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Is obesity associated with lower body temperatures? Core temperature: a forgotten variable in energy balance

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Abstract

The global increase in obesity, along with the associated adverse health consequences, has heightened interest in the fundamental causes of excessive weight gain. Attributing obesity to "gluttony and sloth", blaming the obese for overeating and limiting physical activity, oversimplifies a complex problem, since substantial differences in metabolic efficiency between lean and obese have been decisively demonstrated. The underlying physiological basis for these differences have remained poorly understood. The energetic requirements of homeothermy, the maintenance of a constant core temperature in the face of widely divergent external temperatures, accounts for a major portion of daily energy expenditure. Changes in body temperature are associated with significant changes in metabolic rate. These facts raise the interesting possibility that differences in core temperature may play a role in the pathophysiology of obesity. This review explores the hypothesis that lower body temperatures contribute to the enhanced metabolic efficiency of the obese state.

1. Introduction

Although the history of obesity research is replete with potential physiologic explanations of the "cause" of obesity, no definite abnormalities have been identified that explain why some humans are obese. The time honored explanation of "gluttony and sloth" lays the blame squarely on the obese; but for these reprehensible character traits the obese would be lean, or so goes the well-worn argument. This common attribution, however, oversimplifies a complex problem [1] and cannot be sustained in the light of available evidence. The global epidemic of obesity, moreover, with its untoward health consequences, has forced the question of the cause of obesity into prominence worldwide [2].

2. Individuals differ in metabolic efficiency

It is widely recognized that not all ingested calories taken in excess of energy requirements are stored as fat and that a portion of the caloric excess may be dissipated as heat. *Metabolic efficiency* refers to the relationship between ingested calories and fat storage. Those with more efficient metabolism store a greater proportion of excess calories as fat, whereas, conversely, those whose metabolism is less efficient dissipate more calories as heat. It has, moreover, been decisively demonstrated that individuals differ in their metabolic efficiency [3]; a diet that maintains weight in one individual may cause weight gain in another, despite similar lean body mass and physical exercise.

The Quebec Overfeeding Twin Study of Bouchard and colleagues [3,4] provided clear evidence of such individual differences. In this study, 12 pairs of identical twins were overfed 1000 kcal/d 6 d/wk for 3 months with physical exercise held constant. The results were astonishing: (1) The amount gained varied considerably within the group. (2) The most "efficient" individual gained almost the theoretical amount predicted from the increased caloric intake, whereas the least efficient dissipated 60% of the excess caloric load. The group as a whole dissipated 35% of the increased calories. (3) Variation between twin pairs was greater than variation within twin pairs, implying a genetic factor in energy expenditure.

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3. The energy balance equation

A perspective on these findings is provided by the venerable energy balance equation:

Energy intake = energy output + storage

Energy intake refers to ingested calories; and *storage* refers to change in weight, largely fat. In the Quebec Overfeeding Twin Study [3] cited above, intake was controlled and physical activity was limited; but storage (weight gain) varied considerably, demonstrating that differences in metabolic efficiency result from changes independent of physical activity.

Energy output is the most complex of the components in the energy balance equation and varies considerably among individuals [5]. In sedentary man, a rough approximation of the major compartments of energy expenditure is as follows:

Resting (or "basal") metabolic rate (RMR) accounts for approximately 80% of energy output. About two thirds of RMR is for maintenance of homeothermy (warm-bloodedness); about one third is to maintain cellular integrity, ionic gradients, protein turnover, and the like [6-8] Resting metabolic rate is largely regulated by thyroid hormones, with a minor contribution from the sympathetic nervous system. Resting metabolic rate differs by as much as 600 kcal/d for a 70-kg man [8].

Physical activity (exercise) accounts for about 10% in truly sedentary humans; in addition to intentional activity, this category includes nonpurposeful motion such as fidgeting, which may differ among lean and obese individuals [9], as well as upright posture [10].

