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Nonexercise activity thermogenesis (NEAT): environment and biology

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Levine, James A. Nonexercise activity thermogenesis (NEAT): environment and biology. *Am J Physiol Endocrinol Metab* 286: E675–E685, 2004; 10.1152/ajpendo.00562.2003.—Nonexercise activity thermogenesis (NEAT) is the energy expended for everything that is not sleeping, eating, or sports-like exercise. It includes the energy expended walking to work, typing, performing yard work, undertaking agricultural tasks, and fidgeting. NEAT can be measured by one of two approaches. The first is to measure or estimate total NEAT. Here, total daily energy expenditure is measured, and from it “basal metabolic rate-plus-thermic effect of food” is subtracted. The second is the factorial approach, whereby the components of NEAT are quantified, and total NEAT is calculated by summing these components. The amount of NEAT that humans perform represents the product of the amount and types of physical activities and the thermogenic cost of each activity. The factors that impact a human’s NEAT are readily divisible into environmental factors, such as occupation or dwelling within a “concrete jungle,” and biological factors such as weight, gender, and body composition. The combined impact of these factors explains the substantial variance in human NEAT. The variability in NEAT might be viewed as random, but human and animal data contradict this. It appears that changes in NEAT subtly accompany experimentally induced changes in energy balance and are important in the physiology of weight change. Inadequate modulation of NEAT plus a sedentary lifestyle may thus be important in obesity. It then becomes intriguing to dissect mechanistic studies that delineate how NEAT is regulated into neural, peripheral, and humoral factors. A scheme is described in this review in which NEAT corresponds to a carefully regulated “tank” of physical activity that is crucial for weight control.

energy expenditure; physical activity; obesity; malnutrition

INTRODUCTION TO HUMAN ENERGY BALANCE

Biological entities obey physical laws and, in this regard, humans and mammals obey the laws of thermodynamics. Human energy stores can only increase, and obesity occurs when food intake exceeds energy expenditure (or metabolic rate). Similarly, energy stores can only be depleted when energy expenditure exceeds food intake. Thus the balance between food intake and energy expenditure determines the body’s energy stores. The quantity of energy stored by the human body is impressive; lean individuals store at least 2–3 months of their energy needs in adipose tissue, whereas obese persons can carry a year’s worth of their energy needs. It is the cumulative impact of energy imbalance over months and years that results in the development of obesity or undernutrition.

There are three principal components of human energy balance (Fig. 1): basal metabolic rate (BMR), the thermic effect of food (TEF), and activity thermogenesis. There are also other small components of energy expenditure that may contribute to the whole, such as the energetic costs of medications and emotion.

BMR is the energy expended when an individual is supine at complete rest, in the morning, after sleep, in the postabsorptive

state. In individuals with sedentary occupations, BMR accounts for ~60% of total daily energy expenditure. Three-fourths of the variability in BMR can be predicted by lean body mass within and across species (24, 29). Resting energy expenditure is the energy expenditure at complete rest in the postabsorptive state, at any time of the day, and in general is within 10% of BMR.

TEF (3, 42, 56, 86) is the increase in energy expenditure associated with the digestion, absorption, and storage of food and accounts for ~10–15% of total daily energy expenditure. Many believe there to be facultative as well as fixed components.

Activity thermogenesis can be separated into two components, exercise-related activity thermogenesis and “nonexercise activity thermogenesis” (NEAT) (Fig. 1). The role of exercise in human energy balance will not be reviewed here (please see Refs. 7 and 48), but it should be noted that, for the vast majority of dwellers in developed countries, exercise-related activity thermogenesis is negligible or zero. NEAT, even in avid exercisers, is the predominant component of activity thermogenesis and is the energy expenditure associated with all the activities we undertake as vibrant, independent beings. NEAT includes the energy expenditure of occupation, leisure, sitting, standing, walking, talking, toe-tapping, playing guitar, dancing, and shopping. The enormous variety of components has made NEAT challenging to study and its role in human energy balance difficult to define. NEAT is therefore

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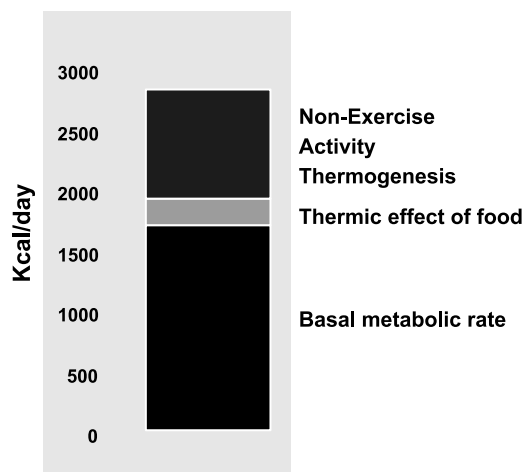


Fig. 1. Components of energy expenditure in sedentary adults.

the most variable component of energy expenditure, both within and between subjects, ranging from ~15% of total daily energy expenditure in very sedentary individuals to 50% or more of total daily energy expenditure in highly active individuals (21, 72, 85). Therefore, its potential role in body weight regulation justifies our scrutiny.

To understand the potential role of NEAT in human energy balance, one must first appreciate the strengths and limitations of available techniques. Little information is available regarding the time period of measurement needed to gain a representative assessment of NEAT. Approximately 7 days (74) of measurement is likely to provide a representative assessment of activity thermogenesis for a given 3- or 4-mo block of time. Such 7-day measurements can potentially be repeated to understand the importance of variables such as season or changing occupational roles. Broadly, NEAT can be measured by one of two approaches. The first approach is to measure or estimate total NEAT. Here, total daily energy expenditure is measured, and from it BMR-plus-TEF is subtracted. The second approach is the factorial approach, whereby the components of NEAT are quantified, and total NEAT is calculated by summing these components. The methodology for measuring NEAT will not be described here but has been reviewed in detail (61).

