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Additional Information

"The Energy Balance Hypothesis of Obesity: Do the Laws of Thermodynamics Explain Excessive Adiposity?"

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The Energy Balance Hypothesis of Obesity: Do the Laws of Thermodynamics Explain Excessive Adiposity?

ABSTRACT

In this work, we reflect upon the energy balance hypothesis of obesity. International organizations, the general population and many scientists hold the belief that obesity is indisputably caused by an imbalance between energy intake and energy expenditure. Most of them argue that the laws of thermodynamics support this view. We identify and review the main arguments used to support this belief, and we explain the reasoning mistakes those arguments harbor. We show that the laws of thermodynamics do not support the idea that obesity is an energy problem nor an energy balance problem more than they do in the growth of any other tissue in the human body. We argue that the validity of the energy balance paradigm for obesity must be questioned. Although correction of a wrong belief is laudable *per se*, in this particular case harm may arise by influencing the way in which obesity prevention is tackled and obese patients are treated.

INTRODUCTION

Prevalence of overweight and obesity has risen significantly worldwide over the past decades⁽¹⁾, while policies, laws and regulations in regard to obesity prevention are based on the idea that excessive energy intake and reduced physical exertion, the so-called obesogenic environments, are driving these trends^(2,3). The scientific study of obesity has been dominated throughout the last hundred years by this energy balance concept, a concept that is presumably based on an indisputable thermodynamic principle: the principle of conservation

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of energy⁽³⁻¹⁶⁾. Under the reign of this paradigm, researchers have focused on the factors that regulate energy intake, such as appetite, satiety, food availability, etc. and the factors that affect energy expenditure, such as sedentary lifestyles. Thus far, this approach has not led to effective therapeutic approaches for obesity nor has proved useful to revert the obesity epidemic. While many articles have pointed to other factors such as genes or hormones or other causes in the obesogenic environment that the individual cannot control, the discussion relies most of the times on the current medical model of obesity: they look for the causes of a positive energy balance, *i.e.* why the individual consumes more energy than they spend. Although correction of erroneous beliefs is desirable *per se*, to hold false beliefs about the cause of obesity can result in enormous harm, diverting efforts and funds to unproductive lines of investigation, resulting in inappropriate medical treatment of patients, impeding the prevention of the condition and even blaming the patient for their weight, therefore promoting weight-stigma⁽¹⁷⁾. We are certainly not suggesting that the laws of physics are suspended when it comes to human body weight, but in this paper we make the case that the energy paradigm for obesity is based on reasoning mistakes.

Energetic research in the nutrition field began in the last years of the 19th and first years of the 20th centuries, when the first human calorimeters were built and the first tables with the caloric content of foods were made available for the general population⁽¹⁸⁾. As the century advanced, the principle that energy had to be conserved was soon interpreted as proof that "obesity is always caused by an overabundant inflow of energy. The excess is deposited as adipose tissue", as Newburgh and Woodwell Johnston stated in 1930⁽⁴⁾. It was progressively assumed that any explanation not based on energy concepts was a direct violation of the law of conservation of energy. Nevertheless, during those years the scientific community was still considering the possibility that instead of "exogenous" the cause of obesity could be

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"endogenous", with tissue "lipophilia" as one of the relevant concepts⁽¹⁹⁾. Those terms were introduced in 1907 by von Noorden⁽²⁰⁾. Endogenous refers to obesity caused by physiological alterations, such as the abnormal secretion of a hormone, while exogenous refers to obesity caused by bad habits, such as an excess of food or poor physical activity. It is worth mentioning that the notion of lipophilia and the knowledge and research from the German and Austrian research communities evaporated with the rise of Hitler and World War II⁽²¹⁾. Although other possible causes for obesity that are also compatible with the First Law of Thermodynamics (FLT) have been proposed since that time, *e.g.* the carbohydrate-insulin model⁽²²⁾, the idea that obesity is caused by a chronic imbalance between energy intake and expenditure is still promoted as an indisputable truth. As a consequence of this belief, experimental results related to obesity are often attributed exclusively to one or both terms of the energy balance formula: calorie intake and energy expenditure⁽²³⁻³¹⁾.

THE FIRST LAW OF THERMODYNAMICS

The energy of a system is the faculty of that system to produce external effects. The external effect could be mechanical or thermal in nature. The First Law of Thermodynamics is the principle of the conservation of energy applied to phenomena involving the production or absorption of heat. In the International System of Units, energy is measured in Joules (J), which is the work done on an object when a force of one Newton acts on that object in the direction of its motion through a distance of one metre. In the food we eat, there is potential energy stored within the chemical bonds of its molecules. A common unit used in regard to the energy content of food is the kilocalorie (kcal), defined as the energy needed to raise the temperature of 1 kg of water by 1°C.

