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Non-exercise activity thermogenesis

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Non-exercise activity thermogenesis (NEAT) is the energy expended that is not from sleeping, eating or sports-like exercise. It ranges from 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 approach is to measure or estimate total NEAT. Here, total daily energy expenditure is measured and from it is subtracted BMR + thermic effect of food. The second is the factoral approach whereby the components of NEAT are quantified and total NEAT calculated by summing these components. The amount of NEAT that human subjects perform represents the product of the amount and types of physical activities and the thermogenic cost of each activity. The factors that affect the NEAT of a human subject are readily divisible into biological factors, such as weight, gender and body composition, and environmental factors, such as occupation or dwelling within a 'concrete jungle'. The combined impact of these factors explains the substantial variance in human NEAT. The variability in NEAT might be viewed as random but human data contradict this perception. It appears that changes in NEAT subtly accompany experimentally-induced changes in energy balance and are important in the physiology of weight change. NEAT and sedentariness may thus be important in obesity. It then becomes intriguing to dissect mechanistic studies that delineate how NEAT is regulated by neural, peripheral and humoral factors. NEAT may be a carefully-regulated 'tank' of physical activity that is crucial for weight control.

Energy expenditure: Physical activity: Obesity: Malnutrition

Human energy balance and non-exercise activity thermogenesis

Biological entities obey physical laws and, thus, human subjects and mammals obey the laws of thermodynamics. Human energy stores can only increase and obesity occur 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 individuals can carry 1 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): BMR; thermic effect of food (TEF); activity thermogenesis. There are also other small components of energy expenditure that may contribute, such as the energetic costs of medications and emotion.

BMR is the energy expended when an individual is laying at complete rest, in the morning, after sleep, in the post-absorptive state. In individuals with sedentary occupations BMR accounts for approximately 60 % of the total daily energy expenditure (TDEE). Three-quarters of the variability in BMR is predicted by lean body mass within and across species (Ford, 1984; Deriaz *et al.* 1992). Resting energy expenditure is the energy expenditure at complete rest in the post-absorptive state and in general is within 10 % of BMR.

TEF (Hill *et al.* 1985; Alessio *et al.* 1988; Kinabo & Durnin, 1990; Reed & Hill, 1996) is the increase in energy expenditure associated with the digestion, absorption and storage of food, and accounts for approximately 10–15 % of the TDEE (Fig. 2). Many researchers believe there to be facultative as well as fixed components.

Abbreviations: NEAT, non-exercise activity thermogenesis; PAL, physical activity level; TDEE, total daily energy expenditure; TEF, thermic effect of food.
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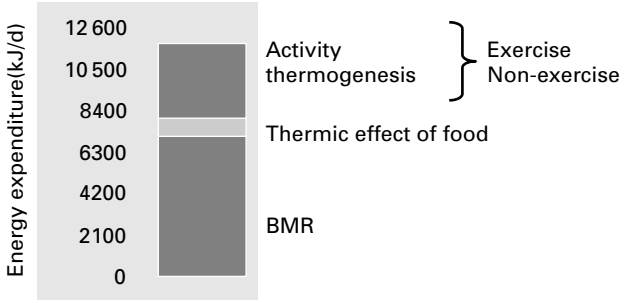

Fig. 1. The components of energy expenditure in sedentary adults.

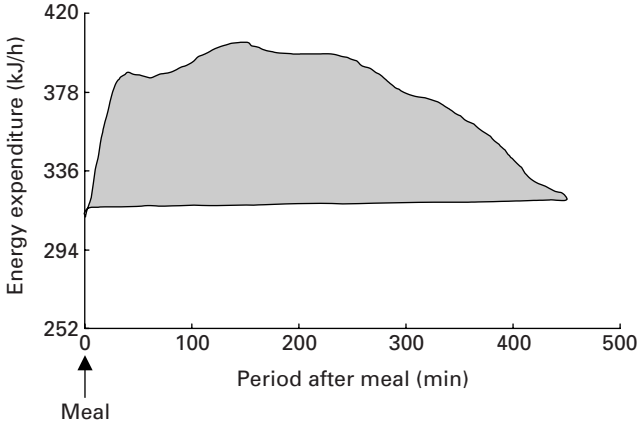

Fig. 2. Thermic effect of food. The subject was given a meal (↑) that comprised one-third of his energy needs for the day. (▨), The area under the curve for the energy expenditure *v.* time curve, which is one-third of the subject's thermic effect of food for the day under study.

Activity thermogenesis can be separated into two components: exercise-related activity thermogenesis and 'non-exercise activity thermogenesis' (NEAT; Fig. 1). The role of exercise in human energy balance will not be reviewed here (see, Jakicic *et al*. 1995; Blundell & King, 1999), but it should be noted that for the vast majority of the populations of 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 undertaken by the human population 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.

