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FGF21 signaling and brown adipose activity gene expressions in male and female mice under fasting and refeeding states

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Motivation and Aim: Brown adipose tissue (BAT) is involved in the body adaptation to starvation and increased food consumption. The main function of BAT is to produce heat. Thermogenesis in BAT is mediated through the BAT-specific uncoupling protein 1 (UCP1). Fasting suppresses UCP1 expression in BAT [1]. Several studies showed that females have more active BAT because sex hormones affect UCP1 expression as well as the adrenergic receptor levels, lipolytic activity and lipid accumulation in brown adipocytes [2]. Fibroblast growth factor 21 (FGF21) recently discovered regulator of lipid and glucose metabolism activates brown adipocytes inducing thermogenic gene expression and caloric expenditure during drug treatment [3]. It is unknown how sex hormones affect on FGF21 signaling in various metabolic states. We investigated the effects of fasting and refeeding on expression of genes of FGF21 signaling and BAT activity in males and females mice.

Methods and Algorithms: Males and females of C57BL mice were decapitated after 24 hours of fasting or after 24 hours of fasting plus 6 hours of refeeding or in the fed state (controle). Plasma hormone concentrations were measured using commercial kits, glucose blood level was determined using a glucometer OneTouch Select, gene expression was evaluated using the qPCR method.

Results: There were no sex differences in alterations of blood hormone levels and BAT mRNA levels in response to fasting. Fasting increased *Ppargc1a* mRNA levels and did not affect the expression of other genes equally in males and females. There were sex differences in hormonal reaction to refeeding because insulin levels were greater and leptin levels were lower in males compared with females although there were no sex differences of the hormone levels in control. Refeeding decreased *Ppargc1a* and *Slc2a1* mRNA levels both in males and females. Furthermore refeeding increased FGF21 mRNA levels and it was significantly lower in males compared to females.

Conclusion: There were sex differences only in FGF21 mRNA levels in response to refeeding. Differential expression of FGF21 might contribute to sex differences in BAT activity, but further research is needed.

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