Abstract

Alzheimer´s disease (AD) and type 2 diabetes mellitus (T2DM) are aging-associated diseases that have rising prevalence in all industrialized countries. AD is a neurodegenerative disease characterized by progressive loss of cognitive functions. It is a complex disease which formation involves both genetic factors and environmental factors. The most important marker associated with this disease is the risk allele ε4 in *APOE* gene. From the latest genome-wide association study emerged another ten candidate genes. As the most significant from those genes appears the minority G allele of rs744373 polymorphism in the gene *BIN1*. AD is connected with many metabolic and immune disorders. To the markers of interest belongs also the new parameter visfatin which can act as a pro-inflammatory cytokine. T2DM is a chronic disease characterized by raised levels of blood glucose, which is also characterized by neurological disorders. In the case of both of these diseases can be found a large number of metabolic disorders. One of the most important disorders is insulin resistance.

This thesis consists of two parts - the biochemical and genetic one. The biochemical part of the thesis studies the visfatin level in patients with AD and healthly control and studies whether visfatin is related to AD. In this part of the thesis has been examined 103 persons in total (39 patients with AD and 64 appropriate healthy controls). The examination included examinations of glucose and lipid metabolism, anthropometric examination to finding the basic anthropometric dimensions and indices calculated from them. Biochemical examination to finding the level of visfatin was performed from blood plasma within the multiplex analysis. Results showed increased levels of visfatin in patients with AD compared with healthy controls. The higher level of visfatin as a pro-inflammatory cytokine can probably reflect the chronic inflammation described in AD. The influence of blood glucose tolerance on the level of visfatin has not been proved.

The genetic part of the thesis studies the influence of the risk ε4 allele in *APOE* gene and minority allele G of polymorphism in the gene *BIN1* on the anthropometric parameters and clinical biochemistry examination of glucose and lipid metabolism. In this part of the thesis were examined 1386 persons in total (417 patients with T2DM, 335 women with gestational diabetes and 634 nondiabetic subjects). Examinations of the studied complex included basic anthropometric measurements, clinical biochemistry examinations of the glucose and lipid metabolism including glucose tolerance test in non-diabetic individuals and genetic analysis focused on candidate genes for AD (*APOE, BIN1*). As a material for genetic analysis has been used DNA isolated from peripheral blood. The frequency of the risk allele ε4 in gene for *APOE*

and minor allele G of polymorphism rs744373 in gene *BIN1* is not significantly different between particular groups. There was confirmed the influence of the risk allele ε4 in gene for *APOE* on lipid metabolism. The holders of this allele had higher level of the overall and LDL-cholesterol. The correlation was not proved in the minor allele G of polymorphism rs744373.

This thesis has contributed to the understanding of the genetic and biochemical background of AD and T2DM. In the genetic part the previously presented influence of the risk ε4 allele on lipid metabolism has confirmed, in the biochemical part a new risk factor – visfatin – was revealed as a likely indicator of chronic inflammation of the brain.

Keywords: Alzheimer's disease, type 2 diabetes mellitus, insulin resistance, visfatin, risk ε4 allele, a polymorphism of the gene *BIN1*