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LETTER TO THE EDITOR

No insulating effect of obesity, neither in mice nor in humans

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TO THE EDITOR: In a study published in this journal in 2016 (6), we observed—unexpectedly and in contrast to common wisdom—that, at least in mice, obesity does not insulate against heat loss. Thus, obese mice do not become more obese because they lose less heat. Our data are summarized in Fig. 1*A* for diet-induced obese mice; we obtained similar data using, e.g., genetically obese *ob/ob* mice. Concerning the insulation, the important issue is that the slope of metabolism (heat production) versus temperature in the cold is the same in the normal ("lean") and the obese mice. This slope represents the heat production that the mice have to maintain to compensate for their global heat loss. The heat loss is "Newtonian" in that it is directly proportional to the difference between the ambient temperature and the "defended" body temperature of the mouse. It can thus be expressed as a simple parameter: the increase in heat production (watt) per degree Celsius difference between the two temperatures (W/°C). ("Insulation" is really the reverse of this and is thus given as °C/W, but it is conceptually simpler to discuss heat loss.) However, whether our observation of the absence of an insulating effect of obesity in mice has relevance for humans has repeatedly been questioned (e.g., Refs. 8, 10).

In this respect, in a recent ambitious and meticulous contribution, Brychta et al. (1) performed similar experiments in humans, in normal versus obese young men. In their abstract and in the text, they state that, in these subjects, obesity insulates. Thus, this would imply that there could be a principal difference between humans and mice in this respect, and such an effect of obesity could also make obesity self-promoting in humans.

However, there may not be such a difference between mice and humans. In Fig. 1*B*, we have drawn the data from Brychta et al. similarly to our data, based on the summary data in their Table 2. First, in agreement with the case in mice, the obese subjects show an increased basal metabolic rate. The reason for this is not fully clear, but both for mice and humans, obesity is associated with a proportional increase in lean body mass (in the subjects of Brychta et al. from 58 to 66 kg), and this is probably the main reason for the increased total metabolic rate (see also Ref. 9). The basal metabolic rate for the lean and the obese subjects is thus approximately the same per lean body weight: 1.5 W/kg [whereas that of the mice is ~15 W/kg lean mass (e.g., Ref. 6)].

However, the important issue is the slope of the heat loss for the obese versus the lean: are the obese more insulated, as stated by the authors? As seen, the slope is in reality almost identical but it is actually slightly (nonsignificantly) *higher* for the obese than for the lean (6.5 versus 5.8 W/°C). Thus, just from this, it can be concluded that also in humans, obesity does not insulate. Why is the heat loss slightly higher in obese than in lean? The difference is understandable as the obese present with a slightly larger body surface area: 2.3 m^2 versus 2.0 m^2 for the lean. As heat is lost through the skin surface, it is reasonable to express the relative heat conductance (insulation) per square meter; this value becomes 3 W per °C per m^2 surface for both the obese and the lean men (2.8 vs. 2.9; less than 5% difference).

It may be mentioned that the mice have a global heat conductance of ~0.03 W/°C (6) and a surface area of ~80–100 cm^2 (4, 5). Thus, it may similarly be calculated that the relative insulation of the mice is also 3 W per °C per m^2. Remarkably, mice and humans are thus equally insulated against heat loss!

