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CORRESPONDENCE

Fat is not just an energy store

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Life-history theory predicts that competition and trade-offs should arise between two processes if they depend on the allocation of the same limited resources. The ubiquity of predators imposes selection pressures on resource allocation and organismal physiology: it has been shown, for example, that acquiring a high level of body reserves, i.e. larger body mass, incurs costs in terms of reduced take-off speed and maneuverability when escaping predators (Krams, 2002, and references therein). However, animals must generally maintain high levels of energy reserves because they are supposed to serve as an 'energetic buffer' against the unpredictability of food access and death by starvation. Hence, regulation of body mass has been generally conceptualized as a trade-off between starvation risk and predation risk.

In a recent review paper, John Speakman (2018) proposed a novel hypothesis on the regulation of adiposity and body mass. Speakman agrees with the idea that the risk of predation selects for low adiposity. However, he concludes that evidence is generally missing to support the risk of starvation as a selective force against low adiposity. Speakman suggests that the risk of disease and the need to survive periods of pathogen-induced anorexia are the main forces selecting for high adiposity. Speakman provides evidence for pathogen-induced anorexia and shows that individuals carrying more fat have a better chance of survival when infected, which provides the basis for the obesity paradox (reviewed in Speakman, 2018).

Overall, we support the novel hypothesis proposed by Speakman. However, it is important to note that fat reserves consist not merely of fat. Adipose tissue is known to be the source of myriad signaling molecules affecting life-history decisions (Wells, 2009). While subcutaneous body fat is viewed as relatively harmless, abdominal or visceral fat is stored around the inner organs and is associated with non-infectious inflammation. Visceral fat contributes to metabolic diseases such as cardiovascular disease and type 2 diabetes as well as mental disorders such as depression (e.g. Rantala et al., 2018). Visceral fat increases the concentration of inflammatory cytokines, which provides a potential mechanistic link between visceral fat and systemic inflammation (Fontana et al., 2007). Thus, metabolism of subcutaneous and visceral fat produces different metabolites and visceral fat is generally considered to be harmful (Qiang et al., 2016).

Nevertheless, both subcutaneous and visceral fat can be used as energy sources during famine, which causes questions about the evolutionary role and functions of visceral fat. This is of crucial importance for the model suggested by Speakman. Interestingly, increasing body mass index (BMI) is associated with increasing body fat content; for any given BMI value, however, people in densely populated South Asian countries tend to have substantially more visceral fat than Europeans (Rush et al., 2004). South Asians have been historically exposed both to regular famines (Fagan, 1999) and to enduring heat stress that may contribute to the spread of infectious diseases (Dunn et al., 2010). Speakman admits that food shortage potentially compromises immune function, increasing susceptibility to disease. Importantly, chronic stress induced by population density and famine may down-regulate testosterone, which is associated with the accumulation of visceral fat (Björntorp, 1991). Therefore, local climate, pathogen prevalence, high density of people and regular famines might have favored increased visceral adiposity in South Asian populations as an adaptation against infections, especially gut-borne ones as suggested by Wells (2009).

We highlight that ecologists and physiologists have to distinguish between subcutaneous fat and visceral fat because the former may generally function as a source of energy while the latter not only accumulates energy for an organism but may also provide protection against parasitic worms, protozoans and bacteria. The mechanism by which visceral fat does this is through toxic compounds and/or by increasing general levels of oxidative stress. However, this may cause phenotypic and functional damage to self-tissue. We suggest that subcutaneous and visceral fat need to be viewed separately in Speakman's model.

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Response to 'Fat is not just an energy store'

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In a recent paper, I suggested that the supposed 'predation–starvation' trade-off model for the regulation of body fat has rather scant evidence to support the 'starvation' side of the trade-off. Instead of starvation risk, I suggested that a likely evolutionary factor driving up levels of stored fat is the risk of infectious disease, and the need to survive through periods of pathogen-induced anorexia (Speakman, 2018). I am glad that in their recent correspondence Krams et al. (2018) state that 'Overall we support the novel hypothesis proposed by Speakman'. They then go on to highlight a potentially important distinction that my paper did not address: the lack of functional equivalence of different fat depots.