Regardless of the difficulties in measuring NEAT and its components, it has long been recognized that NEAT is likely to contribute substantially to the inter- and intra-individual variability in energy expenditure. The argument is if three-quarters of the variance of BMR is accounted for by variance in lean body mass, and TEF represents 10–15 % of the 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 physical activity.

NEAT is the most variable component of energy expenditure, both within and between subjects, ranging from about 15 % TDEE in very sedentary individuals to ≥ 50 % TDEE in highly-active individuals (Ravussin *et al*. 1986; Dauncey, 1990; Livingstone *et al*. 1991). Hence, its potential role in body-weight regulation justifies the scrutiny. First to be discussed is how NEAT is measured. This discussion is not only to inform prospective investigators, but also to provide a methodological background for interpreting published studies. Second, having a sense of the strengths and limitations of these measurement tools, data will be reviewed in order to establish how much energy human subjects expend as NEAT. With an appreciation of the fact that human subjects expend a substantial and highly-variable proportion of their energy expenditure as NEAT, the role of NEAT in the physiology of energy balance will be discussed. Finally, having established that NEAT is a numerically-important component of energy expenditure, and that NEAT is important in the physiological energy balance, it is possible to speculate on the potential mechanism by which NEAT is modulated.

The measurement of non-exercise activity thermogenesis

To understand the potential role of NEAT in human energy balance the strengths and limitations of available techniques must first be appreciated.

First, little information is available regarding the time period of measurement needed to gain a representative assessment of NEAT. Approximately 7 d (Marr & Heady, 1986) of measurement is likely to provide a representative assessment of activity thermogenesis for a given 3- or 4-month block of time. Such 7 d 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, TDEE is measured and from it BMR + TEF is subtracted. The second approach is the factoral approach whereby the components of NEAT are quantified and total NEAT calculated by summing these components. Each approach will now be discussed.

Measurement or estimation of total non-exercise activity thermogenesis

To measure or estimate total NEAT in a sedentary subject, the following formula is applied:

$$\text{NEAT} = \text{TDEE} - (\text{BMR} + \text{TEF}).$$

Hence, completion of this calculation requires data on TDEE, BMR and TEF.

TDEE can be directly measured using a room calorimeter whereby either gas exchange and/or heat loss are measured in a subject confined to a small (e.g. 12 m^2) room for 1 d. These measurements of TDEE are enormously limited because subjects are confined within the room or chamber for the measurement duration and so cannot perform their normal daily activities (Ravussin *et al*. 1986; Sun *et al*. 1994).

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TDEE can be measured in free-living individuals using doubly-labelled water. In the doubly-labelled water method (Schoeller & Taylor, 1987; Coward *et al*. 1988; Goran *et al*. 1993; Black *et al*. 1996; Kurpad *et al*. 1997; Coward, 1998), both the H and O of water are labelled or 'tagged' using stable non-radioactive isotopes ($^2H_2O^{18}$). Elimination of administered $^2H_2O^{18}$ may be used to estimate CO_2 production and energy expenditure. The principle of this technique is as follows. In body water the O is in equilibrium with the O of expired CO_2:

$$CO_2 + H_2O \leftrightarrow H_2CO_3.$$

Thus, if the O in body water is tagged with the tracer O^{18}, the label will distribute not only in body water but also in circulating H_2CO_3 and expired CO_2. Over time, the concentration of the O^{18} in body water will decrease as CO_2 is expired and body water is lost in urine, perspiration and respiration. If the H in body water is tagged with ^2H, the label will distribute only in the circulating H_2O and H_2CO_3. Over time, the concentration of the ^2H label will decrease as body water is lost (some of the H can become portioned into body protein or fat, however). Thus, if both the O and H in body water are tagged with known amounts of tracers at the same time, the differences in the elimination rates of the O and H tracers will represent the elimination rate of CO_2. Subjects are usually given doubly-labelled water orally after baseline samples of urine, saliva or blood have been collected. Time is allowed for complete mixing of isotopes to occur within the body water space and then samples of urine, saliva or blood are collected over 7–21 d. These samples are used for measurements of ^2H and O^{18} enrichments using MS. Changes in ^2H and O^{18} concentrations in body water are then calculated over time and CO_2 production and energy expenditure thereby determined. Energy expenditure can be measured over 7–21 d using doubly-labelled water with an error of approximately 6–8 %. This error can be decreased to a small extent by collecting samples repeatedly over the measurement period rather than by collecting samples only before and after the measurement period.

