thermogenesis in rodents. This study aimed to investigate cold- and meal-induced BAT thermogenesis in healthy men ($n = 14$; age 23.07 ± 0.7 years, BMI $23.22 \pm 0.7\,kg/m^2$) and women at 2 stages of the menstrual cycle (luteal, $n = 9$; age 25.22 ± 1.7 years, BMI $21.56 \pm 0.4\,kg/m^2$ and follicular, $n = 11$; age 24.64 ± 1.2 years, BMI $22.12 \pm 0.9\,kg/m^2$). Cutaneous temperature at the supraclavicular region (human BAT depot) and the manubrium (BAT negative control) were measured at 1 min intervals using infra-red thermography. Cold-induced thermogenesis involved the immersion of one hand into cool (15 °C) water for 5 mins. Once BAT temperature returned to baseline, a liquid meal (Ensure, 10 kcal/kg body weight) was consumed. Thermogenic responses to both diet and cold were greater in females ($P < 0.05$) than males, and this was effect was greater ($P < 0.05$) during the luteal phase of the menstrual cycle. During cold-exposure, the increase in BAT temperature was abrogated ($P < 0.05$) in females during the follicular phase compared to luteal phase of the menstrual cycle. Regression analyses revealed that serum estradiol concentration was correlated to cold- ($P < 0.05$, $R^2 = 0.13$) and meal-induced thermogenesis ($P = 0.07$, $R^2 = 0.10$), whereas meal-induced changes in BAT temperature were inversely correlated with serum testosterone concentration ($P < 0.05$, $R^2 = 0.13$). There was no correlation between BAT temperature and serum progesterone concentration. On the other hand, serum cortisol concentration was inversely related to baseline BAT temperature ($P < 0.05$, $R^2 = 0.17$). In summary, women exhibit greater thermogenic responses to both cold and meal stimuli than men. Furthermore, BAT activity in women is influenced by the stage of menstrual cycle, which relates to fluctuating levels of estradiol.

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Perilipin 5 deletion in hepatocytes remodels lipid metabolism and causes hepatic insulin resistance in mice

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Obesity is associated with dysfunctions in lipid and glucose metabolism, which is linked to the development of insulin resistance and type 2 diabetes. The perilipin (PLIN) family of proteins localize to cellular lipid droplets and control lipid flux within cells by coordinating protein-protein interactions. PLIN5 is expressed in highly oxidative tissues and, in skeletal muscle, controls triglyceride lipolysis and β-oxidation of fatty acids, which in turn helps to maintain insulin sensitivity in this tissue.

The aim of this study was to investigate the role of PLIN5 in regulating hepatic lipid and glucose metabolism in lean and obese mice. To address this aim, we generated PLIN5 liver-specific knockout mice ($Plin5^{LKO}$) by crossing *Plin5* floxed mice with albumin-Cre mice. Hepatocytes isolated from $Plin5^{LKO}$ mice exhibited marked changes in lipid metabolism characterized by decreased fatty acid uptake and storage, decreased fatty acid oxidation that was associated with reduced contact between lipid droplets and mitochondria, and reduced triglyceride secretion.

With consumption of a high-fat diet, $Plin5^{LKO}$ mice accumulated intrahepatic triglyceride, without significant changes in inflammation, ceramide or diacylglycerol contents, endoplasmic reticulum stress or autophagy. Instead, livers of $Plin5^{LKO}$ mice exhibited activation of c-Jun N-terminal kinase, impaired insulin signal transduction and insulin resistance, which impaired systemic insulin action and glycemic control. Re-expression of *Plin5* in the livers of $Plin5^{LKO}$ mice reversed these effects. Together, we show that *Plin5* is an important modulator of intrahepatic lipid metabolism and suggest that the increased *Plin5* expression that occurs with over nutrition may play an important role in preventing hepatic insulin resistance.

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Hunger-sensing AgRP neurons engage the hypothalamic-pituitary-adrenal axis to mediate adaptive responses to stress

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Hunger-sensing Agouti-related peptide (AgRP) neurons in the hypothalamic arcuate nucleus are fundamental to survival. They increase food intake during energy deficit and also facilitate adaptive behaviors to cope with hunger by reducing anxiety and increasing motivation, therefore enabling appropriate food seeking behavior. A fundamental question remains; what are the physiological mechanisms through which AgRP neurons regulate adaptive behaviors. We examined the hypothesis that activation of AgRP neurons in the absence of food engages the Hypothalamic Pituitary Adrenal (HPA) axis to mitigate anxiety associated with acute emotional stress. Using hM3Dq DREADDS, prior activation of AgRP neurons 3-hours before acute restraint stress significantly increased plasma corticosterone 15, 30 and 60 min and ACTH 30 min after stress onset. Anterograde tracing of AgRP neurons using the cre-dependent herpes simplex virus H129 ΔTK-TT confirmed that AgRP neurons target ~30% of CRH neurons in the PVN. In behavioural experiments, prior activation of AgRP neurons reduced anxiety-like behaviour, increased memory recall and promoted food intake after acute stress. Prior activation of AgRP neurons also promoted food-seeking and food consumption in a food-baited novel environment used to evoke acute stress. To determine whether the behaviours were a result of increased circulating corticosterone we pre-treated mice with metyrapone, an inhibitor of corticosterone synthesis and repeated these behavioural experiments. Unexpectedly, inhibiting corticosterone did not influence AgRP-induced behavioural adaptation to stress. Activation of selective AgRP to PVN and AgRP to medial amygdala circuits using retrograde transport of DREADDs from terminal regions induced a significant feeding response. However activation of these circuits in isolation did not influence adaptive behaviour in response to acute stress. Our results suggest AgRP neurons promote an adaptive response to stress independent from increases in plasma corticosterone, however the specific circuits responsible remain to be determined and may require multiple AgRP circuits acting in unison.

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