The remaining 10% is frequently referred to as *thermogenesis*, which means heat production unrelated to physical activity. This component is regulated by the sympathetic nervous system and includes "nonshivering thermogenesis" in response to cold exposure and "diet-induced thermogenesis" in response to dietary intake. These are "adaptive" or "facultative" forms of thermogenesis in that they mediate specific physiologic functions [11]. Although disputed in the past, evidence for adaptive thermogenesis in humans has now been convincingly established [12-14].

It should be emphasized that, for nonsedentary individuals, the activity component may be much greater than 10% of total energy expenditure. Evidence has been developed indicating that the combination of activity plus adaptive thermogenesis accounts for about 44% of total energy expenditure on average, meaning that RMR would constitute about 56% of total energy expenditure in normally active humans [15], as compared with 80% in the truly sedentary.

4. The case for a thermogenic handicap

Inspection of the energy balance equation shows that increases in energy output broaden the range of energy intakes over which balance can be achieved. The overfeeding experiment [3] described above demonstrates that some individuals can achieve energy balance at a greater caloric intake, thereby making them resistant to weight gain. On the other hand, those individuals with more efficient metabolic traits have a diminished capacity to dissipate energy, are prone to obesity, and may be said to have a "thermogenic handicap."

Although the case for differences in metabolic efficiency is convincing, the physiologic bases for such differences remain to be elucidated. Differences in metabolic efficiency may reside in higher or lower basal metabolic rates, a lesser or greater capacity for dietary (adaptive) thermogenesis, or both.

5. Thrifty metabolic traits

A lesser ability to dissipate ingested calories is one example of a thrifty metabolic trait that has evolved to promote survival in the face of fluctuations in food availability. Since the initial formulation of the "thrifty gene" hypothesis by James Neel in 1962 [16], the nature of thrifty traits has been the subject of considerable research and speculation. A recent formulation [17] highlights 2 distinct components: (1) decreased metabolic rate and/or a diminished capacity for "thermogenesis" and (2) decreased insulin sensitivity. These 2 components address the 2 main physiologic imperatives of starvation: energy conservation and protein preservation. A decrease in metabolic rate would lead to more efficient storage of calories as fat, thereby prolonging survival during famine; during periods of abundance and in the face of dietary excess, this trait would predispose to obesity. Resistance to the action of insulin would divert glucose from skeletal muscle, which can use fat-derived substrates, to the brain, an organ almost entirely obligated to the use of glucose. In the presence of famine, insulin resistance would spare muscle breakdown by lessening the need for gluconeogenesis from protein; in the face of an abundant food supply, however, and in association with dietary excess, insulin resistance would predispose to type 2 diabetes mellitus.

Both metabolic efficiency and insulin resistance, moreover, are known to vary among different individuals in the same population. The survival value of these thrifty traits, embedded in our genome by natural selection, underlies the current epidemic of obesity and type 2 diabetes mellitus. The ravages of obesity in once lean indigenous peoples, such as the Pima Indians of the US southwest [18,19], the Aboriginal peoples of Australia [20,21], and the Maoris of New Zealand [22], exemplify the maladaptive side of these thrifty traits in the presence of an abundant high-energy food supply.

6. The sympathetic nervous system and the metabolic response to dietary intake

The prime importance of energy conservation is demonstrated by the decline in metabolic rate that occurs during

starvation, a response that involves suppression of sympathetic nervous system (SNS) activity [23]. Body temperature also falls [24]. This conservative response that limits weight loss during starvation also diminishes the efficacy of low-energy diets in the treatment of obesity [12,14]. The decrease in sympathetically mediated thermogenesis in response to starvation has also raised the reasonable question of whether decreased SNS activity is the cause of the thermogenic handicap in the obese, a question made more compelling by the fact that some hereditary forms of rodent obesity, such as the *ob*/*ob* mouse, do have decreased SNS activity [25,26]. Obesity in humans, however, is not characterized by a state of lowered SNS activity but rather by increased SNS activity [27-30] stimulated by elevated levels of insulin [31,32] and leptin [33,34]. Such a mechanism may be seen as a physiologic adaptation to address the thermogenic handicap of the obese and would tend to mask any thermogenic handicap associated with obesity. In fact, a thermogenic handicap may be more easily demonstrable in obese subjects after weight loss [14]. Although diminished SNS activity does not account for the thermogenic handicap of obesity, sympathetic activation in the obese does, parenthetically, contribute to obesity-related hypertension [35,36]. Reduced responsiveness of thermogenesis to SNS stimulation has not been excluded, however, as a factor in the thermogenic handicap of the obese.