It has long been recognized that NEAT is likely to contribute substantially to the inter- and intrapersonal variability in energy expenditure. If three-quarters of the variance of BMR can be accounted for by variance in lean body mass, and TEF represents 10–15% of total energy expenditure, then the majority of the variance in total energy expenditure that occurs independent of body weight must be accounted for by variance in NEAT. In this paper, the environmental and biological mediators of NEAT will be systematically reviewed. A schema is then proposed to speculate as to how NEAT impacts energy balance.

NEAT: ENVIRONMENT AND BIOLOGY

It is self-evident that there are environmental influences that impact the amount of nonexercise activity that we perform. What is fascinating, however, is to speculate about how much nonexercise activity (so called “spontaneous” physical activity) is biologically regulated.

Table 1. Lifestyle-based prediction of PAL values

Lifestyle	PAL
Chair bound or bed bound	1.2
Seated work with no option of moving around and little or no strenuous leisure activity	1.4–1.5
Seated work with discretion and requirement to move around but little or no strenuous leisure activity	1.6–1.7
Standing work (e.g., housewife, shop assistant)	1.8–1.9
Strenuous work or highly active leisure	2.0–2.4

PAL, physical activity levels, as defined in Ref. 90.

Environmental Influences on NEAT

Occupation. Occupation dramatically impacts NEAT. The impact of occupation on nonexercise activity can be overt, such as the difference between the nonexercise activity of a laborer vs. that of a civil servant (17, 90, 93). Here, activity levels vary severalfold. There are more subtle occupational effects on physical activity. For example, in many populations, where women work both at home and out of the home, their cumulative work burden exceeds that of male cohabitants by several hours per day (60).

A frequently used surrogate of NEAT is physical activity level (PAL), which is total energy expenditure divided by BMR. Black et al. (6a) reviewed PAL values from 574 measurements of total energy expenditure made with doubly labeled water in individuals from affluent societies. It was clear that PAL values varied two- to threefold. Lifestyle and cultural milieu were implicated as major predictors of NEAT and its variability (Table 1).

Impressively, these figures echo those derived from lower-income societies (18, 92) (Table 2).

Concrete urban environment and mechanization. A sedentary lifestyle and a sedentary lifestyle-promoting environment are self-evident to dwellers in high- and middle-income countries. The importance of a population that is sedentary is well illustrated by studies of physical activity levels for individuals moving from agricultural communities to urban environments or by studies of the effects of industrialization (43). In many populations where this has occurred, urbanization is associated with decreased physical activity. Sedentary cues are unmistakable in developed countries, often through services designed to optimize convenience and output at the expense of locomotion. Examples include drive-through restaurants and banks, televisions, escalators, motorized walkways, and washing machines for clothes. In the United States, schools may be built out of the walking distance of the community served, suburbs built without sidewalks, city streets made unsafe for leisure walking or playgrounds unsafe for children to play in. We attempted to directly estimate the cumulative impact of mechanization on

Table 2. PAL values of women and men from low-income countries, reported by intensity of work

	Work Intensity		
	Light	Moderate	Heavy
Women	1.55	1.64	1.82
Men	1.55	1.78	2.10

Intensity of work values are described in Refs. 18 and 92.

NEAT by comparing the energetic costs of mechanized tasks and the manual performance of the same tasks as they would have been performed a century ago (59). It was interesting that mechanization in our crude experiment accounted for 111 kcal per day (Fig. 2), which closely mirrored the estimate of the cost of mechanization given by Hill et al. (44). Thus we were not surprised that sales of labor-saving devices correlate with obesity rates, whereas food intake data did not (Fig. 3).

Gender. Although gender is biologically determined, there are gender-specific environmental cues that impact NEAT. Overall, adult men and women in the US report similar levels of total physical activity, although women are becoming more active (14, 96). In other countries, such as Canada, England, and Australia, men report being 1.5–3 times more active than women (28, 107). In children, there are consistent gender differences, with boys being more active than girls (71, 83). Gender may also influence physical activity in more subtle ways. For example, society and culture may dictate that women work both in the public domain and in the home. When this work burden of women was assessed in agricultural communities, women’s energy needs were found to be 30% greater than predicted (69). There are no data of NEAT for women with similar societal-derived roles in high-income countries. However, there are likely to be environmental influences on NEAT that affect genders differently in all communities.

Education. Groups with more education consistently report more leisure-time physical activity than groups with less education. In the US, highly educated groups are two to three times

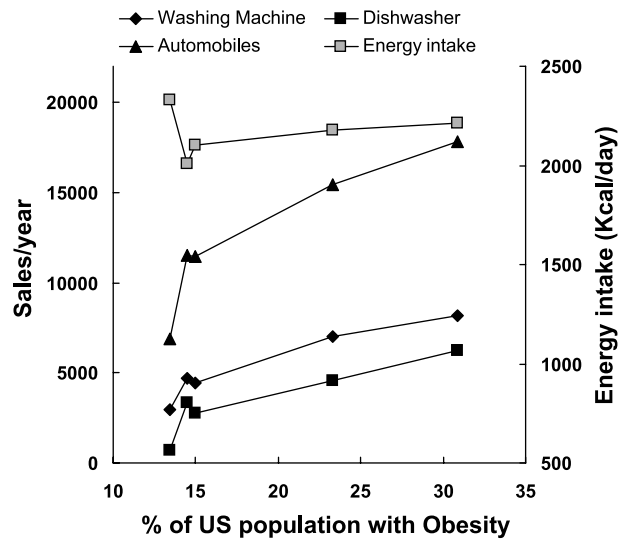


Fig. 3. Sales of domestic machines and energy intake vs. obesity rates for the US population.

more likely to be active than groups with a low level of education (14, 28, 96). This contrasts with low-income countries, where child labor is commonplace. Here, poverty is predictive of greater child labor, and the most impoverished children thereby have the greatest NEAT levels (36, 68).

