



## Entero-insular axis in children with anorexia nervosa

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**Summary** Entero-insular axis plays an important role in generating satiety signal. Thus disturbances in this axis may influence the course of anorexia nervosa. The aim of the study was analysis of the function of the hormonal part of the entero-insular axis in girls with anorexia nervosa. Thirteen girls with anorexia nervosa and in 10 healthy girls were studied. Each girl was subjected to oral glucose tolerance test and standard meal test. Blood was collected before stimulation and within 15, 30, 60, and 120 min thereafter. The concentrations of all peptides were determined by radioimmunoassay commercial kits. Fasted and postprandial levels of these peptides as well as integrated outputs were measured. Fasting insulin concentration was significantly higher in the group of girls with anorexia nervosa than in the control group ( $p < 0.03$ ). What more in girls with anorexia the integrated output of insulin was significantly lower in oral glucose tolerance test than after the meal ( $p < 0.001$ ). Also the integrated output of glucagon in both tests was higher in the group of girls with anorexia than in the control group. The mean output of pancreatic polypeptide and cholecystokinin in anorexia group was significantly higher ( $p < 0.001$  in both cases) than that in the control group but only after the test meal. The integrated outputs of gastric inhibitory peptide in both tests were significantly higher in anorectic girls than those in the control group (oral glucose tolerance test,  $p < 0.02$ ; meal test,  $p < 0.001$ ). However, mean values of the integrated output of glucagon-like peptide 1 in both tests were significantly higher in the control group than in the girls with anorexia ( $p < 0.001$  in each case). Highly significant correlation was found between glucose concentration and the concentrations of insulin, cholecystokinin, and gastric inhibitory peptide in both tests and for the both groups. In the anorectic girls, significant correlation between insulin concentration and the concentration of gastric inhibitory peptide was found after both stimulation tests and between insulin and cholecystokinin

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after oral glucose only. Conclusion: the disturbed secretion of the hormones of entero-insular axis after the meal in anorectic girls may have negative influence on the course of anorexia nervosa. This disease has no effect on the incretin function of cholecystokinin, gastric inhibitory peptide and glucagon-like peptide 1.

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## 1. Introduction

Initially, the term entero-insular axis was defined as a group of signals originating from the intestine that can stimulate, inhibit or modulate insulin secretion (Creutzfeldt, 1979; Unger and Eisentraut, 1969). Currently, it has been accepted that entero-insular axis represents the interaction of signals from the gastrointestinal tract with the whole endocrine part of the pancreas. The endocrine cells of the intestine secrete, among others, such peptides endowed with incretin activity as glucagon-like peptide 1 (GLP-1), gastric inhibitory peptide (GIP), and cholecystokinin (CCK). Besides incretin hormones, also neural connections, as well as direct or indirect actions of food constituents and their metabolites, participate in signals sent from the intestine to the pancreas (Flatt, 1996). In addition to insulin, also glucagon, somatostatin and pancreatic peptide are the effectors of these signals (Creutzfeldt and Ebert, 1988).

Anorexia nervosa has become recently an important epidemiological problem. It is known that hormones, and especially neuropeptides and gastrointestinal peptides play an essential role in pathogenesis of this disease (Gwirtsman et al., 1989). Entero-insular axis, as a functionally isolated system including both pancreatic and intestinal hormones, plays an important role in generating satiety signal. It can be speculated that any disturbance appearing within entero-insular axis may thus influence the course of anorexia nervosa. Therefore, we decided to investigate the possible changes within hormonal part of the entero-insular axis in girls with anorexia nervosa.

## 2. Material and methods

### 2.1. Experimental groups

Twenty-three girls of age between 13 and 16 years (mean age  $14.4 \pm 1.5$  years) treated in the Department of Endocrinology of Children and Adolescents of the Polish-American Institute of Pediatrics in Kraków participated in the study. The Permanent Ethical Committee for Clinical Studies of the Medical College of Jagiellonian University has

approved the protocol of the study. The parents of the studied girls made a written consent for the participation of their children in the study. In 13 girls with body mass index (BMI) of  $14.8 \pm 1.4$  kg/m<sup>2</sup> (mean age  $15 \pm 2$  years) anorexia nervosa was diagnosed basing on the DSM IV criteria. Ten healthy girls with BMI  $22.2 \pm 0.7$  kg/m<sup>2</sup> (mean age  $15 \pm 1$  years) formed the control group. Coexistence of other diseases and any hereditary connections were excluded in all the children.

### 2.2. Experimental protocols

Oral glucose tolerance test (OGTT) and standard meal test were performed in all the studied subjects. Twelve-hours fast was maintained before each test. The test was started in the morning with taking blood sample through the venflon tube installed into the cubital vein followed by oral administration of glucose solution (1.75 g per kg body weight, maximally 75 g) in the case of OGTT or standard breakfast consisting of four pieces of wheat-rye bread (100 g), four slices of ham (50 g), four slices of tomato (100 g) and a glass of orange juice (250 ml). The caloric value of the meal was 555 kcal, in which carbohydrates participated in 60%, protein in 24% and fat in 16%. The composition and caloric value of the meal remained in accordance with the recommendation of the Institute of Food and Nutrition (Warsaw, Poland), for teenage population. The children ate the meal in the separate room, under supervision of nurse or parent. The time of eating was limited to 30 min. All girls finished their breakfast before this time. In the morning after the breakfast, the girls remained in the supervised room, no symptoms of vomiting were observed. Venous blood samples (3 ml) were taken at 15, 30, 60 and 120 min following the administration of stimulant to the cooled glass tubes containing 4 mg EDTA and 0.2 TIU (trypsin inhibitor units) of aprotinin (Sigma, USA). At the same time capillary blood was taken from a finger to the heparinized glass capillary tube. The tubes with blood were put in crushed ice and immediately transported to the laboratory. Blood was then centrifuged at 3000 g and 4 °C. The separated blood plasma was kept frozen at  $-20$  °C until analyzed.

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