7. Resting metabolic rate and homeothermy

Approximately two thirds of RMR is expended in meeting the requirement of homeothermy [6,7], the maintenance of a constant body temperature of about 37°C (98.6°F). In truly sedentary humans where RMR is 80% of total energy expenditure, this means that more than 50% of total energy expenditure is dedicated to maintaining this constant core temperature. In normally active humans where the RMR accounts for 56% of total energy expenditure [15], approximately 37% of total energy output is expended in the maintenance of homeothermy. This impressive contribution that warm-bloodedness makes to overall energy production is exemplified by the difference in energy output between poikilotherms and homeotherms; a mouse has a many fold greater metabolic rate than a lizard of the same weight [37]. This metabolic energy required for homeothermy is thyroid dependent and apparently generated principally in mitochondria throughout the body of warm-blooded animals. The adaptive forms of thermogenesis, in contrast, are regulated by the sympathetic nervous system and generated, at least in part, in brown adipose tissue (BAT) [38]. It is of interest that recent observations using positron emission tomographic scanning have resuscitated interest in functional BAT in adult humans [39,40].

The important relationship of body temperature to metabolic rate is also demonstrated by the effect of temperature elevation on the rate of oxygen consumption. Raising core temperature by 1°C is associated with a 10% to 13% increase in metabolic rate [41]. During starvation, a fall in body temperature occurs, contributing to the decrease in metabolic rate noted in this state [24]. Are differences in body temperature responsible for interindividual variations in RMR? Is it possible that the obese have a lower body temperature than normal-weight persons? Or that, during periods of low energy intake or during sleep, the obese have an exaggerated fall in temperature? Good data appear to be lacking; a recent book on energy metabolism and obesity [42], for example, fails to even mention a potential role for core temperature. Body temperature in the obese is clearly worthy of study given the overriding importance of core temperature as the major factor in energy expenditure.

8. Variation in metabolic rates in different populations

Research involving different human populations has provided considerable evidence for significant interpopulational variation in both RMRs and core temperatures. The pioneering work of DF Roberts [43,44], for example, was among the first to systematically show a link between energy metabolism and environmental temperature in human populations. Roberts found a strong negative correlation between RMRs and mean annual temperature, suggesting that adaptation to regional climatic conditions plays an important role in explaining human variation in metabolic heat production. Subsequent research has confirmed that many populations of the tropics have relatively depressed RMRs for their mass [45,46], whereas indigenous northern, arctic populations tend to have elevated RMRs [47-49].

9. Metabolic rate measurements in the obese

Despite the compelling arguments for a thermogenic handicap in the obese, differences in metabolic rate between the lean and the obese have not been convincingly demonstrated. One possibility for the failure to demonstrate obese-lean differences in RMR relates to the inherent difficulty in making physiologic comparisons between the lean and the obese. When comparing a 70-kg person with a 150-kg individual, how should the results be expressed? What is the appropriate denominator for comparison of oxygen consumption? Clearly, a person-to-person comparison makes no sense given the differences in body mass. Historically, such comparisons have been made by simply standardizing metabolic rate as a function of body mass (kilocalories per kilogram), fat-free mass (kilocalories per kilogram fat-free mass), or surface area (kilocalories per square meter) [50]. Much recent work, however, indicates that standardizing RMR as simple ratios of mass or surface area leads to spurious conclusions about variation in metabolic efficiency [51].

