# OBSERVATIONS CONCERNING THE CYBERNETIC HORMONAL MECHANISMS AND THE INFLUENCING FACTORS ON EATING BEHAVIOR

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***Abstract:*** *The author of the paper aims to analyze the hormonal mechanisms and the factors that influence the eating behaviour. The main hormones involved are also analyzed: leptin, ghrelin, thyroid hormones. The author carries out further analyses into the elements of eating habits in relation to genetic and environmental causes, orienting the researches towards monogenic and polygenic directions as well as towards hyper-caloric consumption, physical inactivity, insomnias, night eating or the use of drugs that induce obesity. The conclusions unveiled by the present study emphasize the mechanisms for hormonal regulation as well as the lifestyle elements that lead to profound deteriorations in the eating behaviour.*

***Key words:*** *leptin, ghrelin, eating behavior.*

## 1. Introduction

Researchers have reached the conclusion according to which the modifications in eating behavior (for instance excessive desire for food) are caused by hormonal regulation and auto-regulation of the organism. A particular modification which leads to eating behavior disorders and which is widely spread is obesity. We make reference to the lack of the hormone called leptin, which disturbs the metabolism and makes people eat in excess although they are not hungry. The change in the eating behavior which causes obesity is nowadays a major problem of public health, recording a prevalence of about 30-40% in Romania. In order for this phenomenon to be controlled it is important to take into account certain processes of our organism, i.e. neuro-hormonal regulations and influencing factors.

As for the modifications in the eating behavior, which brings about weight gain and loss, the organism needs three important processes, namely: rest, elimination of remnants and energy consumption. These are the elements that induce the relation between "body and mind", relation that is based on *neuro-hormonal mechanisms*. The hormones, which function as mediators, send impulses to the nervous system warning it when nourishment is needed or when the satiety threshold is reached. These hormones are leptin and ghrelin, both of them being involved in the regulation and auto-regulation of eating behavior.

The influencing factors are either *genetic* or lifestyle-oriented, the modification in the food habits and in the level of physical activity being more and more often attributed to the *environmental factors.*

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## 2. System of Neuro-Hormonal Regulation

Once leptin has been discovered, the neuro-modulation of hunger and satiety mechanisms proved to be a complex mechanism. The main role of leptin in regulating body weight consists of sending the signal of satiety to the hypothalamus, reducing this way the food intake and the fatty deposits. Likewise, leptin plays important roles in carbohydrates metabolism, bony system development and reproduction. Unlike animals, where a deficit of leptin was noticed, the obese humans are usually resistant to leptin, having increased circular levels. In the few cases of leptin deficiency discovered in humans, leptin administration determined a reduction of food intake and significant weight loss [6], [11].

The two hormones, i.e. *leptin* and *ghrelin*, are the main actors in the cybernetic process of eating behavior regulation, more precisely in generating or ceasing the sensation of hunger. Their specificity is well known in the specialist literature [22].

Thus, the specialist literature mentions that **leptin** is a hormone secreted by the subcutaneous adipose tissue as response to the fatty deposit. Leptin is connected to the brain by alpha-melanocortin receptors inhibiting the neuropeptide Y and causing satiety. Provided the fatty level decreases, the level of leptin decreases as well and the appetite increases. Experimentally, mice, which are genetically unable to secrete leptin, turn obese because they do not recognize the "stop" command.

We must state that leptin is secreted during sleep hours, which means that 7 hours of night sleep are absolutely necessary to prevent disturbances in eating behavior. Males have lower concentrations of leptin as compared to females [10]. The lowest concentrations of leptin were recorded at noon and the highest ones at midnight [19]. The lack of sleep increases the "taste" for carbohydrates - this phenomenon is explained through the fact that the lack of sleep affects the production of leptin which, as shown before, is responsible for the state of satiety. A reduction in the level of leptin entails an increasing need to consume foods rich in carbohydrates.

**Ghrelin**, a hormone made up of twenty-eight amino-acids, is secreted by the empty stomach and stimulates the appetite. In a healthy body, two-three hours after breakfast the empty stomach secrets the ghrelin which, once in the brain, commands the appetite. The eating behavior modifies, we start thinking of lunch and we soon eat. The regulation is then done, namely the food commands the level of gherlin to decrease and together with it the appetite of the respective person, as shown in Figure 1 [22].

The specific eating behavior of a person on diet increases the ghrelin level not only before meals but almost permanently and in time it erodes the will. The genetic code translates this mechanism through hunger/ starvation.

