

Abstract:

Obesity is a complex multifactorial disease and one of the most significant health challenges of our time. The prevalence of overweight and obesity continues to rise globally in both adults and children. Excess body weight in early life is often associated with additional metabolic complications, and most obese children remain obese into adulthood, which brings further health risks. Despite intensive research into the causes and mechanisms leading to the development of excessive body weight, certain aspects of this condition remain unclear.

This thesis consists of two separate studies representing possible approaches to the investigation of the genetic background of obesity.

The first part of the thesis presents a cross-sectional study of 1,947 Czech adolescents, which involved an association study examining the effect of physical activity on body composition and metabolic health. The study also evaluated the impact of the rs686989 polymorphism in the *ZBTB16* gene on selected anthropometric and biochemical traits related to overweight and obesity. The results demonstrate a positive influence of physical activity on certain anthropometric and metabolic traits in both male and female adolescents, albeit with some gender-specific differences. Additionally, it was found that the rs686989 polymorphism in the *ZBTB16* gene may have a modest effect on anthropometric and biochemical parameters, although this effect is very subtle.

The second part of the work consists of a longitudinal study in which the technique of massive parallel exome sequencing was used to identify variants potentially associated with polygenic obesity in a group of patients with suspected monogenic obesity. The frequency of the identified variants was subsequently analyzed in a group of individuals with higher risk of obesity and compared to a group of non-risk individuals. The frequency of the identified variants did not differ significantly between the two groups.

The thesis demonstrates the diversity of the etiopathogenesis of polygenic obesity and the challenges in its research.

Key words: polygenic obesity, sport activity, *ZBTB16*, whole exome sequencing, COPAT