Indeed, the magnitude of measurement error in the independent and dependent variables may be sufficiently large to swamp physiologically meaningful differences in relative metabolic efficiency. Parenthetically, measurements of core temperature can be made precisely and are free of the conundrum imposed by differences in body size because core temperature is regulated centrally for the whole body.

10. Is core temperature lower in the obese?

Lowering body temperature is an established strategy used by homeotherms to conserve energy. Some animal models of obesity, including the obese (*ob*/*ob*) mouse [52,53] and the Zucker fatty (*fa*/*fa*) rat [54], are hypothermic compared with lean controls. Hibernation and the lesser state of shallow torpor wherein the temperature falls at night are energy-saving adaptations used by a variety of mammals [55,56] and even some human populations such as the Australian Aboriginals [57]. A decrease in body temperature, in fact, occurs at night in relation to the sleep cycle in human populations [58,59]. A fall in body temperature occurs during starvation, as noted above, and in hypoglycemia, an acute state of energy deprivation [60-62]. Recent evidence implicating fibroblast growth factor 21 in the metabolic response to fasting supports the important adaptive role that temperature plays in the adaptation to starvation. In addition to stimulating lipolysis, fibroblast growth factor 21 lowers temperature and induces torpor [63]. Lower temperature has also been linked to obesity in mice with BAT ablation [64].

Does core temperature contribute to the well-documented differences in RMR displayed within all populations [65]? Might individual variations in temperature drop at night or during therapeutic low-energy diets contribute to a “thrifty trait” conferring an increase in metabolic efficiency and contributing to the thermogenic handicap described above? The relationship between core temperature and obesity has received limited attention; of the currently available data, some [65-67], but not all [68,69], support an inverse association between temperature and obesity. Twenty-four–hour temperature monitoring, correlated with daily activities, should answer the question.

11. Quantitative significance of changes in core temperature

Some quantitative considerations, although crude, also serve to demonstrate the potential importance of core temperature. A positive balance of 3500 to 4000 kcal results, theoretically, in the deposition of 1 lb of fat. Walking 1 mile, a normal-sized individual burns about 100 kcal, the amount of energy contained in 10 potato chips and equivalent to 5% of a total energy intake of 2000 kcal/d. A 1°C increase in core temperature, by comparison, would increase metabolic rate by 10% to 13% [41]. In the example of extreme sedentary existence cited above where metabolic rate approximates 50% of overall energy output (or about 1000 kcal for a normal-sized person), a 1°C increase in core temperature increases expenditure of 100 to 130 kcal/d. Such an individual could achieve energy balance eating 100 to 130 kcal more per day than one with a 1.0°C lower body temperature. Individuals with the 1°C lower core temperature, thus, would have a thermogenic handicap of about 100 to 130 kcal/d or about 3000 to 4000 kcal/mo. In 1 month, this would account for 1 lb of fat, 12 lb in 1 year, and about 120 lb in a decade, all else being equal. In the normally active example described above where RMR constitutes 37% of total energy expenditure, the impact is less but still impressive. Under these circumstances, the thermogenic handicap of a 1°C lower core temperature might approximate 74 to 96 kcal/d or about 2200 to 2900 kcal/mo. Greater falls in temperature, perhaps during sleep or in response to low-energy diets, would have correspondingly greater effects.

12. Summary

Given the importance of RMR in overall energy output and the importance of homeothermy as the major component of RMR, core temperature should be evaluated as a potential cause of individual differences in metabolic efficiency in humans. Assessing core temperature in the obese can be done, furthermore, without the confounding need to normalize energy expenditure per unit of body mass. In these studies, assessment of core temperature should be done for prolonged periods, should sample day and night temperatures, and should assess the impact of fasting and low energy intake on obese and lean individuals. Cross-sectional, and especially longitudinal, population-based studies could define the role of core temperature in the pathogenesis of obesity. Information gained in such studies, along with research into the central nervous system regulation of temperature set point and the regulation of mitochondrial metabolism, might enable the development of new therapeutic strategies designed to enhance energy output.

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