Low ambient temperature lowers cholecystokinin and leptin plasma concentrations in adult men

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Abstract
Background: Low ambient temperature increases appetite. The mechanisms of this phenomenon have not been elucidated. The aim of this study was to investigate the effect of short exposition to low ambient temperature on the plasma concentration of leptin and cholecystokinin.

Methods: Sixteen healthy men, age 24.6 ± 3.5 years, BMI 22.3 ± 2.3 kg/m², participated in the study. The concentrations of plasma CCK and leptin were determined twice - before and after the 30 min. exposition to + 4° C by RIA kits.

Results: The CCK concentration before the exposition to low temperature was 1.1 pmol/l, and after 0.6 pmol/l (p<0.0005). The mean values of leptin before exposition (4.7 ± 1.54 µg/l) were also significantly lower than after the exposition (6.4 ± 1.7 µg/l; p<0.0005).

Conclusions: It has been concluded that CCK and leptin participate in the short-term regulation of energy balance following exposition to low temperature by potentiating the feeling of hunger.

BACKGROUND
The amount of the ingested food is regulated in healthy individual by feelings of hunger and satiety. In hypothalamus there are two contrariwise interacting centers: hunger center (nucleus ventrolateralis) in the lateral part of hypothalamus and satiety center in the ventromedial nucleus. In physiological conditions, hunger center and satiety center remain in dynamic balance. The activity of these two centers is modified by several central and parenteral factors, the hormones, cholecystokinin (CCK) and leptin, among others.

CCK is an enterohormone belonging to the gastrin family. It is synthesized and secreted by the I cells localized mainly in the jejunum in response to food stimuli. In gastrointestinal tract CCK regulates mainly the motility and contraction of smooth muscles, and acts as a potent stimulant of secretion of pancreatic enzymes. CCK also participates in the central and parenteral regulation of feeding process [1]. Parenterally, CCK acts on diminishing the amount of the ingested food through the activation of the CCK-A receptors and following increase in the efferent impulse of vagus nerve to the central nervous centers [2]. The parenteral effect is additionally intensified by the relaxation of gastric muscles. In turn, CCK acts centrally by directly stimulating hypothalamic CCK-B receptors [1]. Gibbs et al. [1] observed that in rats CCK administered parenterally lowers the amount of the ingested food. In animal experiments, intraventricular administration of CCK receptor antagonists or specific antibodies increases feeding activity [2].

Leptin, a hormone synthesized mainly by white adipose tissue, has the structure similar to that of cytokines. Blood plasma concentration of leptin depends directly on adipose tissue mass and correlates with body mass index (BMI) [3]. It is thought that leptin plays a role of peripheral signal informing on the cumulated body stores of energy and thus participating in the long-term regulation of the amount of ingested food [3]. Acting at the level of central nervous system, leptin lowers the amount of ingested food by inhibiting the expression of neuropeptide Y (NPY) and the peptide bound to the agouti protein (AGRP). It also activates the expression of proteins connected with the propiomelanocortin group (POMC) [4].

It is known that the environmental temperature influences the amount of ingested food. Exposition to high ambient temperature results in the reduction of the amount of ingested food. Low ambient temperature, in term, causes a considerable increase of appetite. For the time being, the mechanism underlying the changes of the amounts of the
ingested food in relation to the environmental temperature has not been elucidated. CCK and leptin are one of humoral factors, which could be involved in the regulation of appetite due to changes of environmental temperature. Therefore the aim of this study was to investigate the effect of the short exposition to low ambient temperature on the blood plasma concentration of leptin and cholecystokinin.