Another theory, which has been widely debated over the past few years, concerns the role of the *thyroid gland* and its relation to obesity. It seems that a direct connection between obesity and the dysfunctions of the thyroid gland has not been clearly traced. Beside a suggestive clinical picture, the causes of weight excess (especially in case of obesity) must be looked for especially in the lifestyle and nourishment of the respective person. More and more studies seem to destroy the myth of the direct relation between hypothyroidism and obesity. Actually, the contrary was proved, i.e. gaining weight brings about the inhibition of the thyroid function. The more unstable the weight, which is due to repeated diets ("yo-yo" effect: loosing weight fast - regaining the

initial or more weight, soon after interrupting the diet), the tighter the relation; thus, a vicious circle is formed, leptin holding an important role as a major hormone regulating the appetite and the caloric indigestion. Leptin is produced in the adipose tissue, then, through blood circulation, it goes to the brain where it gives information about the fatty deposits, according to the flow shown in Figure 1.

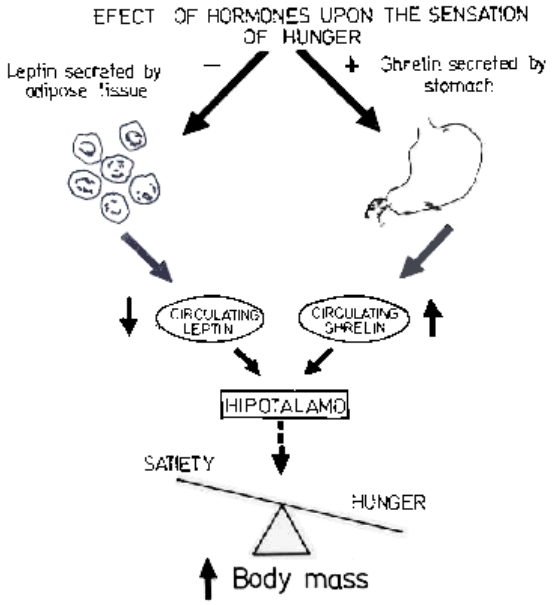


Fig. 1. *Neuro-hormonal regulation of the eating behavior*

Moreover, along the human evolution, the leptin - thyroid gland relation was important for survival. During the periods of hunger the organism uses the adipose tissue as "fuel". Thus, the level of leptin that goes to the brain decreases, which leads to the decrease in the basal metabolic rate and energy consumption. If this mechanism didn't exist the occurrence of malnutrition would be faster. Therefore, the hypothyroid status is the answer the organism gives to hunger. Provided there is not enough nourishment the adipose tissues are regenerated and only when the latter have reached the previous level the "thyroid" is allowed to increase the basal metabolic rate. This is the way through which the organism recovers after periods of hunger/starvation, which are nowadays known as "diets".

Similarly, the food excess determines, among others, the triglycerides excess, namely fats in blood that thicken the leptin, preventing it from reaching the brain. Thus, the *resistance to leptin occurs*: the brain records deficit of leptin as period of hunger and despite the continuous excessive feeding it continues to maintain the basal metabolic rate low, favoring the occurrence of overweight.

### 2.2. Regulating Mechanisms in Relation with the Adipose Tissue

The distribution of the adipose tissue is the consequence of an interaction between genetic and environmental factors. As for the arrangement, at about 20% female and

2% male in perimenopause period the adipose tissue is viscerally located [16].

The secretion of leptin is directly correlated with the mass of the subcutaneous adipose tissue. The adipose cell, which was long considered inert as far as the secreting role was concerned and with exclusive role for lipids deposit, has lately revealed its capacity of secreting a multitude of substances (adipokines, cytokines) with a role in regulating the insulin-resistance, satiety, inflammation, sexual function, endothelial function etc. The most important substances are adiponectin, leptin, visfatin, resistin, omentin, tumor necrosis factor-α (TNF-α), interleukin-6 and angiotensin II [5], [8].

Obesity is characterized by an increased concentration of leptin, which might make us believe that the effects of leptin are expressed, especially the anorectic effect. Unfortunately, the hyperleptinemia within obesity and type 2 diabetes (DZ2) is characterized through leptin-resistance [7] which is similar to insulin-resistance. The role of leptin in insulin-resistance is controversially debated, the tendency being that of accepting a favoring effect of insulin-resistance [1]. Women have higher daily concentrations as compared to men, but mechanisms are not clearly detected [15].