Seasonal variations in physical activity. Limited data are available regarding differences in NEAT during different seasons. Who volitionally walks to work in the rain? Data from Canada suggest wide differences in time spent in physical activity due to season. Time spent in an activity was twice as high during the summer months as in the winter months (53). Common sense dictates and data confirm that occupational NEAT is very seasonally dependent in agricultural communities, where workloads vary cyclically (27, 80, 92).

Thus, although few objective data exist with respect to how much and what types of nonexercise activities people perform, it is clear that a variety of cultural and/or environmental factors impact NEAT. It is difficult from existing data to quantify the impact of NEAT vs. exercise. However, what is clear is that NEAT is highly variable and dramatically affected by environmental factors, in particular occupation and environmental cues that promote a sedentary lifestyle.

Biological Influences on NEAT

At the simplest level, there is ample evidence that components of NEAT have mechanistic drives. For example, picture the schoolgirl shivering while waiting for the bus. Cancer cachexia patients and starving individuals with food intakes of <500 kcal (64) have very low physical activity levels, whereas patients with hyperthyroidism are tremulous and easily startled (76, 91). What is more challenging is to derive the role of NEAT in human energy balance and to understand whether and how the central integration of this process occurs.

Biological factors and the thermic efficiency of physical activities. A determinant of NEAT is the energetic efficiency with which nonexercise activities are performed (Fig. 4) (67). It is recognized that even trivial movement is associated with substantial deviation in energy expenditure above resting val-

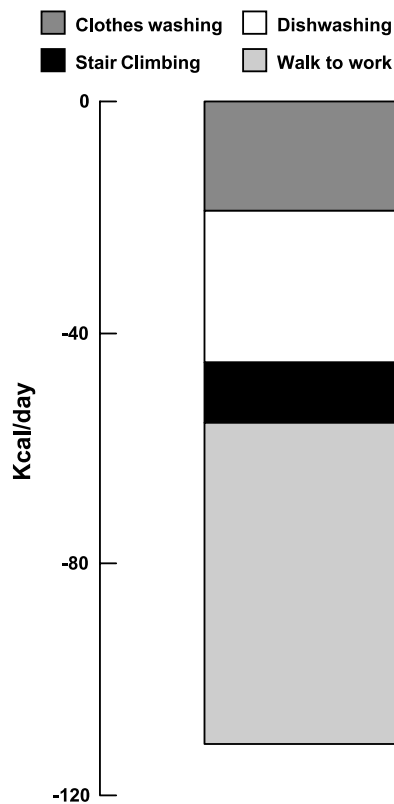


Fig. 2. Energy costs of combined daily tasks in healthy subjects (n = 122). Subjects completed the indicated tasks with and without the aid of equipment or machines while energy expenditure was measured. See *Concrete urban environment and mechanization*.

ues. For example, mastication is associated with deviations in energy expenditure of 20% above resting (62). Very low levels of physical activity, such as fidgeting, can increase energy expenditure above resting levels by 20–40% (67). It is not surprising, then, that ambulation, whereby body weight is supported and translocated, is associated with substantial excursions in energy expenditure (40). Even ambling or browsing in a store (walking at 1 mph) doubles energy expenditure, and purposeful walking (2–3 mph) is associated with doubling or tripling of energy expenditure. When body translocation was logged with a triaxial accelerometer, the output from this unit correlated with nonresting energy expenditure (11). This implies that ambulation may be a key component of NEAT. The energy costs of a multitude of occupational and nonoccupational physical activities have been charted and tabulated (1, 2). What is noteworthy is the manifold variance in the energy costs of occupation-dictated activities, ranging from <1 multiple of resting energy expenditure (MET), such as typing, to 5–10 MET, such as wood cutting, harvesting, or physical construction work.

Several factors affect the energetic efficiency of physical activity.

BODY WEIGHT AND THERMIC EFFICIENCY. It requires more energy to move a larger body than a smaller one. Several investigators have demonstrated that the energy expended during weight-bearing physical activity increases with increasing body weight (12, 79). It is less clear whether work efficiency varies with body composition, independent of body weight. Some studies (12, 38, 82, 105) have found no differences in weight-corrected work efficiency between obese and nonobese subjects, whereas others (23, 73) have found a greater work efficiency in the obese.

EFFECTS OF CHANGES IN BODY WEIGHT ON THERMIC EFFICIENCY. There is controversy as to whether work efficiency changes with weight loss. Several studies have reported that energetic efficiency is reduced after weight reduction. Foster et al. (31) measured the energy cost of walking in 11 obese women before weight loss and at 9 and 22 wk after weight loss. They determined that the energy cost of walking (after control for loss of body weight) decreased substantially by 22 wk after weight loss. They estimated that with a 20% loss of body weight, subjects would expend about 427 kJ/h less during

walking than before weight loss. Geissler et al. (34) compared energy expenditure during different physical activities and found that it was ~15% lower in the postobese than in control subjects. DeBoer et al. (22) found that sleeping metabolic rate declined appropriately for the decline in fat-free mass when obese subjects lost weight, but that total energy expenditure declined more than expected for the change in fat-free mass. Similar results were obtained by Leibel et al. (60), who speculated that increased work efficiency may be partially responsible for weight regain after weight loss.