Having measured TDEE, determinations of BMR and TEF are needed to calculate NEAT. BMR is invariably measured using an indirect calorimeter, whereby O_2 consumption or CO_2 production, or both these variables, are measured. Energy expenditure is then calculated by means of established formulae (Weir, 1949; Cunningham, 1990). Indirect calorimeters vary in sophistication and cost (Jequier & Felber, 1987). In the laboratory ventilated open-circuit calorimeters are most often used. Here, expired air is collected by means of a mouthpiece, mask or hood, or from a sealed chamber (Sun *et al*. 1994; Levine *et al*. 2000). The air is then mixed, the rate of flow is measured and O_2 and/or CO_2 concentrations determined. Measurements to within 1 % of chemical standards can be achieved using these devices. In the field Douglas bags or portable expiratory open-circuit calorimeters can be used. The Douglas bag (Douglas, 1911; Yoshida *et al*. 1981; de Groot *et al*. 1983; Lum *et al*. 1998) comprises a polyvinyl chloride (or other leak-proof material) bag of approximately 100–150 litres (Daniels, 1971). After collection of the expired air in the bag, the volume is measured and a sample analysed to determine O_2 and/or CO_2 concentrations. The technique is highly operator dependent, and under optimal conditions the error of energy expenditure measurements undertaken with Douglas bags can be small (< 3 %). A variety of portable expiratory open-circuit systems have been devised (Consolazio, 1971; Sujatha *et al*. 2000; McLaughlin *et al*. 2001; Rietjens *et al*. 2001). In most systems expiratory flow O_2 and/or CO_2 concentrations are measured. Although less precise than laboratory-based instruments, their flexibility allows BMR to be measured readily.

Where calorimeters are not available BMR can be estimated by calculation, as it is related to body size. A variety of age-, gender- and population-specific formulae have been published specifically for this calculation (Shetty *et al*. 1996). Caution is advised when such formulae are applied because BMR is a numerically large component of NEAT and body weight only accounts for about three-quarters of the variance in BMR. Hence, numerically-important errors may be introduced by such an approach.

TEF is often not measured but rather estimated or ignored when determining NEAT. TEF can be measured by providing a subject with a meal (using one-third of the subject's daily weight-maintenance needs) and the energy expenditure in response to the meal is calculated from the area under the time *v*. energy expenditure curve (Fig. 2). The area under the curve for this meal is then multiplied by 3 (in this laboratory) to give total TEF per d. Other investigators multiply TDEE by 0·10 to provide a crude estimate of NEAT. Alternatively, TEF is ignored and assumed not to be a crucial variable because it is numerically small.

Thus, it is possible to directly measure total NEAT. TDEE can be measured even in free-living individuals using doubly-labelled water. BMR + TEF optimally should be measured using an indirect calorimeter, but can be estimated if necessary. Especially where TEF has not been measured, TDEE is frequently expressed relative to BMR to provide an index of physical activity. The physical activity level (PAL) is TDEE/resting metabolic rate. PAL values (and similar indices) are important, as they are often used to compare physical activity between the population and population sub-groups. It should be noted that PAL corrects TDEE for body size because of the previously mentioned relationship between BMR and body weight. For sedentary subjects the PAL is approximately 1·5, but this level can increase to approximately 3·5–4·5 under conditions of extreme NEAT. It is impressive that the cumulative error for measurements of PAL can be approximately 7 %, considering that the measurements are performed in free-living unrestrained individuals. The major limitation of measuring total NEAT or PAL is that no information is obtained about the components of NEAT. It is therefore difficult to implicate specific mechanisms from total NEAT or PAL.

The factoral approach to measuring non-exercise activity thermogenesis

This approach is frequently used for estimating NEAT in free-living individuals. First, a subject's physical activities are recorded over the time period of interest (e.g. 7 d). The energy equivalent of each of these activities is determined.

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The time spent in each activity is then multiplied by the energy equivalent for that activity. These values are then summed to derive an estimate of NEAT. The advantage of this approach is that the components of NEAT can be defined.

There are two pivotal issues that are key when using the factoral method to measure NEAT. First, how accurate are the activity records? Second, how accurate or representative are the determinations of the energy costs of the activities?

Quantifying physical activities

Non-specific information about habitual and occupational activity can be obtained using questionnaires, interviews or time-and-motion studies. Predictably, substantial errors are introduced through inaccurate recall and inadequate data recording. These approaches can be applied for following trends in certain activities, particularly in relation to occupational practices (United Nations University, 1989).

Activity diaries are often used to record the nature and amount of time spent performing activities over the period of interest (Ferro-Luzzi *et al*. 1990). This procedure has several limitations, as subjects may show variable literary and/or innumeracy, they may report their activities inaccurately or incompletely and/or may alter their normal activity patterns during periods of assessment. To limit these sources of error, one approach is to have trained enumerators follow subjects and objectively record subjects' activities (United Nations University, 1989). This procedure is time consuming and expensive but potentially a valuable source of accurate and objective data.

