Abstract

Fibroblast growth factor 21 (FGF21) is a unique peptide hormone involved in the energy homeostasis, as well as in the regulation of glucose and lipid metabolism. Numerous animal studies suggest that FGF21 may be used as a potential treatment for obesity and type 2 diabetes mellitus. It was found out, that FGF21 counteracts the development of obesity presumably by increasing energy expenditure through activation of thermogenesis in brown and white adipose tissue. FGF21 apparently also inhibits lipolysis. However, the specific mechanism of action of FGF21 is not clear.

In our experiments we studied the antiobesogenic effects of FGF21 on mice model of diet-induced obesity at thermoneutrality. It is assumed that this model approach (in contrast to housing mice at standard laboratory temperature) mimics closely the metabolic status of humans. During the 4- to 8-day FGF21 treatment we observed a gradual reduction of lipid content in the brown and white adipose tissue and liver, especially in combination with β_3-adrenergic stimulation. We have confirmed that FGF21 inhibits lipolysis and also stimulates browning in certain adipose tissue depots. Furthermore, we have found that the effect of FGF21 on fatty acid secretion by adipose tissue is not mediated by changes in the fatty acid re-esterification rate, but rather by changes in lipolysis. Although we did not observe any beneficial effect of FGF21 on glycemic profile of obese mice in basal conditions, in combination with β_3-adrenergic stimulation FGF21 synergistically reduced blood glucose levels, which may also be related to changes in adipose tissue (i.e. to inhibition of lipolysis).

Our results thus support the theory of the key role of adipose tissue for the manifestation of the antiobesogenic and antidiabetic effects of FGF21.

Key words

White adipose tissue, obesity, metabolic flexibility, β-adrenergic stimulation, FGF21