Alternatively, Froidevaux (33) measured the energy cost of walking in 10 moderately obese women before and after weight loss and during refeeding. Total energy expended during treadmill walking declined with weight loss but was entirely explained by the decline in body mass. Net efficiency of walking did not change. Poole and Henson (82) also found no change in efficiency of cycling after caloric restriction in moderately obese women. Weigle and Brunzell (101) demonstrated that ~50% of the decline in energy expenditure with weight loss was eliminated when they replaced weight lost by energy restriction with external weight worn in a specially constructed vest (101).

Thus, although it is clear that total energy expenditure declines with weight loss, the extent to which changes in work efficiency contribute to this decline is controversial. It is an important question, because if work efficiency truly changes, it implies that a mechanism may exist to define the work efficiency of NEAT activities and impact energy balance.

ROLE OF SKELETAL MUSCLE METABOLISM IN DETERMINING WORK EFFICIENCY. Differences in skeletal muscle morphology and/or metabolism may play a role in differences in work efficiency. Henriksson (41) suggested that changes in muscle morphology in response to energy restriction lead to changes in the relative proportion of type I vs. type II fibers in human subjects. Some studies suggest that type II fibers have a greater fuel economy than type I fibers (19, 103). Because type II fibers appear to be better preserved during starvation than type I fibers (41), overall fuel economy and work efficiency may increase after energy restriction and loss of body mass. However, a recent study on muscle fiber type before and after an 11-kg weight loss in obese females did not show any changes in the fiber type distribution (97).

The potential contribution of skeletal muscle differences to differences in work efficiency between weight-stable lean and obese subjects is more controversial. Data suggest that obese subjects oxidize proportionally more carbohydrate and less fat than lean subjects in response to perturbations in energy balance (94, 109, 110), and that differences in morphology/metabolism of skeletal muscle and sympathetic nervous system activity (6) may underlie some of the whole body differences (16, 110). However, it is not clear to what extent such differences contribute to differences in work efficiency. Furthermore, such differences may arise from genetic and environmental causes.

GENETIC CONTRIBUTIONS TO WORK EFFICIENCY. Very little information is available to allow estimation of the genetic contribution to differences in work efficiency. When the energy costs associated with common body postures (sitting, standing) and low-intensity activities (walking, stair climbing, and the

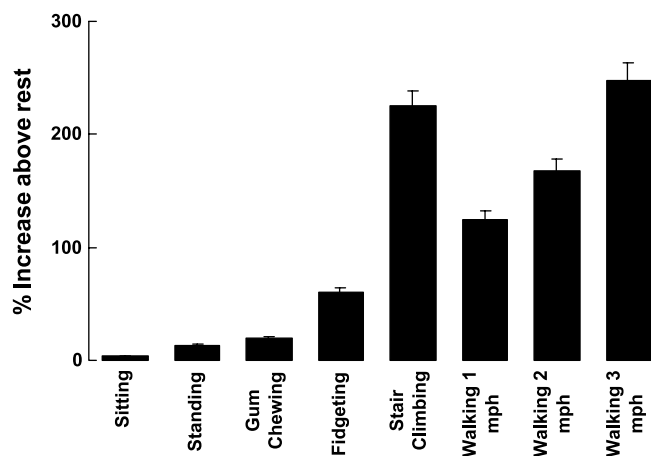


Fig. 4. Energy expenditure of varied low-level activities.

like) were measured in 22 pairs of dizygotic and 31 pairs of monozygotic sedentary twins, there was a genetic effect for energy expenditure for low-intensity activities (from 50 to 150 W), even after correction for differences in body weight (10). No genetic effect was seen for activities requiring energy expenditure greater than six METs. These observations hint at an intriguing possibility, namely, that the efficiency of NEAT activities may be genetically programmed.

AGE AND WORK EFFICIENCY. Work efficiency for NEAT activities may vary with age. For example, children are ~10% more energy efficient during squatting exercises than adults (98). However, there is little information available to evaluate the effects of aging on work efficiency. Skeletal muscle mass is often lost as a subject ages, and if the loss involves a greater proportion of type I vs. type II fibers, work efficiency could increase with age.

EXERCISE TRAINING AND WORK EFFICIENCY. If the work efficiency of NEAT activities varies as a function of muscle morphology, exercise-induced effects in skeletal muscle could be important for NEAT. Alterations in exercise can alter the fiber type proportions of skeletal muscle as well as induce changes in enzyme activities. Aerobic exercise training results primarily in the transformation of type IIb into type IIa fibers, whereas transformation of type II fibers into type I fibers is not common unless the exercise training has been extremely intense over a long period of time. Type I fibers have a greater mitochondrial density and are more oxidative and more fatigue resistant than type IIb fibers. Type IIb fibers are glycolytic in nature, with lower mitochondrial content, and are more prone to fatigue. Type IIa fibers are intermediate in their mitochondrial content and, in humans, closely resemble type I fibers in oxidative capacity. However, an overlap of oxidative capacity exists between fiber types. Type I and type IIa fibers are more energy efficient than type IIb fibers, and the proportions of these fiber types will vary according to the type of exercise training performed. It has been shown that, even independent of fiber type alterations, the activities of important enzymes in oxidative and glycolytic pathways can be modified as a result of exercise training and can lead to improvements in metabolic efficiency. Training may increase work efficiency whereby elite runners and cyclists average lower energy expenditures (15% for running and $\leq 50\%$ for swimming) at specified velocities compared with untrained individuals (45, 46, 89). Here, the concept is introduced whereby exercise directly affects NEAT through change in work efficiency.

