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Title of the diploma thesis: The impaired change in plasma long-chain acylcarnitine level as a marker of insulin resistance

Insulin resistance presents one of the factors that could lead to type 2 diabetes mellitus (T2DM). Increased levels of long-chain (LC)-acylcarnitines are associated with obesity and T2DM and recent studies suggest that LC-acylcarnitines could play a role in the development of insulin resistance. Early diagnosis of insulin resistance would help to prevent the onset of T2DM and the development of associated complications.

The purpose of this study was to determine whether the measurements of the changes in acylcarnitine concentrations during the glucose tolerance test (GTT) could be used as a novel marker of insulin resistance. After intraperitoneal administration of glucose in high fat diet (HFD)-fed C57bl/6N, db/db mice and respective controls the concentrations of glucose, insulin, glycated haemoglobin, free fatty acids (FFAs) and acylcarnitine levels in the fasted state and subsequently at 1 and 2 hours after GTT were measured. Utilization of glucose was determined by the measurement of the rate of 2-[1,2-^{3}H]-deoxy-D-glucose ([^{3}H]-DOG) uptake in insulin-sensitive tissues. Measurements of biochemical parameters and [^{3}H]-DOG uptake in tissues demonstrated that HFD mice represent a model of early stage insulin resistance, while db/db mice develop type 2 diabetes with severely impaired glucose metabolism. The decrease of plasma LC-acylcarnitine levels during the GTT in control mice was higher in comparison to mice with insulin resistance. Moreover, in db/db mice there was no change in plasma LC-acylcarnitines during GTT. Thus, the impaired change in LC-acylcarnitine concentration could be considered as a diagnostic marker of muscle-specific insulin resistance.

Keywords: type 2 diabetes, insulin resistance, acylcarnitines