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PERSPECTIVES

Brown adipose tissue – not as hot as we thought

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The article by Blondin *et al.* (2015) in the current issue of *The Journal of Physiology* brings together and expands upon three adipose/muscle-related concepts that emphasize the importance of understanding physiology before jumping to conclusions when new findings are reported.

First, the excitement following the reports of brown adipose tissue (BAT) in 2009 (Cypess *et al.* 2009; van Marken Lichtenbelt *et al.* 2009; Virtanen *et al.* 2009) has spawned a number of additional, enthusiastic reports of human BAT activity (Orava *et al.* 2011). Some authors suggest that BAT accounts for up to 20% of the cold-stimulated increase in energy expenditure in humans (Cypess *et al.* 2009). In the rush to characterize BAT as the next frontier in obesity treatment investigators have largely ignored the obligate relationship between energy expenditure and oxygen delivery, which in turn is dependent upon blood flow and tissue mass. Adipose tissue blood flow is notoriously low relative to metabolically active tissues (Summers *et al.* 1996; Karpe *et al.* 2002), and it turns out that BAT is not an exception. Even during cold exposure BAT blood flow averages only 13 ml (100 g tissue)$^{-1}$ min^{-1} (Muzik *et al.* 2012, 2013). Under conditions of normal oxygen saturation and 16 g dl^{-1} of haemoglobin, 100 ml of arterial blood contains only 21.3 ml of O_2. With an average total body BAT volume of 57 ml, the amount of oxygen delivered to total body BAT would be only ∼1.6 ml min^{-1}. Furthermore, BAT oxygen extraction is reported to be ∼56% (Muzik *et al.* 2012). Thus, under steady-state, cold-stimulated conditions, average whole-body BAT oxygen consumption should be ∼1 ml min^{-1}, very similar to that measured using oxygen isotopes and PET approaches (Muzik *et al.* 2012). This is underwhelming considering the cold-induced increase in oxygen uptake of ∼270 ml min^{-1} that was observed by Blondin *et al.* (2015). The BAT oxygen uptake data (Muzik *et al.* 2012, 2013) are consistent with the limited total body BAT glucose uptake relative to the increase in total glucose disposal in response to cold (Blondin *et al.* 2015). Even individuals at the high end of BAT blood flow (25 ml (100 g tissue)$^{-1}$ min^{-1}; Orava *et al.* 2011) and with 100 g of total body BAT, actual BAT thermogenesis would account for only ∼1% of the increase in energy expenditure above basal induced by cold exposure.

The second important observation is the contribution of subclinical muscle shivering to cold-induced increases in muscle glucose uptake and presumably energy expenditure. Blondin *et al.*'s careful and extensive use of surface electromyography showed that muscle contraction (shivering) is the major component of the increase in whole-body glucose uptake. This suggests that investigations directed at the role of muscle, rather than BAT, will be more promising.

Finally, the observation by Blondin *et al.* (2015) that the cold-induced increase in non-esterified fatty acid release from adipose tissue lipolysis relates to the activation of BAT is important. It is consistent with animal data indicating that the sympathetic innervation of BAT and white adipose tissue (WAT) is similar (reviewed in Vaughan *et al.* 2014). This implies that variations in sympathetic activation or the sensitivity to such activation is similar in human BAT and WAT. If the former, then variations in observed BAT activation during cold exposure could reflect more of a central nervous system sympathetic response to cold rather than a peripheral, e.g. BAT, difference.

In summary, the findings of Musik (Muzik *et al.* 2012, 2013) and Blondin *et al.* (2015) suggest to me that BAT is most likely a vestigial and largely irrelevant tissue when it comes to adult human energy expenditure. They also provide some renewed excitement about the role of muscle in resting energy expenditure.

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Additional information

Competing interests

None declared.

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