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Effect of melanocortin obesity on insulin signaling in female and male mice

In the human population, melanocortin obesity is more common than other forms of genetic types of obesity. In mice mutation "Yellow" in the Agouti locus (Ay) decreases melanocortin receptor activity, induces hyperphagia, adult onset obesity and insulin resistance. It remains unknown if there are sex differences in molecular mechanisms of insulin resistance at melanocortin obesity. We investigated effects of melanocortin obesity on adipose tissue, glucose tolerance, insulin sensitivity, insulin and glucose blood levels, and mRNA level of insulin signaling genes (INSR, IRS1/2, PIK3CD) in liver, muscle and adipose tissue (WAT) in females and males at 30 weeks of age. We have shown that both Ay-females and Ay-males have impaired whole body insulin sensitivity: females had glucose intolerance and fed hyperinsulinemia, and males had impaired insulin sensitivity and fasted hyperinsulinemia. However, the molecular mechanisms of insulin resistance were different in Ay-females and Ay-males. We found sex specific effects of melanocortin obesity on insulin signaling in liver and adipose tissue, whereas obesity did not affect insulin signaling in muscles. In females, obesity was associated with decreased hepatic INSR and IRS2 mRNA levels, and increased WAT INSR and PIK3CD mRNA levels, and in males, obesity was associated with increased hepatic PIK3CD mRNA level and decreased WAT INSR mRNA level. The data suggest that sexual differences in mechanisms of insulin resistance should be considered for correction of metabolic syndrome at melanocortin obesity.

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Biography

Iakovleva T V has graduated from Novosibirsk University. At the University, she studied the properties and function of estradiol secreted by the adrenal gland. She then studied effects of color mutations (Agouti and non-Agouti) on the function of pituitary-adrenal system in females and males of Arvicola terestris; effects of colour mutation Agouti yellow on the function of pituitary-adrenal system in mice C57Bl and; effects of melanocortin system and estradiol on obesity development and insulin sensitivity in females of C57Bl mice. She studied mechanisms underlying the development of insulin resistance and expression of insulin signal transduction genes in females and males of C57Bl mice during the development of melanocortin and diet-induced obesity and presented work is the part of her study on sex characteristics of the FGF21 regulatory effects.

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