The leptin secretion is stimulated by insulin, having a reduced effect at insulin-resistant persons [12]. It seems that not only the hyper-insulin but also the hyper-glycemia contribute to modulating the leptin secretion [17]. Leptin, at its turn, decreases the insulin synthesis, closing up a regulation flow.

The involvement of the adipose tissue in endocrine processes allows us to understand its role as active organ; by acting upon it, we can determine the central, cardiovascular and metabolic nervous effects. For this very reason, the adipose tissue has turned very interesting for therapeutic interventions and the future will certainly lead to the occurrence of treatments that aim especially at influencing its secreting constellation. We must have in view that the secretion presents diurnal variations and the concentration of certain adipokines modifies postprandially, depending on the food composition but especially on the way of preparation. The research data regarding the effects of benfotiamine on the concentration of adiponectin are preliminary and they call for long-term validation through studies. Nevertheless, the hypothesis is very interesting especially within the context of well-known effects of benfotiamine in treating diabetic neuropathy [18] as well as its beneficial effects upon the function of endothelial cells [14].

## 3. Influencing Factors in Eating Behavior

The influencing factors are genetic, environmental and psychosocial factors that have separate or mutual influence as far as the eating behavior is concerned.

### 3.1. Genetic Factors

The genetic factors were indicated on account of the fact that there are many persons who, despite the weight loss that followed a diet and physical exercise-based program, do not succeed in maintaining the weight obtained for a longer time. The genetic studies help us identify sub-groups of individuals who can be sensitive or resistant to certain modifications of environmental factors. For instance, researches suggested that the family environment is very likely to influence obesity [21], [23].

Within this context, studies on families and adopted twins provided significant proof regarding the genetic cause of obesity. The rate of transmission varied between 10% (at adopted twins) and 80%

(at monozygotic twins). Similarly, the studies carried out on monozygotic twins showed a concordance for hereditary predisposition of weight excess of about 0.7-0.9, as compared to dizygotic twins, in their case the concordance ranging from 0.35 to 0.45 [9], [13].

A few cases with deficit of leptin receptor were discovered; the respective individuals, despite a normal weight at birth, gained weight in the first months of life, followed by hyperfagia, hypogonadotropic hypogonadism and affection of thyrotropin secretion. The recent data suggest that about 5% of the obese children present MC4 or POMC mutations [2], [4].

The current genetic studies and the recently used technologies have enabled the discovery of new genes with potential involvement in the pathogenic character of obesity; the most commonly studied genes have been those on chromosomes 2p, 10p, 5p, 11q and 20q. The researches in the field of genetics have showed that the obesity may be the result of a single anomaly that may lead to the energy unbalance. The individual variations of the adipose tissue are determined, to a great extent, by multiple genetic factors (polygenic obesity). The studies emphasized more possible loci but the chromosome 2p21 has been most frequently encountered in relation to obesity. This area of chromosome 2 includes the POMC gene as well, the mutations at this level being encountered at about 0.8% of obese children [1].

Determining genetic factors became very important once their influence was more frequently noticed at persons with severe obesity installed at young ages. Identifying key molecular elements involved in maintaining the energetic balance proved to be very interesting for conceiving new diets or diet-therapy methods. Likewise, current studies have showed that strict diets are not very efficient in the long term without a change in lifestyle, including the eating behavior.

### 3.2. Environmental Factors

As stated before, the change of eating habits as well as of the degree of physical activity emphasize more and more frequently the environmental factors. Eating habits are a risk factor for obesity. Consuming foods rich in calories - sugary products, excess of fats, gaseous drinks with extra sweeteners - as well as the inappropriate hours for meals stand for the main causes of weight excess. In most developed countries the consumption of hypercaloric foods is abundant. Their availability in stores, fast food restaurants and their consumption at various social-cultural events favors the occurrence of obesity.

In certain ethnic groups, the incidence of obesity is increased due to specific eating habits, partially conditioned by religious customs or climatic conditions, which do not allow for the availability of foods with reduced calorie content, such as fruits and vegetables, throughout the whole year. The consumption of alcohol is another important factor involved in the etiology of the central type obesity due to an increased caloric contribution (1 gram of alcohol releases 7 calories). Smoking is often followed by the occurrence of central obesity, reversible after giving up smoking. The diminution of physical activity and a sedentary life style, encouraged by the rhythm of modern societies, generate the energetic unbalance, giving rise to a surplus of calories from foods as compared to those burned through physical effort, even at persons without an excessive energetic contribution. The relation between obesity and physical inactivity is bidirectional, the weight surplus determining at its turn the decrease of appetite for physical effort. The lack of

physical activity was proved to be an independent risk factor for cardiovascular diseases and sugar diabetes type 2, increasing the risk of mortality.