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For our purposes, we can consider the human body, as defined by its external limits (*e.g.* our skin), as an open thermodynamic system. The internal energy is the total energy within the boundaries of a system. According to the FLT the change in internal energy (ΔU) in this system is equal to the net potential energy added by the food intake (food energy) minus the net heat lost by the system (Q) minus the work done by the system (W):

$$\Delta U = (\text{food energy}) - Q - W. \tag{1}$$

If we rename "food energy" as CI (Calories In) and ΔU as ΔE , and we define CO (Calories Out) as W + Q, *i.e.* the net energy loss as heat and work, we can rewrite Eq. (1) in its most-popular form:

$$\Delta \mathbf{E} = \mathbf{CI} - \mathbf{CO}.$$
 (2)

THE ENERGY BALANCE PARADIGM FOR OBESITY

The energy balance paradigm for obesity postulates that the obvious cause of obesity is a sustained positive energy balance, where energy balance (EB) is a formula defined as CI- $CO^{(4,5,32-34)}$ (see Fig. 1). Correspondingly, this paradigm assumes that dietary interventions for weight loss only work if they provide an overall reduction in energy intake and/or increase energy losses⁽³⁵⁻³⁸⁾. Since the energy paradigm for obesity is different from the FLT, in this paper we refer to it as the CICO (Calories In, Calories Out) hypothesis.

We analyze below the main reasoning mistakes that support the CICO hypothesis.

The energy balance equation is not a formula

As stated previously, the CICO hypothesis stipulates that weight gain occurs because caloric intake exceeds energy expenditure, or, in other words, that overcomsumption and underactivity are the obvious causes of obesity. This conclusion derives from the

interpretation of Eq. (2) as a formula that can be used on its own to deduce what causes obesity or how to reverse it. In this section, we use a simple model of the human body, based on four different compartments (see Fig. 2), to explain why this interpretation is defective. For the sake of clarity, we make explicit that we call equation to a relationship that defines a restriction, and we call formula to an expression that tells how to compute something. Both equations and formulas have an equal sign, but its meaning is different: in an equation the equal sign means that both sides of the equal sign are numerically equivalent, while in a formula the meaning is an assignment, *i.e.* the expression on one side of the equal sign is evaluated and it is assigned to the variable on the other side, which must be already isolated. A formula is true no matter its inputs, while an equation only is true for specific values of the variables in the equation, which are called the solution of the equation. A formula is evaluated while an equation must be solved.

In Fig. 2, the rectangles symbolize compartments and the arrows represent mass/energy exchanges. For reasons of clarity, we will consider that fatty acids are the only matter that is exchanged among compartments, that long term accumulation of fatty acids only occurs in the adipose tissue and that no conversion from other macronutrients to fatty acids exist. These simplifications do not affect the conclusions of the present analysis. Under these conditions, the net energy that enters the Enterocytes, Blood and Muscle compartments (considered as a single compartment) in a specific period of time is assumed to be zero:

$$\mathbf{E}_{\mathrm{IN}} - \mathbf{E}_{\mathrm{OUT}} - \mathbf{E}_{\mathrm{lg}} + \mathbf{E}_{\mathrm{ll}} = \mathbf{0},$$

where E_{IN} is the energy increase associated to the fatty acids that have entered the body, E_{OUT} is the energy loss associated to the fatty acids that have been oxidized and E_{Ig} and E_{Il}

are the energies associated to the fatty acids that have entered and exited the adipose tissue, respectively.

If we call $\Delta E_{AT} = E_{lg} - E_{ll}$ to the net energy accumulation in the adipose tissue, we get:

$$\Delta E_{\rm AT} = E_{\rm IN} - E_{\rm OUT}.$$
 (3)

If we call factors that affect E_{IN} , E_{OUT} and lipogenesis/lipolysis x_i , y_i and z_i , respectively, we can rewrite Eq. (3) as:

$$\Delta E_{\mathrm{AT}}(\boldsymbol{z}_1, \boldsymbol{z}_2, \dots, \boldsymbol{z}_p) = E_{\mathrm{IN}}(\boldsymbol{x}_1, \boldsymbol{x}_2, \dots, \boldsymbol{x}_n) - E_{\mathrm{OUT}}(\boldsymbol{y}_1, \boldsymbol{y}_2, \dots, \boldsymbol{y}_m), \quad (4)$$

which is analogous to Eq. (2).