Alternatively, instrumentation can be used to record or quantify human activities. A variety of such instruments are available. Some kinematic techniques are specific for use in confined spaces, e.g. radar tracking, floor pressure-pad displacement and cine photography (Mayer, 1966; Schutz *et al*. 1982). These instruments are precise but subjects are confined and so normal daily activities are impossible. Other kinematic techniques have been used in free-living individuals and generally focus on pedometers and accelerometers of varying sophistication. Pedometers typically detect the displacement of a subject with each stride. However, pedometers tend to lack sensitivity because they do not quantify stride length or total body displacement. Overall, pedometer output is poorly predictive of NEAT (Gretebeck & Montoye, 1992) but potentially of value for quantifying walking (e.g. to determine compliance with a walking programme). Accelerometers detect body displacement electronically with varying extents of sensitivity (uniaxial accelerometers in one axis and triaxial accelerometers in three axes). Portable uniaxial accelerometer units have been widely used to quantify non-exercise activity (Pambianco *et al*. 1990; Melanson & Freedson, 1995; Bassett *et al*. 2000). However, these instruments are not sufficiently sensitive to quantify the physical activity of a given free-living individual, but rather they are of potential value for comparing activity levels between groups. Greater precision has been obtained using triaxial accelerometers (Bouten *et al*. 1994; Westerterp & Bouten, 1997; Levine *et al*. 2001*b*). In free-living subjects data from these devices correlates reasonably well with TDEE (measured using doubly-labelled water)/ BMR (i.e. PAL values; Bouten *et al*. 1996). Kinematic approaches can be more sophisticated still. Data on movement (gathered using a triaxial accelerometer) and body position (determined using inclinometers) can be combined in free-living individuals to further characterize human activities every 0·5 s and capture > 80 % of the NEAT (Levine *et al*. 2001*a*).

A host of newer technologies are under development that may aid in quantifying NEAT. For example, the utility of motion tracking using global positioning systems has not been fully defined for human studies, although it is limited because global positioning systems do not work indoors and have a precision of about 3 m. Global positioning systems will require further evaluation and validation before their role in measuring NEAT is defined.

Thus, it is possible to quantify physical activity using one or several tools of variable precision and sophistication. What is essential is that the appropriate and feasible tool is used to address the hypothesis of interest in the population under study.

Measuring the energy cost of non-exercise activities

The energy costs of non-exercise activities are readily measurable, although often published tables that list the energetic costs of physical activities are used.

To measure the energy cost of a given physical activity, an indirect calorimeter is most often used, as described earlier. The configurations most suitable are the ventilated hood, Douglas bag and portable calorimeter systems. Here, instead of the measurement being performed at rest, it is performed during the activity of interest. Reliable and precise measurements both in the laboratory and field settings are thereby obtainable. At best, the energy costs for each of a subject's activities would be measured. This procedure is rarely practical except in studies with very few subjects.

The tables that list the energetic costs of physical activities are inexpensive and convenient (Ainsworth *et al*. 1993, 2000). However, substantial, albeit systematic, errors can be introduced. First, the tables may not include the precise activity the subject performed. Second, the energy cost for a given activity may be highly variable between subjects, even independent of gender and weight. Third, calorimetric methods for measuring the energy costs of activities have not been standardized between investigators, so that precision and accuracy of data in the activity tables cannot always be assured. To limit the errors introduced by activity tables, population-, gender- and age-specific group means for the energy costs of the majority of the studied subjects' activities should be available.

It is because of the difficulty of measuring total NEAT and/or its components that so little information is available on the role of NEAT in physiology or human health. It would be possible to combine the total and factoral approaches to better clarify the impact of NEAT on human energetics and health. However, engaging in such endeavours necessitates investigator and capital investment.

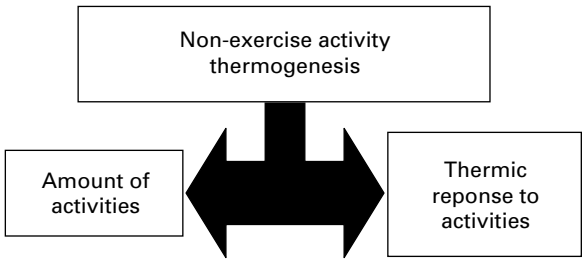

Fig. 3. Schematic representation of the conceptual components of non-exercise activity thermogenesis.

The amount of non-exercise activity thermogenesis that human subjects perform

To systematically understand the amount of NEAT that subjects expend, it is first necessary to quantify and define the energy efficiency of the non-exercise activity (Fig. 3). The limited volume of data on total NEAT in human subjects can then be placed in perspective.

The amount of non-exercise activity

It is difficult to gain true estimates of non-exercise activities for free-living individuals because the variety of non-exercise activities is so enormous and the ability to quantify them is so poor. What transpires from reviewing available data is, not surprisingly, that a variety of factors affect NEAT.

Occupation. The impact of occupation on non-exercise activity can be overt, e.g. when comparing the non-exercise activity of a labourer *v*. a civil servant (Chave *et al*. 1978; Shetty *et al*. 1996; Smith *et al*. 2000). Here, activity levels vary several-fold. There are more subtle occupational effects on physical activity. For example, in many populations in which women work both in the home and out of the home, their cumulative work burden exceeds that of male cohabitants by several hours daily (Levine *et al*. 2001*c*).

