GLUCOCORTICOID-MEDIATED EFFECTS OF *Mif* DEFICIENCY AND FRUCTOSE - ENRICHED DIET ON ENERGY METABOLISM IN THE MOUSE LIVER

Ljupka Gligorovska, Ana Teofilović, Nataša Veličković,
Danijela Vojnović Milutinović, Gordana Matić and Ana Djordjevic

Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia

Introduction: The macrophage migration inhibitory factor (MIF) is a proinflammatory cytokine involved in the regulation of energy metabolism and glucocorticoid action in the liver. Genetic deletion of *Mif* may contribute to the development of systemic insulin resistance, especially in the setting of fructose overload that can be associated with perturbed hepatic metabolism.
The aim: The aim of the present study was to elucidate the impact of combined effects of *Mif* deficiency and dietary sugar on energy metabolism and insulin sensitivity in the liver of male mice.
Methods: Wild type (WT) and *Mif* deficient ($MIF^{-/-}$) C57Bl/6J mice were used to analyze the effects of 9-week 20% fructose-enriched diet on energy intake, and indicators of insulin sensitivity and glucocorticoid receptor (GR) signaling. Deregulation of Akt signaling pathway was used as a hallmark of hepatic insulin resistance. Changes in energy metabolism were estimated by AMP-activated protein kinase (AMPK) and SIRT1 protein levels.
Results: All fructose-fed animals had increased energy intake, while elevated APMK and SIRT1 protein levels compared to the WT ones. Although enhanced glucocorticoid prereceptor metabolism was observed in all fructose-fed mice, GR protein level was increased only in $MIF^{-/-}$ animals. *Mif* deficient animals exibited impaired systemic insulin sensitivity. However, the impaired hepatic insulin signaling, revealed by decreased pAkt/total Akt ratio, was observed only in fructose-fed $MIF^{-/-}$ animals.
Conclusion: The results showed that *Mif* deficiency under the conditions of dietary fructose overload leads to systemic insulin resistance, and impaired hepatic insulin signaling and energy metabolism, possibly through enhanced glucocorticoid signaling.

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