Eq. (4) is not a formula. It is an equation, and it cannot be solved by evaluating only one side of the equal sign. It should be noted that the usual definition of the "energy balance" formula as CI-CO creates the wrong perception that the right-hand side from Eq. (2), or equivalently from Eq. (4), can be computed on its own, disconnected from the physiological behavior of ΔE , and then assigned to the variable on the left-hand side of the equal sign. In the CICO formula, the equal sign has the same meaning as an assignment symbol in programming languages:

$$\Delta E \leftarrow CI - CO. \tag{5}$$

In the CICO formula, causes (assumed to be CI and CO) are on one side of the equal sign and a single effect (assumed to be ΔE) is on the other. But the FLT equation does not express a causal relationship as implied by this assignment process. As shown in Fig. 3, the interpretation of Eq. (4) as causal is equivalent to the surgical removal of the physiological dependences of $\Delta E^{(39)}$. In the unwarranted use of the FLT equation as a formula, it is

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implicitly assumed that a variable has been isolated on the left-hand side of the equation, or, in other words, that CI and CO are not dependent on the changes that may happen in the ΔE term as a result of direct effect of physiological/hormonal factors on this term. It should be noted that the CICO formula is a correct computation of the accumulated energy only if its minuend and subtrahend are the numerical values obtained by solving Eq. (4).

The consequence of the misinterpretation of an equation as if it were a formula is that the adipose tissue is assumed to be a lifeless mass that accumulates from the residue of the food intake after energy needs have been met. This misinterpretation leads to unfounded conclusions about the causes of obesity or what to do to reverse it.

Unsure temporality

For relationships to be causal, the cause needs to precede the effect. Since excessive body fat accumulation is associated with a net energy accumulation in the body, this fact is usually interpreted as proof that a positive energy balance (more energy in than out) is the cause of obesity. Or, in other words, the effect (i.e. energy accumulation) is considered to be the cause because it is present in obesity.

We can clearly see this mistake thanks to the example in Fig. 4: we can think of a period of time (Period #1) where there is body fat gain but the energy stored in other formats in the body decreases to the same extent as fat increases and, therefore, there is no net positive energy balance in the whole body. On a subsequent period of time (Period #2) those other stores restore their previous level. In the combination of both periods, there has been body fat accumulation and the energy balance has been positive, but the energy balance was only positive after body fat was already increased. Under the conditions of the example, the effect

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(*i.e.* body fat accumulation) happens without the alleged cause (*i.e.* positive energy balance) preceding it. Therefore, it is hypothetically possible to gain weight and body fat in the long term in a situation where a positive energy balance cannot be the cause of body fat accumulation because it does not precede the effect.

Related to the temporality problem, it is conceptually possible to gain or lose body fat while the body weight does not change or goes in the other direction. This possibility has been obtained in several experimental studies in humans and animals^(40–47). If the effect can happen without the concurrency of the presumed cause, this proves that the cause is not warranted by an inviolable law of physics.

Causality inferred from a correlation

It is never possible to correctly deduce a cause for obesity from the FLT. In this Section, we explain how this mistake is made.

In the CICO hypothesis, an energy imbalance is considered to be a "requisite" for weight gain, a condition that must be met for energy accumulation to happen. But the causal language and implications are unwarranted since the cause of fat accumulation could lie in the physiological regulation of the ΔE term, neither in the CI nor in the CO terms. We illustrate this point with an analogy for fat accumulation in the body (see Fig. 5). In the analogy, we have a water tank that has two compartments named A and B, which are joined through a pipe that has a control valve. In part A, there is an incoming flow of water (Water IN, WI). An overflow pipe discharges excess water (Water OUT, WO) in part A. In this system, once the overflow level is reached you cannot increase the amount of accumulated water by regulating WI. It is also not possible to regulate WO, since it is not under our direct

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control. Therefore, more WI than WO cannot cause water accumulation in this system. But when the control valve is opened, water starts to accumulate in the tank, specifically in part B. While this happens, the water balance (WI minus WO) is positive, but that is a symptom, not the cause of the water accumulation nor it is a requisite: water accumulation didn't wait for a positive water balance to start. What this analogy shows is that even when "more in than out" happens always that there is an accumulation —because it is a tautology, *i.e.* just another way of saying "accumulation"—, more in than out is not necessarily the cause nor a prerequisite for accumulation. In this analogy, focusing on what regulates WI and WO to understand water accumulation would be a mistake, because it is the "physiology" of the tank what really determines whether there is accumulation or not. We could say that it is the avidity of the tank for accumulation what determines if there is accumulation, not WI minus WO.