The concrete or urban environment. The importance of population sedentariness is well illustrated by studies of PAL for individuals moving from agricultural communities to urban environments, or of the effects of industrialization (Hill & Peters, 1998). In many populations in which this transition has occurred, urbanization has been associated with decreased physical activity. Sedentary cues are unmistakable in developed countries, often through services designed to optimize convenience and throughput at the expense of necessitating locomotion. Examples include drive-through restaurants and banks, televisions, escalators, motorized walkways and clothes' washing machines. In the USA schools may be built beyond walking reach of the community served, suburbs may be built without pavements, city streets may be felt to be unsafe for leisure walking or playgrounds may be unsafe for children to play in.

Genetic background. Genetics may play a role in determining the amount of non-exercise physical activity performed (Bouchard *et al*. 1991). Based on twin and family studies, the heritability for PAL is estimated to be between 29 and 62 %. Analysis of self reports of physical activity from the Finnish Twin Registry, consisting of 1537 monozygotic twins and 3057 dizygotic twins, estimated a 62 % heritability level for age-adjusted physical activity (Kaprio *et al*. 1981). Analyses of self-reported physical activity from the Quebec Family Study, consisting of 1610 members of 375 families, showed a heritability level of 29 % for habitual physical activity (Perusse *et al*. 1989). It is recognized here (and later; see p. 675) that the boundaries between non-exercise- and exercise-related energy expenditure may be poorly defined. Nonetheless, it is intriguing to speculate that genetics directly affect NEAT, i.e. it could be that the twin of a labourer selects to be a lumberjack rather than an office worker.

Age. Studies have consistently shown a decline in physical activity with aging in men and women (Caspersen & Merritt, 1995; Yusuf *et al*. 1996; Bijnen *et al*. 1998). 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 (Yusuf *et al*. 1996).

Gender. Overall, adult men and women in the USA report similar levels of total physical activity, although women are becoming more active (Caspersen & Merritt, 1995; Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996). In other countries, such as Canada, UK and Australia, men report being 1·5–3 times more active than women (Ford *et al*. 1991; Yeager *et al*. 1991). In children there are consistent gender differences, with boys being more active than girls (Pratt *et al*. 1999; Livingstone, 2000). Gender may 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. Where this situation occurs in agricultural communities women's energy needs were found to be 30 % greater that predicted (Levine *et al*. 2001*c*).

Body composition. There is substantial data to suggest that overweight individuals show lower activity levels than their lean counterparts (Thompson *et al*. 1982; Pacy *et al*. 1986). This finding appears to be repeated across all ages, for both genders and for all ethnic groups. It is not possible to ascertain whether the effects of body composition on non-exercise activities occur independent of weight.

Education. Groups with more education consistently report more leisure time physical activity than groups with less education. In the USA high-education groups are two to three times more likely to be active than low-education groups (Ford *et al*. 1991; Caspersen & Merritt, 1995; Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996). This situation contrasts with that of low-income countries, in which child labour is commonplace. Here, poverty is predictive of greater child labour, and the most impoverished children thereby have the greatest NEAT levels (Grootaert, 1998; Levine *et al*. 2002).

Seasonal variations in physical activity. Limited data are available regarding differences in the amount of physical activity performed during different seasons. Who volitionally walks to work in the rain? Data from Canada

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suggest wide differences in time spent in physical activity associated with season. Time spent in activity was twice as high during the summer months compared with winter months (Katzmarzyk *et al*. 2001). Common sense dictates, and data confirm, that occupational NEAT is greatly seasonally dependent in agricultural communities in which workloads vary cyclically (Singh *et al*. 1989; Ferro-Luzzi *et al*. 1990; Pastore *et al*. 1993).

Thus, although little objective data exist on how much and what types of non-exercise activities individuals perform, it is clear that there are a variety of cultural and environmental factors that affect physical activity. It is difficult, from existing data, to quantify the impact of NEAT *v*. exercise. However, what is clear is that NEAT is highly variable and dramatically affected by factors such as those discussed earlier and by a variety of other variables that are yet to be clearly defined. Also, genetics may subtly affect self-selected physical activity, perhaps through job and/or leisure-time choices.

The energy costs of non-exercise activities

The other major determinant of NEAT is the energetic efficiency with which non-exercise activities are performed (Figs. 3 and 4). It is recognized that even trivial movement is associated with substantial deviation in energy expenditure above resting values. For example, mastication is associated with deviations in energy expenditure of 20 % above resting values (Levine *et al*. 1999*a*). Very low levels of physical activity such as fidgeting can increase energy expenditure above resting levels by 20–40 % (Levine *et al*. 2000). It is not surprising then that ambulation, whereby body weight is supported and translocated, is associated with substantial variations in energy expenditure (Haymes & Byrnes, 1993). Even ambling or browsing in a store (walking at 1·6 km/h) doubles energy expenditure and purposeful walking (3·2–4·8 km/h) is associated with doubling or tripling of energy expenditure. When body translocation was recorded using a triaxial accelerometer, the output from this unit correlated with non-resting energy expenditure (Bouten *et al*. 1996). This relationship implies that ambulation may be a key component of NEAT. The energy costs of a multitude of occupational and non-occupational physical activities have been charted and tabulated (Ainsworth *et al*. 1993, 2000). What is noteworthy is the many-fold variance in the energy costs of occupation-dictated activities, ranging from $< 1 \times$ resting energy expenditure (e.g. typing) to 5–10$\times$ resting energy expenditure (e.g. during wood cutting, harvesting or physical construction work).

