Is a reduction in brown adipose thermogenesis responsible for the change in core body temperature at menopause?

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Following menopause, women are at a greater risk of becoming obese and suffering from associated cardiometabolic diseases [1,2]. The transition towards greater visceral adiposity and metabolic dysregulation after menopause is likely to be a consequence of changes in energy metabolism, primarily mediated by a reduction in circulating sex hormones such as estrogen or progesterone [1,2]. In the current issue of cardiovascular endocrinology, Neff et al. [3] describe that core body temperature is lower in women who have reached menopause, reaching temperatures similar to that of men. Their observation that the lower core body temperatures in those women who had reached menopause raises the possibility that this little studied factor could itself play a role in the increase in disease risk after this time [1,2], although whether the associated higher BMI and adiposity is an effect of age or the menopause per se cannot be determined from their study. Although the researchers acknowledge that the study was an exploratory post-hoc analysis of data synthesized from temporally distinct studies, it is worth further consideration, given current interest in brown adipose tissue (BAT) as a therapeutic target to combat cardiometabolic diseases [4]. BAT is a thermogenic organ located mainly in the supraclavicular regions and in much smaller amounts [5] in other locations such as surrounding the kidneys and heart. Most abundant at birth [6], BAT is responsible for nonshivering thermogenesis and the maintenance of thermal homeostasis. This is achieved through nonshivering thermogenesis, which is mediated by the sympathetic nervous system and involves the oxidation of lipids and glucose in BAT to produce heat. This process is particularly important during infancy and early childhood when the need for heat production is greatest. In adults, BAT activity is reduced, and its contribution to total body heat production is minimal. However, BAT activity can be increased in response to cold exposure, and it remains a potential therapeutic target for the treatment of obesity and related cardiometabolic disorders.

Fig. 1

Overview of phenotypic differences between premenopausal/postmenopausal women and possible mechanisms involved. Histological image adapted from Ravussin and Galgani [26].
through the uncoupling of oxidative metabolism from ATP production through mitochondrial uncoupling protein 1, which dissipates chemical energy as heat [7]. We now know that a majority of adults retain metabolically active BAT into adulthood [8], in declining amounts with age, and that sex hormones such as estrogen are likely to play a key role in the development of brown adipocytes and their function [9,10]. Preclinical research has long demonstrated that exogenous sex hormones play a key role in the metabolic activity of BAT, and more recently it has been shown that cerebroventricular estradiol administration stimulates BAT function, increasing core body and BAT temperatures [11–13].

Another feature of the study by Neff and colleagues is the large variation in body temperatures within women irrespective of age, and this appears to be most marked in the group described as postmenopausal. Although the authors do not define how many of the so-called postmenopausal women in the study were still experiencing hot flushes, a stage already known to be associated with lower body temperature, [14,15] and a truly age-matched group of men is omitted, their observations fit with studies showing that women are more sensitive to cold compared with men [8,16]. This is likely to be a primary factor contributing to their higher incidence of BAT [17]. Moreover, a recent small study in premenopausal women demonstrated a potentially important relationship between salivary cortisol and basal temperature of BAT within the neck [18]. A combination of differences in the hypothalamic–pituitary–adrenal axis, BAT abundance, stress and thermal sensitivity could explain the large variation in body temperatures of healthy women. These relationships may shift after menopause as BAT activity declines.

However, whether a decline in BAT after menopause occurs in humans and, therefore, contributes to greater BMI and fat mass remains to be determined. Given the role of BAT in metabolic homeostasis [19,20] and the recent associations between BAT activity and cardiovascular events [21], investigation of changes in BAT around the meno-pause and any effects of hormone replacement therapy are warranted. Maintenance of active BAT after the menopause has potential to attenuate the development of adiposity. Future investigations would require well-matched groups as differences in age, body mass and seasonality can all have a significant impact on BAT functionality as highlighted by the authors. Future studies should use additional methods as core body temperature measurements to determine thermal homeostasis and should include supraclavicular skin temperature [22–25] and thermal imaging [22,25] to assess BAT function (Fig. 1).

Acknowledgements
Conflicts of interest
There are no conflicts of interest.

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