GENDER AND WORK EFFICIENCY. There are several reports that female athletes, unlike male athletes, are more energy efficient than their sedentary counterparts (20, 50, 77). There are reports in the literature of increased energy efficiency in female runners (77), dancers (20), and swimmers (50) compared with sedentary females. Most reports make conclusions regarding energetic efficiency on the basis of indirect rather than direct measurements of energy intake and/or expenditure. For example, Mulligan and Butterfield (77) concluded that female runners had increased energy efficiency because their self-reported energy intake was less than their estimated energy expenditure. However, in the few studies in which both intake and expenditure were measured directly, no evidence of increased energy efficiency was seen in female runners (88) or cyclists (47). Thus the questions of whether female athletes show a different energy efficiency than sedentary females is controversial.

Whether there are inherent gender differences for the efficiency of nonexercise activities is open to speculation but could readily be studied.

Genetic background. Several independent lines of evidence point toward a genetic role for NEAT (8). Animal data demonstrate that NEAT clusters for murine strain (4). On the basis of twin and family studies, the heritability for physical activity level is estimated to be between 29 and 62%. Analysis of self-reports of physical activity from the Finnish Twin Registry, consisting of 1,537 monozygotic and 3,057 dizygotic twins, estimated a 62% heritability level for age-adjusted physical activity (51). Analyses of self-reported physical activity from the Quebec Family Study, consisting of 1,610 members of 375 families, showed a heritability level of 29% for habitual physical activity (81). When 12 pairs of twins were overfed by an estimated 84,000 kcal over a period of 100 days, weight and fat gain clustered for "twinness"; this could only have been through concordant changes in energy expenditure. This in turn was likely to be through NEAT, because changes in BMR and TEF could not account for the twin-associated relationship (9). Nonetheless, it is intriguing to speculate that genetics directly impact NEAT. Perhaps the twin of a laborer is predisposed to becoming a lumberjack rather than an office worker.

Age. Studies have consistently shown a decline in physical activity with aging in men and women (5, 14, 108). Some data suggest that the "aging-gap" is closing. During the period from 1986 to 1990, activity levels increased more in elderly subjects than in young adults (108). One wonders whether the sarcopenia of aging contributes to NEAT.

Gender. We overfed 16 healthy subjects by 1,000 kcal/day for 8 wk; four of these subjects were women. There was a 10-fold variance in fat gain (0.4–4.2 kg). The four persons who gained the most fat were women [3.4 ± 0.7 (SD) kg] compared with fat gain for men (2.1 ± 1.1 kg). Women did not increase their NEAT with overfeeding on average ($\Delta\text{NEAT} = -2.1 \pm 102$ kcal/day), whereas men did by 438 ± 184 kcal/day. It would be intriguing if women modulate NEAT differently from men. Could this be a means to preserve fat stores with increased workloads? Could this have impacted the allocation of work tasks in labor-intensive environments?

Body composition. There are substantial data to suggest that overweight individuals show lower NEAT levels than their lean counterparts (78, 95). This appears to be true across all ages, for both genders, and for all ethnic groups. It is not possible to ascertain whether effects of body composition on nonexercise activities occur independently of weight.

Behavioral issues. What is fascinating to speculate is that a person with a high "programmed NEAT" might select a more active job (e.g., car washing or ambulatory mail delivery) than a person with a lower biological drive for NEAT (e.g., civil service). The mechanism of the volition for selection of occupation has not been defined.

Total NEAT in energy homeostasis. There is evidence that NEAT is important in human energy homeostasis. NEAT is the key predictor of non-BMR energy expenditure, and BMR is largely predicted by body size or lean body mass. NEAT then becomes the crucial component of energy expenditure that is most variable and least predictable. Consider the energy expenditure of a person who works as a road layer but then

becomes a secretary. For this example, it is self-evident that variations in NEAT can result in severalfold variations in total energy expenditure independent of body size. What is not self-evident is whether changes in NEAT contribute to the mechanism by which adipose tissue accumulates.

Further insight into total NEAT comes from Westerterp's observation (104) that, in free-living individuals, the cumulative impact of low-intensity activities over greater duration is of greater energetic impact than short bursts of high-intensity physical activities (104). Thus, for a given individual, his/her NEAT is defined by the total energetic cost of occupational plus nonoccupational activities, which in turn are influenced by the sedentary conditions of the individual's microenvironment (e.g., workplace) and macroenvironment (e.g., country).

Changes in NEAT with positive energy balance. Several studies have employed an overfeeding paradigm to determine whether energy expenditure changes during forcible overfeeding. On balance, these studies have demonstrated that, as overfeeding occurs, NEAT increases (87). In one such study, twelve pairs of twins were overfed by 1,000 kcal/day above estimated resting needs. There was a fourfold variation in weight gain, which had to represent substantial variance in energy expenditure modulation, because food intake was clamped. This variance in energy expenditure response could not be accounted for by changes in resting energy expenditure alone, and so, indirectly, NEAT is implicated. What was also fascinating was that twinning accounted for some of the inter-individual variance in weight gain, suggesting that the NEAT response to overfeeding is in part genetically determined.