The specificity of such eating behavior leads to obesity, its parameters being revealed in Table 1 by the specialist literature [19].

Table 1

*Classification of obesity following the deteriorations of eating behavior*

| Item | Category | IMC [kg/m$^2$] | Type of obesity |
|---|---|---|---|
| 1 | Overweight | under 18.5 | - |
| 2 | Normal | 18.5 - 24.9 | - |
| 3 | Overweight | 25.0 - 29.9 | - |
| 4 | Obesity | 30.0 - 34.9 | I |
| 5 | Advanced obesity | 35.0 - 39.9 | II |
| 6 | Morbid obesity | over 40.0 | III |

### 3.3. Psychological and Social Factors

Lifestyle and especially the eating behavior make many obese persons no longer able to control food impulses in response to stress, depression, loneliness, anger and other emotions. This theory is NOT agreed by all specialists, since many people with normal weight have psychological problems without deteriorations of eating behavior. Moreover, obesity does not disappear once the psychological problems are solved. On the other hand, there are many categories of individuals with eating behavior disorders, such as bulimia, hyperphagia, excessive alcohol, excessive consumption of sugary products (carbohydrate-craving), episodes of excessive hunger, followed by increased food intake, excessive night-eating.

Other psycho-social factors mentioned by researchers [3] can also cause obesity - women during the pregnancy period, lactation, menopause - some drugs that decrease the rate of metabolism, stimulate the appetite and water retention (Table 2); endocrine diseases (Table 3).

The complexity of psycho-social factors leads to a de facto balance. In this sense, Friedman would say that "people have the illusion that they can control the quantity of food they consume and this is true for a short period of time, but in the long term the biological drive to eat enough and to regain normal weight almost always overcome the control over conscience".

*Medicines that may lead to overweight* Table 2

| Item | Medication |
|---|---|
| 1 | Tricyclic antidepressants (amitriptyline, imipramine) |
| 2 | Antiepileptic (carbamazepine, valproate) |
| 3 | Antipsychotic (haloperidol, chlorpromazine) |
| 4 | Corticosteroids |
| 5 | Beta-adrenergic blocking agents |
| 6 | Serotoninergic Antagonistic (cyproheptadine, magestrol) |
| 7 | Certain contraceptive steroids |
| 8 | Insulin, sulfonylurea agents, tiazolidindions) |

*Hormonal disorders that may lead to overweight* Table 3

| Item | Endocrine disease | Mechanism and manifestations |
|---|---|---|
| 1 | Cushing Syndrome | Hypercortisolism and central-type obesity, which occurs through the involvement of neuro-endocrin pathways (leptin, corticotropin stimulating hormone, neuropeptide Y) and the sympathetic nervous system |
| 2 | Hypothyroidism | The metabolic rate decreases; it usually does not cause significant weight excess |
| 3 | Polycystic ovary syndrome | The increase in the circulating level of testosterone and androstenedione and the decrease in the sex hormones binding protein determine the central type obesity and insulin resistance |
| 4 | Hypothalamic obesity | It is characterized by affecting the appetite and the hypothalamic centers of satiety |

## 4. Conclusions

The eating behavior is linked to the mechanisms of neuro-endocrine regulation and in particular to leptin and ghrelin hormones in the satiety - hungry relation. Excess weight is not due to the thyroid gland, but rather to lifestyle. The leptin - thyroid gland relationship influences the basal metabolic rate, an eloquent example being that of diets for loosing weight. The excess of triglycerides in blood leads to leptin resistance and to overweight. The involvement of the adipose tissue in endocrine processes allows us to understand its role as an active organ. Obesity, through an increased concentration of leptin, is rather characterized by leptin resistance; as for the relation to insulin, further studies are required.

Eating behavior is influenced by genetic environmental and psycho-social factors, which have either separate or mutual action. Determining the genetic factors has become important since their influence was observed at people with severe obesity installed at young ages. The identification of key molecular components involved in maintaining the energy balance has proved to be particularly interesting for the conception of new diets and diet-therapy methods. Among the environmental factors, the hyper-caloric consumption, alcohol consumption, physical inactivity, smoking, insomnias, night eating or the use of certain drugs that favor obesity, are the lifestyle elements leading to profound deteriorations of eating behavior.

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