It should be noted that the water tank analogy is a counterexample that disproves the argument that, since the FLT must be fulfilled, a positive energy balance is always the cause of obesity. In the counterexample, the FLT is satisfied but the cause of the accumulation is not a positive energy balance. Since the premise is true and the conclusion is false, the argument is demonstrated invalid.

An additional analogy may be useful to understand the mistake of inferring causality from a mathematical equation. Let us assume (see Fig. 6) that a group of A tourists wants to visit the top floor of the Eiffel Tower, but the amount of admission tickets are limited and they only can buy B tickets. The rest C of the group decides to visit a different monument in Paris. Although it is true that the number of turists that visits the top floor can be computed as B = A - C, we cannot say that A - C determines B, because, for a given A, the term that is set by

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its own dependences is *B*, not *C*. B = A - C is correct as an equation, but the causal interpretation of the equal sign is unwarranted. When the CICO hypothesis postulates that CI minus CO determines the changes in body fat/weight there is an implicit assumption: that CO is set on its own before the changes in body fat/weight are. That assumption is not rightfully derived from the FLT.

As a final note, other authors have proposed obesity models that are centered in the adipocyte physiology^(22,48). In these models the driving forces for fat accumulation are hormones and the availability of dietary triglycerides. The mere existence of these models, in which the causal pathway relating energy balance to fat storage flows opposite to the causality direction in the CICO hypothesis, demonstrates that the causality assumed as obvious in the CICO hypothesis does not derive from the FLT.

DISCUSSION

Obesity is a rapidly growing public health problem that affects an increasing number of countries worldwide⁽⁴⁹⁾. Because according to the dominant discourse obesity is caused by individual behaviour, *i.e.* too much food and too little exercise, when governments around the world have included obesity in their public health agendas, the measures they contain seek to curb energy consumption and increase physical activity. However, programs to address obesity have been unable to produce any significant improvements in body fatness⁽⁵⁰⁾. At the same time, obesity treatment for those of us who already have excess weight is based on the same paradigm: to lose weight it is usually recommended to cut calories, *e.g.* 500 kcal/d less, because the current belief is that to lose fat you have to consume less energy than you spend. Often people fail to achieve any weight loss at all, and the failure

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is then blamed on the obese people, who are accused of either not trying hard enough or being inaccurate about how much energy they ate or spent^(51,52). It is worth remarking that the longoutcomes of scientifically controlled weight loss programs term are rather disappointing^(53,54). Moreover, the current energy paradigm may cause harm. First, obesity is associated with multiple diseases, such as cardiovascular disease, type 2 diabetes, hypertension, stroke, some cancers, etc.⁽⁵⁵⁾. Second, it can be argued that this paradigm fosters weight stigma because it conveys the idea that body weight is a modifiable risk factor, something we can achieve just by eating less or moving more. Experimental research in psychology consistently shows that obese people are stigmatized because body weight is perceived to be caused by factors within personal control⁽⁵⁶⁾. Third, obese and overweight individuals face multiple forms of prejudice and discrimination because of their weight⁽⁵⁷⁾, e.g. they may be disadvantaged in workplace interactions, evaluations and employment outcomes as a result of negative weight-based stereotype. In our opinion, the failure of the energy paradigm both to stop the obesity epidemic and to help obese people to revert their excess weight should be enough to lead the scientific community to question the validity of the energy paradigm for obesity. Moreover, there is a more compelling argument for a reevaluation of the current belief system: it can no longer be asserted that a chronic energy imbalance is the obvious cause of obesity when some researchers defend proposals that do not comply with the CICO hypothesis while being fully respectful of the thermodynamics laws. Such is the case of the carbohydrate-insulin hypothesis⁽²²⁾, for example. The mere existence of a plausible alternative hypothesis should inevitably lead to a reconsideration of the validity of what is still commonly regarded as the only cause of obesity allowed by those laws. Since that is not the case, we argue that one of the reasons why the CICO hypothesis is

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not questioned at all is that it lacks a definition that is both rigorous and falsifiable. As this hypothesis makes no predictions, no observable situations, if actually observed, can be interpreted as a refutation of the theory. The cause of the non-scientific status of this hypothesis is presumably the false belief that the CICO hypothesis and the FLT are one and the same, and, therefore, no further validation of the hypothesis is required nor refutation is possible. This fact highlights the relevance of analysing if the CICO hypothesis and the FLT are really one and the same.