NEAT was directly implicated in the physiology of weight gain when 16 sedentary, lean individuals were carefully overfed by 1,000 kcal/day (63). All components of energy expenditure and body composition were carefully determined. There was a 10-fold variation in fat gain and an 8-fold variation in changes in NEAT. Those individuals who increased their NEAT the most gained the least fat with overfeeding, and those individuals who failed to increase their NEAT with overfeeding gained the most fat (Fig. 5) (63). Studies are too sparse to define how changes in the amount of nonexercise activity interplay with changes in energy efficiency; the bulk of evidence suggests that increases in the amount of physical activity predominate. Changes in BMR and TEF were not predictive of changes in fat gain. These data strongly imply that NEAT may counterbalance fat gain with positive energy balance, when appetite is clamped.

Changes of NEAT with negative energy balance. With underfeeding, physical activity and NEAT decrease. Chronic starvation is known to be associated with decreased physical activity (49, 55, 70). Whether those individuals who are susceptible to ready fat loss are those who fail to decrease NEAT with underfeeding has not been established. However, let us argue that, with a prolonged energy deficit of 500–600 kcal/day, BMR decreases by ~10% (i.e., ~200 kcal/day). This assumes a sustained decrease in lean body mass (LBM) that may not actually occur (13, 15, 25, 30, 32, 37, 75, 99), and TEF decreases by ~0–50 kcal/day (26, 102). Hence, NEAT has to decrease by ~200–300 kcal/day once fat loss reaches a plateau. In one study with severe energy reduction (800 kcal/day) (60), decreases in NEAT likely accounted for 33% of the decrease in total daily

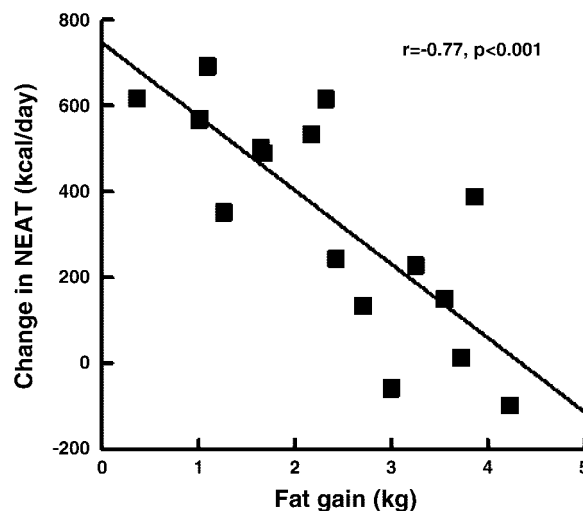


Fig. 5. Changes in nonexercise activity thermogenesis (NEAT) with overfeeding. Healthy subjects ($n = 16$) were overfed by 1,000 kcal/day over baseline energy needs. Fat gain, on the x-axis, was determined from dual X-ray absorptiometry. Change in NEAT was calculated from NEAT values measured before and after overfeeding: $\text{NEAT} = \text{TDEE} - (\text{BMR} + \text{TEF})$, where TDEE is total daily energy expenditure, BMR is basic metabolic rate, and TEF is the thermic effect of food.

energy expenditure (TDEE) in lean subjects, 46% in obese subjects with 10% weight loss, and 51% in obese subjects with 20% weight loss (60). If NEAT decreases with negative energy balance, is it because the quantity of physical activities decrease or because there are decreases in energy efficiency, or both? Studies to date have not definitively answered this question. With severe energy reduction (420 kcal/day) in obesity, maximal $\dot{V}O_{2\text{max}}$ and energy expenditure at submaximal loads may decrease (54); however, with less severe energy restriction, $\dot{V}O_{2\text{max}}$ appears unchanged (52). Thus the balance of information suggests that NEAT decreases with negative energy balance. It is unclear whether the effect is through decreased amounts of activity, altered energetic efficiency, or both.

Overall, there are a multitude of biological effectors of NEAT. It appears that with weight gain, NEAT increases, and with weight loss, NEAT decreases. This creates an intriguing scenario whereby NEAT might act to counterbalance shifts in energy balance. It could be that these changes in NEAT, along with those that affect BMR and TEF, are small and swamped by changes in energy intake. However, consider that some subjects who were overfed by 1,000 kcal/day increased NEAT by >600 kcal/day. This argues that changes in energy expenditure and NEAT may be quantitatively important in the physiology of body weight regulation. Let us now consider the mechanism by which NEAT is modulated.

MECHANISM OF NEAT REGULATION

Very little is known about the mechanism by which NEAT is regulated, for several reasons. First, very few data are available regarding the physiological modulation of NEAT. Second, despite the evidence that NEAT is altered with changing energy balance, no information is available with respect to which components of NEAT are specifically altered. It is not known which components of NEAT predominate, or which

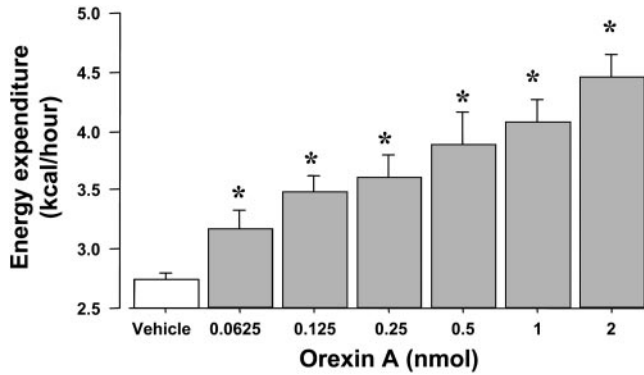


Fig. 6. Effect of orexin on NEAT when injected into the paraventricular nucleus of the rat.