So, why do Brychta et al. conclude differently – that obesity insulates? This is because Brychta et al., apparently without a clearly stated motivation, choose not to use the direct data discussed above but instead to use a normalized value in their running text presentation. They use insulation expressed as a function of each subject's basal metabolic rate (BMR), rather than as the global value per subject. The interpretation problem arises then because both obese mice and obese humans have higher basal metabolic rates than their lean counterparts (cf. Fig. 1, *A* and *B*). Thus, the actual heat conductivity/insulation values are expressed as a percentage of the basal metabolic rate—but this rate is in its turn determined by the obesity as such, as it is secondary to the increase in lean body mass that is a consequence of the obesity. Due to this division, the apparent heat conductance becomes lower—and the apparent insulation thus becomes higher—than when it is expressed as actual heat. Indeed, if we recalculate our earlier mouse data in this way, we would also obtain an apparent lower heat conductance (apparent higher insulation) in obese versus lean mice (0.07% BMR/°C vs. 0.09% BMR/°C). However, the level of the basal metabolic rate is really not of relevance for the interpretation of the data concerning insulation [except that it may be said to explain why the so-called lower critical temperature (the temperature below which metabolism is increased to counteract heat loss) is lower in the obese human subjects (21°C) than in the lean subjects (23°C); in this respect, human subjects behave fully as predicted from the physics of heat transfer].

Although it may be understandable to consider that metabolic data should be "normalized" in some way, such normalizations are often misleading. The issue here is akin to the long-discussed issue concerning the metabolic rate of obese animals and humans versus lean (2, 3, 7). Indeed, when

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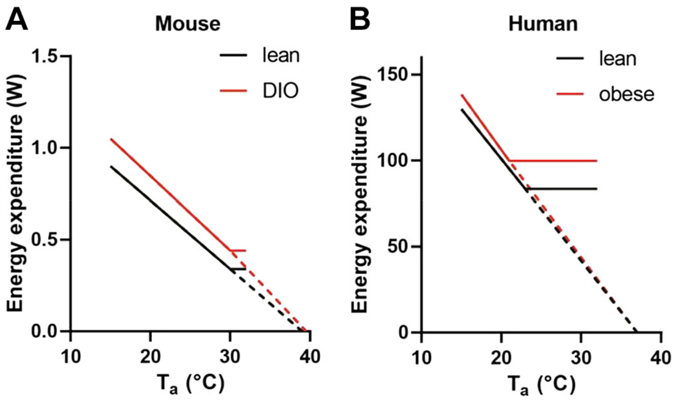

Fig. 1. Comparison between the metabolic behavior of mice and humans. *A*: mouse data. Figure is drawn based on values underlying Fig. 6A in Fischer et al. (9). The metabolic rate at 30°C has been taken as the thermoneutral zone rate. *B*: human data. Figure is drawn based on values found in Table 2 in Brychta et al. (1). The basal metabolic rate, given as 72 and 86 kcal/hr in lean and obese, is recalculated to 84 and 100 W. Lower critical temperature is stated as 23°C in lean and 21°C in obese. Insulation is stated as 0.20 and 0.18°C/kcal/hr; this is recalculated as heat conductance (inverted and converted to W/°C). In both *A* and *B*, the dotted lines extrapolate to the defended body temperature.

expressed per kilogram body weight, obese mice and humans have a lower metabolic rate than the lean, and this has been put forward as an explanation of their obesity. However, when expressed as metabolism per animal/subject, the rates are not lower, and decreased metabolism cannot explain obesity.

Concerning the insulation we discuss here, it is clear that what we mean when we discuss whether obesity insulates is whether an obese person in the cold has a lower metabolism than a lean person in the cold. As seen in Fig. 1, this is never the case: the obese has a higher or a similar metabolism at any ambient temperature. [This is also the conclusion from indirect data analysis by Nahon et al. (9).]

By expressing the insulation in a "normalized" way, Brychta et al. conclude in the "expected" way, i.e., that obesity insulates. It is hard to accept that it does not; such a conclusion is both counterintuitive and contradicts common and textbook wisdom. However, both our earlier mice studies and the human studies now published make it clear that this common wisdom is probably erroneous: despite what is generally thought, obesity in itself does not insulate, neither in mice nor in humans.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

A.W.F. analyzed data; A.W.F. prepared figures; A.W.F. and J.N. drafted manuscript; A.W.F., B.C., and J.N. edited and revised manuscript; A.W.F., B.C., and J.N. approved final version of manuscript; J.N. interpreted results of experiments.

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