Other authors have previously argued for the unsubstantiated *a priori* assumptions regarding causal relationships based on appeals to the FLT. Hugo H. Rony⁽⁵⁸⁾ explained that even if a positive caloric balance may be regarded as the cause of fatness when fatness is artificially produced by forced excessive feeding, the cause of obesity could be different when it develops spontaneously. In his words, a positive caloric balance can be a result rather than a cause of the condition. Pennington⁽⁵⁹⁾ also pointed out that the law of conservation of energy makes no distinction between cause and effect and that physiologic metabolic processes or forces could be the ones that established a positive or negative energy balance, and not the other way around. Taubes⁽⁶⁰⁾ also pointed out that the energy balance notion is tautological or, in other words, based on circular logic, and that the fact that we have to take in more calories than we expend to get fatter tells us nothing about cause. He explained that what is currently regarded as cause may be just an effect of the lipophilic behavior of the adipose tissue. Wells and Siervo^(61,62) agreed that a positive energy balance is simply a truism that cannot explain why weight gain occurs. In their words, the direction of causation in obesity aetiology is less clear than is commonly assumed and it should be questioned if the simplified interpretation of the energy balance equation with regard to obesity causation is misleading.

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Hebert et al. (63) argued that a priori assumptions about cause have been uncritically accepted in scholarly dialogues. They specifically pointed out that the FLT provides a "true but inadequately simplistic and inherently tautological" description of the energy imbalance that is associated with weight gain, and that the use of the FLT to explain secular changes in body weight is nonadherent to Hill's criteria for judging causality. Concretely, they argued that invoking the FLT fails the specificity and temporality criteria, while it also provides little useful information for assessing other criteria (e.g. the strength of the association, consistency across different sources of evidence, plausibility, etc.). In their words, "the flawed logic that naturally flows from naive appeals to the FLT and energy balance (e.g. increased caloric intake must lead to increased obesity) has biased research funding decisions and the choice of study designs, operational definitions of variables, choice of measurement methods, and analytic procedures." They added that "we should not be satisfied with tautological statements based on the FLT." Chandaria⁽⁶⁴⁾ also explained that a specific causality is not embedded in the FLT. He argued that in CICO calories-in and calories-out are independent variables and weight gain is a fully dependent variable, which implies that calories-in and calories-out cause weight gain, but, he said, there is no theoretical reason for causality not to operate in the reverse direction. Camacho and Ruppel⁽⁶⁵⁾ also proposed a revision of the current concept for the causes of obesity. In their opinion, the idea that a positive energy balance results in fat mass or that individuals aiming to lose weight should look for a negative energy balance has not provided an efficient framework against the obesity epidemic and may even foster stigma and prevent tackling strategies from being efficient. They also hypothesize that food composition could increase our body's capacity for fat production and storage, leading to an increased intake of the fattening foods. They

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mentioned that under this hypothesis "laziness" and "gluttony" would actually be the symptoms of obesity and overweight, whereas the cause would be a hormonal imbalance.

Although other authors have previously pointed out problems in the energy balance paradigm, our aim is to answer an important question: how this paradigm is wrong. As we have explained in the present paper, a specific and unwarranted behavior of the adipose tissue is implicitly assumed in the CICO hypothesis.

Fig. 7 provides a non-exhaustive list of examples of wrong arguments used to defend the CICO hypothesis.

CONCLUSIONS

For more than a century it has been widely believed that the cause of obesity is deceptively simple: a chronic energy imbalance. This has led to the conclusion that the only factors that are relevant to study how to prevent and how to treat obesity are those that affect energy intake and/or energy expenditure. This belief is promoted as indisputable since it is assumed to be a corollary derived from the fact that energy is neither created nor destroyed, only changes form. In this paper, we have explained the reasoning mistakes that support the energy balance paradigm. The most important one of those mistakes is the assumption that the adipose tissue cannot change by itself (while the other tissues/organs would adapt to its changes). That assumption is implicitly included in the arguments used to defend the energy balance hypothesis, specially in the misinterpretation of the FLT equation as a formula that tells us how and why the fat/energy stores in the body change.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Vicente Torres conceived the first draft of the article. All authors contributed to the development of subsequent draft versions.