MATERIAL AND METHODS
Sixteen healthy men, mean age 24.6 ± 3.5 years, BMI 22.3 ± 2.3 kg/m², participated in the study. The subjects were placed in the cold room for 30 min at the temperature of +4°C. At the time of exposition to the low temperature, the subjects were dressed in light clothing: trousers, shirt and sweater. The subjects were after overnight fast and the experiment was done in the morning. The venous blood was taken from the antecubital vein to the cooled tubes containing EDTA and aprotinin (Sigma) twice – before and after the exposition. Blood was immediately centrifuged and plasma distributed to several tubes according to the assay plan, and frozen at –70°C, until assayed. The day after, control experiment was performed with the participation of the same subjects at room temperature (21°C) by applying the same protocol.

The concentrations of CCK and leptin were determined by using RIA kits (Eurodiagnostica, Sweden, for CCK, and Linco Research, Inc., USA, for leptin determination). The sensitivity of CCK assay was 0.3 pmol/l with precision (CV) <5%, that of leptin assay 0.5 ng/ml with precision <10%.

The results were subjected to statistical analysis. Mean values were compared by applying the paired t-test, with the probability p<0.05 considered as a proof of significance. Correlation coefficients were calculated by using the parametric approach. All statistical calculations were done with the use of Statistica 5.0 and Excel 98 software.

RESULTS
The mean value of CCK concentration before the exposition to low temperature was 1.1 pmol/l, and after the exposition 0.6 pmol/l (Fig.1).
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Figure 2
Figure 2: Mean values of plasma leptin concentrations in patients before and after exposition to cold (4 centigrade). The statistical difference is between individual results by applying paired t-test.

In the control experiment no significant changes neither in leptin nor CCK concentrations were observed (Fig 1 and 2). No significant correlation was found between CCK and leptin concentrations, both before and after exposition to low temperature.

DISCUSSION
The thermostatic theory of appetite is based on the observation that high ambient temperature inhibits appetite and motor activities in animals. Exposition to low temperature elicits hyperphagia and considerably increases motor activity of the organism [8]. Recent studies confirmed a short-term limitation of the amount of ingested food under the influence of high environmental temperature [9]. The mechanisms underlying the changes in the amount of ingested food in relation to the ambient temperature have not yet been elucidated.

The results of the present study demonstrated a statistically significant decrease in the plasma concentration of CCK (p<0.0005) after a short exposition to low temperature. It has been concluded on the basis of this observation that CCK participates in the short-term regulation of energy balance following exposition to low temperature by potentiating the feeling of hunger and thus increasing the amount of the ingested food. It has been known that a fall in the concentration of CCK elicits hunger and causes an increase in feeding activity [2]. The mechanism of this phenomenon may be both peripheral and central. There could be down regulation of central CCK-B receptors as well as peripheral CCK-A receptors that in term activate vagus nerve [10].

The available data on the effect of low temperature on leptin secretion are controversial. The experiments of Hardie et al. and Cancello et al. suggest that short exposition to low temperature decreases the secretion of leptin in non-obese mice [11,12]. On the other hand, according to Melnyk et al. and Bing et al. long-term exposition to low temperature has no effect on leptin secretion in non-obese mice [13,14]. In humans it was observed that an elevated body temperature caused a decrease in leptin concentration, while a fall of body temperature brought about an increase in the concentration of this hormone [15,16,17]. It was also observed that low temperature causes a decrease in the blood serum concentration of leptin in healthy women [15]. Also the results of this study demonstrated a significant (p<0.0005) decrease in leptin concentration in healthy men after a short exposition to low ambient temperature confirming the view that this hormone may participate in the short-term regulation of energy metabolism [16]. Inasmuch as also fasting lowers the concentration of leptin, the observed fall of leptin concentration following the exposition to low temperature may be one of the factors responsible for the enhancement of appetite observed in low environmental temperature. This fall may originate from the activation of the sympathetic nervous system. Low ambient temperature stimulates -3-adrenergic receptors thus increasing cellular concentration of cyclic AMP that leads to a decrease of leptin synthesis by adipocytes [10].

CONCLUSION
The leptin and CCK are involved in adaptation to short-term acute cold exposure.

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