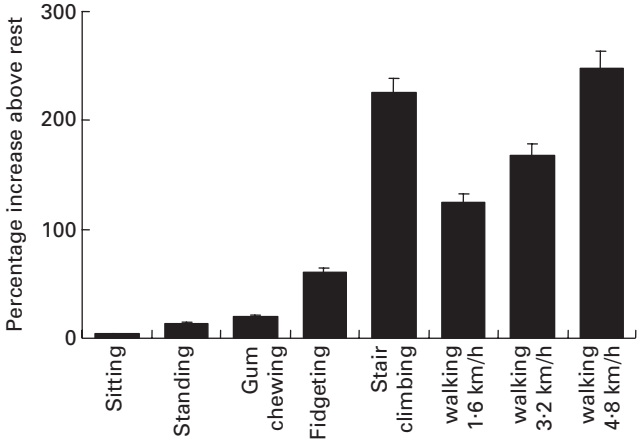

Fig. 4. The effect of selected activities on energy expenditure in human subjects. (From Levine *et al*. 2000.)

Several factors affect the energetic efficiency of physical activity.

Body weight. It requires more energy to move a larger body than a smaller one. Several investigators have demonstrated that the energy expended in physical activity during weight-bearing physical activity increases with increasing body weight (Passmore, 1956; Bray *et al*. 1977). It is less clear whether work efficiency varies with body composition, independently of body weight. Some studies (Hanson, 1973; Whipp *et al*. 1973; Bray *et al*. 1977; Poole & Henson, 1988) have found no differences in weight-corrected work efficiency between obese and non-obese subjects, while other studies (Dempsey *et al*. 1966; Maloiy *et al*. 1986) have found greater work efficiency in the obese.

Effects of changes in body weight. There is controversy as to whether work efficiency changes with weight loss. Several studies have reported that energetic efficiency is reduced following weight reduction. Foster *et al*. (1995) measured the energy cost of walking in eleven obese women before weight loss and at 9 and 22 weeks post weight loss. They determined that the energy cost of walking (after controlling for loss of body weight) decreased substantially by 22 weeks 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*. (1987) compared energy expenditure during different physical activities and found that energy expenditure was about 15 % lower in the post-obese subjects compared with controls. de Boer *et al*. (1986) 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*. (1995), who speculated that increased work efficiency could be partially responsible for weight regain following weight loss.

Alternatively, Froidevaux *et al*. (1993) measured the energy cost of walking in ten 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 & Henson (1988) also found no change in efficiency of cycling after energy restriction in moderately-obese women. Weigle & Brunzell (1990*a*,*b*) demonstrated that about 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.

Thus, while 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

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changes, it implies that a mechanism may exist to define the work efficiency of NEAT activities and affect energy balance.

Role of skeletal muscle metabolism in determining work efficiency. Differences in skeletal muscle morphology or metabolism may play a role in differences in work efficiency. Henriksson (1990) suggested that changes in muscle morphology in response to energy restriction lead to changes in the relative proportion of type I *v*. type II fibres in human subjects. Some studies suggest that type II fibres have a greater fuel economy than type I fibres (Wendt & Gibbs, 1973; Crow & Kushmerick, 1982). Since type II fibres appear to be better preserved during starvation than type I fibres (Henriksson, 1990), overall fuel economy and work efficiency may increase following energy restriction and loss of body mass. However, a recent study on muscle fibre type before and after an 11 kg weight loss in obese females did not show any changes in the fibre type distribution (van Aggel-Leijssen *et al*. 2002).