It is well established that in humans, and other animals, white adipose tissue is distributed in different depots. A distinction is often made between visceral fat, located around the viscera and vital organs, and subcutaneous fat, which is located outside the peritoneum. In terms of their role as stores of energy, these different depots are functionally equal, and in my 'predation–disease' trade-off model, as well as the earlier predation–starvation models (McNamara and Houston, 1990), no distinction was made between these stores. Krams et al. (2018) suggest this is a mistake and that these depots are not functionally equivalent in terms of their consequences. Visceral fat in particular is regarded as a major contributor to metabolic diseases, such as type 2 diabetes and cardiovascular disease, while subcutaneous fat is considered to be relatively benign.

This raises the interesting question of why individuals would ever choose (evolutionarily) to store fat viscerally if it has these disadvantageous consequences. This is an interesting question. Krams et al. (2018) point out that at any given body fatness, South Asians store more fat viscerally than Caucasians (Europeans). They suggest this is because such populations have high population densities leading to chronic stress, have historically been exposed to regular famines and have high levels of infectious disease. Together, they suggest these factors may have favoured greater visceral adiposity because it provides a defence against 'parasitic worms, protozoans and bacteria' through the production of 'toxic compounds and/or by increasing general levels of oxidative stress'. These statements are not referenced, but appear to originate in Wells (2009), which is cited elsewhere in their paper.

While there is possibly a difference between Caucasian and South Asian populations in exposure to pathogens, there is little evidence to support the suggestion that these populations have historically endured greater levels of famine than populations in Europe (see Speakman, 2006). In addition, until recently (post-agricultural revolution), populations of humans were universally quite small, so stress caused by high population density also seems an unlikely evolutionarily important factor.

An additional (or alternative) factor to pathogen exposure driving the difference in the distribution patterns of fat storage between South Asians and Caucasians may be the ambient temperatures they experience (Pond, 1992). As I noted in my disease–predation trade-off paper (Speakman, 2018), fat serves not only as a store of energy: by virtue of its low water content, fat also has a lower thermal conductivity than lean tissue (Cohen, 1977). Hence, if distributed subcutaneously, it provides a barrier to heat loss. This function of the subcutaneous fat layer in cetaceans (or blubber) has been known for many decades. For example, in the novel *Moby Dick*, written in 1851, Herman Melville wrote 'For the whale is indeed wrapped up in his blubber as in a real blanket… It is by reason of this cosy blanketing, that the whale is enabled to keep himself comfortable in all weathers, in all seas, times, and tides'. In humans, subcutaneous fat seems to play a similar role. Individuals with greater adiposity cool down more slowly when immersed in cool water, and do not need to elevate their metabolic rate as much to defend this slower cooling rate. However, a thick insulative layer of fat that retards heat loss in the cold may restrict the capacity to lose heat in hot conditions. As the capacity for heat dissipation may be an important limiting factor in endotherms (Speakman and Krol, 2010), a thick layer of subcutaneous fat may be a disadvantage in many circumstances. It has been suggested that the distribution of fat stores in tropical animals may reflect these heat dissipation issues (Pond, 1992). Humans living in the tropics may also redistribute their fat stores away from the subcutaneous fat, and into visceral fat depots to facilitate heat loss. This would also then explain why visceral obesity is an issue not only in South Asian countries but also across India, the Middle East and North Africa.

Overall there are probably adaptive reasons explaining the distribution of body fat in humans, and in modern societies, where humans live long enough to develop metabolic disorders, these differences may have important downstream consequences for differential susceptibility to metabolic disease. This is a valid question and Krams et al. (2018) are correct in highlighting it. However, as they admit, as regards energy storage, the subcutaneous and visceral stores are functionally equivalent, and hence the distribution issue is separate from the question of regulation of the total amount of fat to be stored, which was the primary question addressed in my previous paper (Speakman, 2018). This separation is emphasized by the fact the single nucleotide polymorphisms (SNPs) that are linked to fat storage level (body mass index: e.g. Locke et al., 2015) occur in a largely non-overlapping set of genes to those SNPs associated with fat distribution (waist to hip ratio: e.g. Held et al., 2010).

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