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FIGURE LEGENDS

Fig. 1 The energy balance paradigm for obesity. This paradigm postulates that although the development of obesity is multi-factorial, the main reason is always a positive energy balance. Such positive energy balance results from an increased intake of energy from foods or beverages or a reduced energy expenditure.

Fig. 2 Compartmental model of the human body. In this figure, mass/energy fluxes are represented with arrows. f_{lg} : flux associated to lipogenesis; f_{ll} : flux associated to lipolysis; f_{IN} : flux associated to the fatty acids that enter the body; f_{OUT} : flux associated to fatty acid oxidation

Fig. 3 Causality and the First Law of Thermodynamics. The CICO hypothesis is a causal model, not the First Law of Thermodynamics.

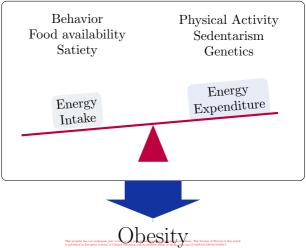
Fig. 4 The temporality problem. This figure shows a hypothetical case where there are body energy and fat gain but there is no causality between body fat gain and body energy balance.

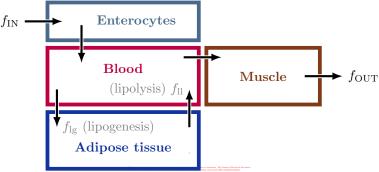
Fig. 5 Water tank analogy. In a the valve is closed and water does not fill part B. When the valve is opened in b, the system accumulates water, but the cause of the accumulation is not that more water comes in than goes out, nor more water coming in than going out can be considered a requisite for water accumulation in this system.

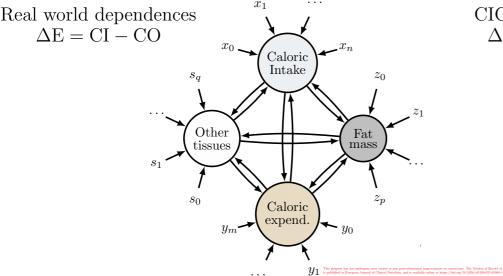
Fig. 6 Tourist visit analogy.

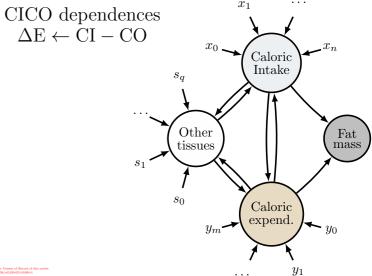
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Fig. 7 Wrong propositions that are propagated as though they are facts.

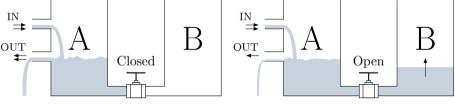






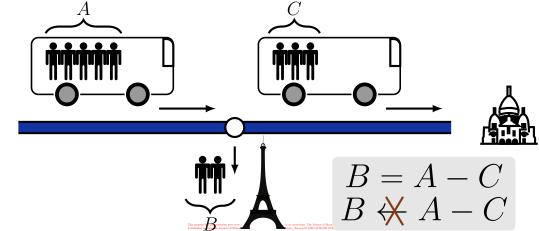


	Energy Stores		
	Adipose tissue	Others (muscle, liver, etc)	Total
Period 1	Increased	Decreased	No change
Period 2	No change	Increased	Increased
Period 1+2		No change	Increased



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Presumptions erroneously accepted as facts

"According to the First Law of Thermodynamics, obesity results from a chronic energy imbalance".

"Our body fat is determined by the difference between calorie intake and energy expenditure".

"Positive energy balance is the essential ingredient required to store more body fat and become overweight".

Explanation

No causality can be rightfully derived from that law. Moreover, it is a wrong application of the principle of energy conservation to only consider the energy stored in the adipose tissue.

To assume that the only energy that can change is the one stored in the adipose tissue is a wrong application of the principle of energy conservation.

The claim that the relationship between two events is necessary or inevitable (rather than occasional or coincidental) helps to confuse correlation with causality. A "positive energy balance" is neither a requisite nor a condition that must be met. A priori it is just an unavoidable characteristic of any energy accumulation, since it is another way of saying energy accumulation. The false sense of necessity comes from a tautology and there is no causal information in tautologies. The use of

This preprint has not undergone peer review or any "requisite" in this context ocan be article is published in European Journal of Clinical Nutrition, and is available online at https://doi.org/10.1039/e1143021-010644 considered as an ambiguity fallacy.