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 (Zurlo *et al*. 1990, 1994; Thomas *et al*. 1992) and that differences in morphology or metabolism of skeletal muscle and sympathetic nervous system activity (Blaak *et al*. 1994) may underlie some of the whole-body differences (Chang *et al*. 1990; Zurlo *et al*. 1994). 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 etc.) were measured in twenty-two pairs of dizygotic sedentary twins and thirty-one pairs of monozygotic sedentary twins there was a genetic effect for energy expenditure for low-intensity activities (from 50 W to 150 W), even after correction for differences in body weight (Bouchard *et al*. 1989). No genetic effect was seen for activities requiring energy expenditure $> 6 \times$ resting energy expenditure. These observations hint at an intriguing possibility, i.e. 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 about 10 % more energy efficient during squatting exercises than adults (Villagra *et al*. 1993). 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 *v*. type II fibres, 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, exercised-induced effects in skeletal muscle could be important for NEAT. Alterations in exercise can change the fibre-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 fibres, while transformation of type II fibres into type I fibres is not common unless the exercise training has been extremely intense over a long period of time. Type I fibres have a greater mitochondrial density, are more oxidative and more fatigue-resistant than type IIb fibres. Type IIb fibres are glycolytic in nature, have a lower mitochondrial content, and are more prone to fatigue. Type IIa fibres are intermediate in their mitochondrial content and, in human subjects, closely resemble type I fibres in oxidative capacity. However, an overlap of oxidative capacity exists between fibre-type groups. Type I and type IIa fibres are more energy efficient than type IIb fibres and the proportions of these fibre types will vary according to the type of exercise training performed. It has been shown that, even independently of fibre-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 swimmers average lower energy expenditures (15 % for running and ≤ 50 % for swimming) at specified velocities compared with untrained individuals (Holmer, 1974; Holmer *et al*. 1974; Sharp *et al*. 1992). Here, the concept is introduced whereby exercise directly affects NEAT through changes 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 (Dahlstrom *et al*. 1990; Mulligan & Butterfield, 1990; Jones & Leitch, 1993). There are reports in the literature of increased energy efficiency in female runners (Mulligan & Butterfield, 1990), dancers (Dahlstrom *et al*. 1990) and swimmers (Jones & Leitch, 1993) as compared with sedentary females. Most reports make conclusions regarding energetic efficiency based on indirect rather than direct measurements of energy intake and/or expenditure. For example, Mulligan & Butterfield (1990) concluded that female runners had increased energy efficiency since 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 (Schulz *et al*. 1992) or cyclists (Horton *et al*. 1994). Thus, the question of whether female athletes show a different energy efficiency compared with sedentary females is controversial. Whether there are inherent gender differences for the efficiency of non-exercise activities is open to speculation, but could readily be studied.

Total non-exercise activity thermogenesis in human subjects and its variability

Data readily demonstrates the marked variance in NEAT. Black *et al*. (1996) reviewed PAL values from 574 measurements of total energy expenditure, made using doubly-labelled 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

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Table 1. Lifestyle-based prediction of physical activity levels (PAL) (from Gorzelniak *et al*. 1998)

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

Table 2. Physical activity levels for women and men from low-income countries, grouped according to intensity of work (from Singh *et al*. 1989; Coward, 1998)

	Work Intensity		
	Light	Moderate	Heavy
Women	1·55	1·64	1·82
Men	1·55	1·78	2·10

values echo those derived from lower-income societies (Singh *et al*. 1989; Coward, 1998; Table 2).

Further insight into total NEAT comes from Westerterp's (2001) observation 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. Thus, for a given individual NEAT is defined by the sum of the energetic costs of occupational plus non-occupational activities, which in turn is influenced by the sedentariness of the individual's microenvironment (e.g. workplace) and macroenvironment (e.g. country). What is fascinating is to speculate that an individual with a high 'programmed NEAT' might select an active job (e.g. car washing or ambulatory mail delivery) despite living in a sedentary country such as the USA.

The role of non-exercise activity thermogenesis in physiology

That NEAT should play a role in human energy homeostasis is not that surprising. 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 an individual 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 several-fold 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.

Changes in non-exercise activity thermogenesis 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 (Schoeller, 2001). In one such study twelve pairs of twins were overfed by 4·2 MJ (1000 kcal)/d 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 'twinness' accounted for some of the inter-individual variance in weight gain. This finding suggests that NEAT responsiveness with overfeeding is in part genetically determined.

NEAT was directly implicated in the physiology of weight gain when sixteen sedentary lean individuals were carefully overfed by 4·2 MJ (1000 kcal)/d (Levine *et al*. 1999*b*). All components of energy expenditure and body composition were carefully determined. There was a tenfold variation in fat gain and an eightfold variation in changes in NEAT. Those individuals who had the highest increase in their NEAT gained the least fat with overfeeding, and those individuals who failed to increase their NEAT with overfeeding gained the most fat (Fig. 5). Studies are too sparse to define how changes in the amount of non-exercise 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.

