1. ABSTRACT

Anorexia nervosa (AN) still remains a highly morbid condition with the highest mortality of any other psychiatric disorder. Beside acute refeeding techniques, no specific interventions have been proven effective in changing the long-term course of AN. Extreme reduction of food intake and hyperactivity characteristic for this starvation status result in severe weight and fat loss together with multiple endocrine perturbations, altered glucose and lipid metabolism as well as in delayed gastric emptying and other gastrointestinal complications.

Loss of adipose tissue is beside disturbances in thermoregulation, lipolysis and lipogenesis associated with altered production and release of adipose tissue-derived proteins, so-called adipocytokines, that play an important role in the autocrine and paracrine regulation of adipose tissue metabolism as well as in the endocrine regulation of metabolism of other peripheral tissues. Furthermore, some of adipocytokines act in the central nervous system to regulate energy balance. Similarly, altered food ingestion in patients with AN could be related to changed production and/or action of gastrointestinal hormones. Thus, both adipose tissue-derived and gastrointestinal hormones could inform central nervous system about acute (food intake) as well as about long-term (fat stores) energy disbalance in peripheral systems.

In the present Thesis, the roles of leptin and resistin, as the representatives of adipocytokines, and ghrelin, the gastrointestinal hormone, in the pathophysiology of AN have been studied. Although alterations in many endocrine systems have been clearly described in patients with AN, the role of these recently characterized proteins in patients with AN is not definitive. The research focused on the role of resistin in human physiology as well as in pathophysiologic conditions, such as malnutrition, brought rather contradictory data. However, the participation of both leptin and ghrelin in the long-term regulation of energy balance as well as in the acute regulation of food intake is well established.

The unique technique of microdialysis allows direct *in vivo* sampling of interstitial fluid from the studied tissue. Moreover, microdialysis is conseptually simple and the principle of the technique could be likened to capillary. The limitation of the procedure is a molecular weight of the tested and/or applicated molecules. That is the practical reason of limited using of *in vivo* microdialysis to measure proteins. Although microdialysis has been used since 1987 in more than 3000 clinical trials mainly in the muscle and adipose tissue and has been described as a suitable technique for *in vivo* measurement of concentrations or dynamic changes in concentrations of glucose, adenosine, glycerol, aminoacids etc., as long as I know, *in vivo* concentrations of adipocytokines have not been explored. Thus, in this Thesis the

unique microdialysis technique has been modified and used for *in vivo* measurement of leptin and resistin levels in the extracellular space of abdominal adipose tissue for the first time.

The present Thesis is divided on abstract, introduction, results, discussion and conclusions. In the introduction part, author is presenting an overview on the experimental field closely connected with the studied questions. The text of introduction also includes the original results of the author and embedded graphs. The result and discussion parts are submitted together in a form of original articles of the author (3 published and 2 submitted for publishing). Finally, the conclusion part summarizes the main results of this Thesis.