components predominantly change during fluxes of energy balance. In the absence of this information, it has not been possible to further elucidate the mechanism by which NEAT impacts energy expenditure and energy balance. Third, there is ample evidence to demonstrate the impact of environment and culture on NEAT. Hence, in the minds of some, effort may not be warranted to define the biological mechanism by which NEAT is modulated. Fourth, understanding that NEAT represents the energy expenditure associated with spontaneous physical activity, the concept of a unifying mechanism by which NEAT is driven is difficult to grasp. Thus, for a host of reasons, very little is known about the mechanism driving NEAT.

Is there sufficient evidence that NEAT is modulated in physiology to warrant resource allocation to better understand its mechanism? On balance, it appears that NEAT is modulated during shifts in energy balance. The strong negative correlation between increases in NEAT and fat gain during overfeeding supports this contention, as do the consistent studies demon-

strating that physical activity and NEAT decrease during negative energy balance.

How might one start to investigate the mechanism by which NEAT is modulated? A simple starting point might be to understand its components. For example, if future studies showed that, during positive energy balance, ambulation energy expenditure increases and accounts for the vast majority of the changes in NEAT, this might suggest that the mechanism that drives ambulation energy expenditure is pivotal for understanding NEAT. One might then want to define whether it is the amount or the energy efficiency of walking that is crucial; both may occur together. Thus, by systematically evaluating NEAT and its components, the mechanism of NEAT may become clearer.

The next question is one of concept. Is it conceivable that there are any putative moderators of NEAT? Interestingly, several substances are known to increase NEAT. These include thyroxine. Hyperthyroidism in humans is associated with increased spontaneous physical activity (100), and a direct effect of hyperthyroidism on NEAT has been demonstrated in animals (65). The sympathetic nervous system (84) and neurohumoral factors such as the orexins (58, 106) also have the potential to impact NEAT (Fig. 6) (57). Thus, albeit crude, examples do exist whereby specific mediators of spontaneous physical activity have been identified. There is certainly evidence that there are humoral and central mediators of NEAT, at least in animals.

To date, little is known regarding the mechanism by which NEAT is modulated. This is because there is a paucity of data regarding how NEAT and its components are modulated in physiology. However, as information becomes available, hypothesis-driven research will allow a further elucidation of the mechanism of NEAT. It is intriguing to speculate that there are specific neuromediators of NEAT, and this can be conceptualized in a unifying hypothesis.

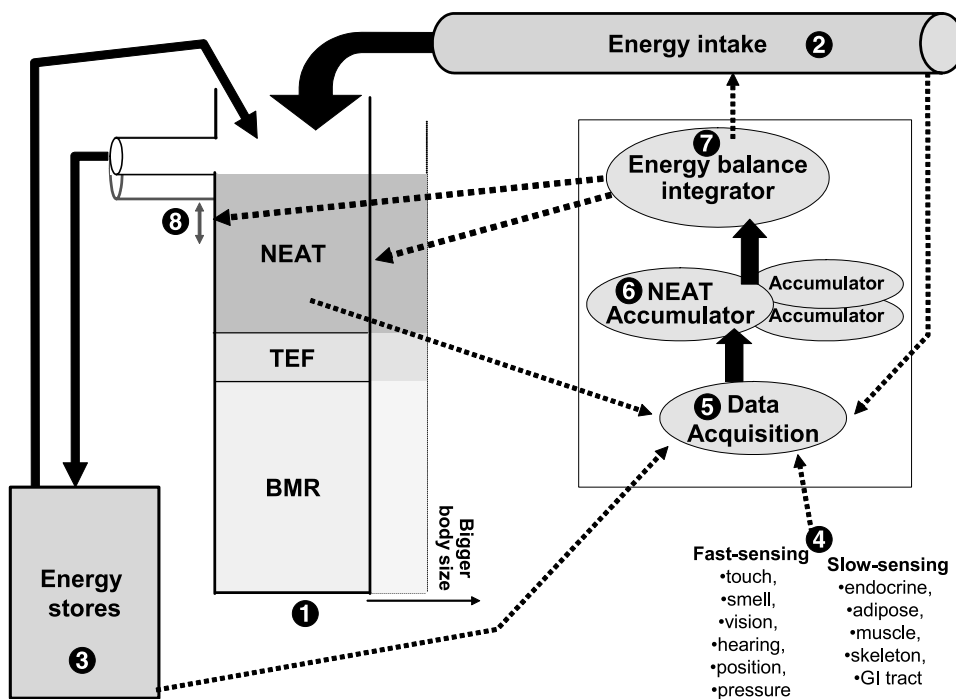


Fig. 7. A cartoon to explain the modulation of NEAT in the context of human energy balance. Continuous arrows represent energy flow through the system; broken lines represent putative signaling pathways (neuronal or blood-borne). Circled numbers are explained in the text.