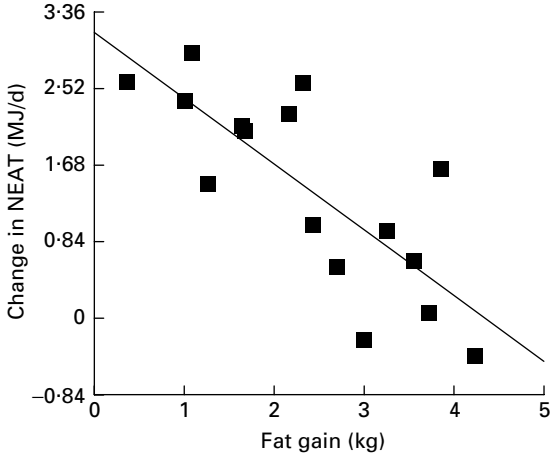

Fig. 5. Changes in non-exercise activity thermogenesis (NEAT) with overfeeding. Healthy subjects (*n* 16) were overfed by 4·2 MJ (1000 kcal)/d over baseline energy needs. Fat gain was determined using dual x-ray absorptiometry and change in NEAT was calculated from NEAT measured before and after overfeeding (NEAT = TDEE – (BMR + TEF), where TDEE is total daily energy expenditure, TEF is thermic effect of food); r –0·77, $P < 0·001$. (From Levine *et al*. 1999*b*.)

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Changes of non-exercise activity thermogenesis with negative energy balance

With underfeeding, physical activity and NEAT decrease. Chronic starvation is known to be associated with decreased physical activity (Leyton, 1946; Keys *et al*. 1950; James *et al*. 1988). Whether those individuals who are susceptible to ready fat loss are those who fail to decrease NEAT with underfeeding has not been established. However, if it is argued that with a prolonged energy deficit of 2·1–2·5 MJ (500–600 kcal)/d BMR decreases by approximately 10 % (i.e. approximately 0·84 MJ (200 kcal)/d; assuming a sustained decrease in lean body mass that may not actually occur; Mathieson *et al*. 1986; Hammer *et al*. 1989; Cavallo *et al*. 1990; Foster *et al*. 1990; Wadden *et al*. 1990; Burgess, 1991; Donnelly *et al*. 1991; Fricker *et al*. 1991) and TEF decreases by approximately 0–0·21 MJ (0–50 kcal)/d (Even & Nicolaidis, 1993; Weinsier *et al*. 1995), then NEAT has to decrease by approximately 0·84–1·26 MJ (200–300 kcal)/d once fat loss reaches a plateau. In one study with severe energy reduction (3·36 MJ (800 kcal)/d; Leibel *et al*. 1995), decreases in NEAT apparently accounted for 33 % of the decrease in TDEE in lean subjects, 46 % in obese subjects with a 10 % weight loss and 51 % in obese subjects with a 20 % weight loss (Leibel *et al*. 1995). If NEAT decreases with negative energy balance, is it because the quantity of physical activities decreases or that energy efficiency decreases, or both? Studies to date have not definitely answered this question. With severe energy reduction (1·76 MJ (420 kcal)/d) in obesity maximal O_2 consumption and energy expenditure at submaximal loads may decrease (Keim *et al*. 1990), although with less-severe energy restriction maximal O_2 consumption appears unchanged (Katzel *et al*. 1995). 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 or altered energetic efficiency, or both.

Overall, it appears that with weight gain NEAT increases and with weight loss NEAT decreases. This relationship creates an intriguing scenario whereby NEAT might act to counterbalance shifts in energy balance. It could be that these changes in NEAT together with those that affect BMR and TEF are small and swamped by changes in energy intake. However, some subjects overfed by 4·2 MJ (1000 kcal)/d increased NEAT by > 2·5 MJ (600 kcal)/d, which suggests that changes in energy expenditure and NEAT may be quantitatively important in the physiology of body-weight regulation. This factor in turn raises the question as to whether NEAT contributes to pathological perturbations in energy balance.

The mechanism of non-exercise activity thermogenesis

Very little is known about the mechanism by which NEAT is regulated, for several reasons. First, very little data is available on the physiological modulation of NEAT. Second, despite the evidence that NEAT is altered with changing energy balance, no information is available on which components of NEAT are specifically altered. It is not known which components of NEAT predominate, or which 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 affects 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 researchers 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 that demonstrate that physical activity and NEAT decrease during negative energy balance.

How might an investigation of the mechanism by which NEAT is modulated be started? 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 accounted for the vast majority of the changes in NEAT, it is possible that the mechanism that drives ambulation energy expenditure is pivotal for understanding NEAT. It might then be necessary to define whether it is the amount of walking 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, including thyroxin. Hyperthyroidism in human subjects is associated with increased spontaneous physical activity (Weetman, 2000). The sympathetic nervous system (Ravussin, 1995) and neuro-humoral factors such as the orexins (Williams *et al*. 2000; Kotz *et al*. 2002) also have the potential to affect NEAT. Thus, albeit crudely, examples do exist whereby specific mediators of spontaneous physical activity have been identified.

To date little is known about the mechanism by which NEAT is modulated. This situation is a result of the paucity of information on 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. If each week begins with a tank of NEAT akin to a tank of petrol, the size of which could be determined genetically, then when the tank is empty on a given Friday afternoon, the weekend is spent recumbent operating only the remote control. Conversely, if on Friday the NEAT tank is still half-full, then that becomes the weekend that the overgrown shrubs in the back yard become removed.

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