THE NEAT HYPOTHESIS OF ENERGY BALANCE REGULATION

This concept is detailed in Fig. 7. (The bold numbers within parentheses that follow in text appear as numbers within filled circles in Fig. 7). The components of energy expenditure are shown in (1). The balance among energy intake (2), energy stores (3), and energy expenditure is in constant flux, and data from each component are sensed. This is self-evident; otherwise we would never stop eating, or know that after a day of hanging plasterboard, we are “exhausted.” It seems likely that NEAT signals are derived from known pathways (4), and it is likely that there are numerous NEAT-sensing pathways, since NEAT has many environmental cues and includes many behaviors. The signals can be divided into fast-response elements, such as the startle response (66), and slow-response elements, such as thyroid hormone. These signals converge at a data acquisition center (5) that is likely to lie within a primal part of the brain, such as the hypothalamus, because all animals regulate energy balance. Once the data on the various NEAT signals are rectified into a common signal, the data acquisition center signals the NEAT accumulator (6), which is an invented concept to allow the ready explanation of energy balances. The NEAT accumulator is constantly summing the net amount of NEAT per unit time.

What is the minimum energetic data set? It could be argued that the only variable the body needs to monitor is energy stores. The trouble with this one-element sensing system is that, for appetite to increase when energy stores decrease, the current energy intake needs to be sensed so that a change can be instituted. We know that when energy intake is experimentally increased, NEAT increases. It appears that NEAT is modulated exquisitely to predicted susceptibility and resistance to fat gain (Fig. 5). The only way NEAT could be modulated is if baseline NEAT were sensed. Thus accumulators for NEAT, energy intake, and energy stores seem likely. Whether BMR and/or TEF are signaled to accumulators is difficult to resolve. Certainly, weight gain is associated with increased BMR and TEF, and the converse occurs with weight loss. Also, three-quarters of the variance of BMR is predicted from LBM, but one-quarter is not. This unaccounted-for variance of several hundred kilocalories per day could be crucial in energy homeostasis. A counterpoint, however, is that when uncoupling of oxidative phosphorylation occurs in humans (39), weight loss occurs. Thus, when BMR is exogenously increased, it is not completely sensed in a putative BMR accumulator; otherwise (in this schema), body weight would remain unchanged. At the very least, we should be careful not to assume that BMR and TEF are not being sensed.

Data from the NEAT accumulator is then fed to the energy balance integrator (7), which also receives data from the energy intake and energy stores accumulators, and possibly those for BMR and TEF. The energy balance integrator is akin to a bank account, where financial expenditure counterbalances income. For a bank account to be in balance, total spending has to equal income. A mortgage is analogous to BMR (i.e., a large obligate payment with little room for maneuver unless one undergoes major transactions at the bank). Food cost is analogous to TEF, i.e., a small, obligate, but variable expense whereby one can choose to cook, eat fast-food, or dine in expensive restaurants. What remains after the mortgage and

food bills are paid is “surplus income” or NEAT. Interestingly, for many, most of the surplus income is taken up with transportation costs (car loan), just as locomotion accounts for most of NEAT! The amount of surplus income (NEAT) that is not spent (expended) goes into a savings account, i.e., tissue energy stores (3), predominantly adipose. Now argue that there is a salary cut. The mortgage (BMR) is essentially fixed, a little can be cut from food expenses (TEF), but the majority of the decrement has to come from either “surplus income” (NEAT) or depletion of savings (adipose tissue). Conversely, say income increases by \$1,000 this month. Again, the mortgage (BMR) is essentially fixed. A little more can be spent on food (TEF). How is the excess \$800 dealt with? It is either going to be used to purchase a variety of objects (increased NEAT), or it is going into the savings account (adipose tissue). More likely, some will be spent (NEAT) and some will be saved (adipose). Thus the energy balance integrator (7) may directly modulate NEAT in response to changes in energy intake, presumably by altering the threshold at which excess energy is filtered into energy stores (8). The above schema is presented to illustrate several concepts in human energy balance and NEAT, to provoke debate, and most important, to serve as a hypothesis-testing platform to better understand NEAT and the modulation of energy balance.

Suppose that, at the beginning of each week, Sally Sloth starts her week with a tank of NEAT akin to a tank of gasoline. The size of Sally's NEAT tank is genetically determined. When she arrives home on Friday afternoon, her NEAT tank is empty. Sally then spends the weekend recumbent, operating only the remote control of her television. In contrast, Sally's coworker, Francine Fidget, comes home from the identical job on Friday afternoon. Francine's NEAT tank is genetically twice the size of Sally's and is still half-full. Francine spends the weekend removing overgrown shrubs from her back yard and painting her basement. Sally and Francine then go to New Orleans for 2 wk of feasting. Sally gains 5 pounds, because her NEAT does not change. Francine eats the same gorgeous food but spends her nights dancing at jazz clubs, thereby increasing her NEAT and not gaining a pound. Thus, could obesity be a thrifty state whereby NEAT does not increase in response to caloric excess fueled by an environment in which surplus calories and inactivity are permissive? Conversely, is restrictive anorexia nervosa a state in which caloric restriction is not countered by decreased NEAT? Superb technologies and committed, sharing scientists can readily solve these questions.

In conclusion, NEAT is likely to serve as a crucial thermoregulatory switch between excess energy being stored and that being dissipated.

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Pages E675–E685: Levine JA. “Nonexercise activity thermogenesis (NEAT): environment and biology” (doi:10.1152/ajpendo.00562.2003; <http://ajpendo.physiology.org/cgi/content/full/286/5/E675>). I apologize that, in my article, there were direct quotes from the article by Hill JO, Saris WHM, and Levine JA, “Energy expenditure and physical activity,” In: *Handbook of Obesity* (2nd ed.), edited by Bray GA and Bouchard C, New York: Marcel Dekker, p. 631–655, and that this work was not cited, although the coauthors, with their agreement, were acknowledged in my article.

