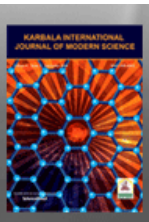

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Neurophysiology and Endocrine Responses to Hunger and Satiety Mechanisms: The Brain-Gut Crosstalk

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Background: Obesity is a main public health problem which substantially increases the risk of many diseases. The complex neural circuitry controls energy homeostasis and food consumption by the incorporation of hormonal and neural signals. Circulating hormones, in specific the gut hormones, have been found to be very important in appetite regulation. These hormones transfer energy situation signs to the brain throughout three principle paths: the circulation system, activation of the vagus nerve, and direct modification of main brain regions such as the hypothalamus and brainstem. The control of food eating is not exclusively dependent on the homeostatic processes, rather it includes reward mechanisms in which the brain plays a key role. Highly palatable foods, especially those high in sugar and fat, have clear impacts on brain circuits through activating main reward-related areas such as the nucleus accumbens and prefrontal cortex. Frequent exposure to these stimuli increases neural replies, causing increased ingestion due to the over activation of reward systems, which contributes to weight gain and obesity. **Objective:** This review aims to give an overview of the relationship between obesity and food eating from a neuroscientific view, and highlight the interaction between the central nervous system and the endocrine system in appetite and energy homeostasis regulation. Also, it investigates how energy-dense foods affect reward paths, contributing to overeating and obesity. **Key Findings:** The findings indicate that the hypothalamus and reward circuits play a vital role in energy homeostasis. Also, hormonal signs, such as leptin and ghrelin, regulate the feeding behavior, affecting weight regulation. **Conclusion:** Understanding the neuroendocrine basis of the eating behavior and addiction to highly palatable food is important for improving the non-surgical strategies for therapeutic obesity. **Recommendation:** Future research should aim to explore targeted interventions that adjust the reward pathways.

Keywords

Hypothalamus: Obesity; Arcuate Nucleus; High-palatable Foods; Endocrine Hormone

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REVIEW ARTICLE

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Recommendation: **Future research should aim to explore targeted interventions that adjust the reward pathways.**

Keywords: Hypothalamus, Obesity, Arcuate nucleus, High-palatable foods, Endocrine hormone

1. Introduction

Food eating is a primary mechanism for survival, and it is one of the greatest human pleasures. One of the important keys for living a healthy life is a suitable nutrition which depends on eating a variety of foods that contain the nutrients the body needs to maintain health, feel comfortable, and obtain energy. These elements include: proteins, carbohydrates, fats, water, vitamins, and minerals [1].

Over the past decades, the World Health Organization's (WHO) recommendations confirmed that suitable nutrient consumption participates in strengthening and promoting the immune system, decreasing the risk of the non-communicable diseases, and basically, increasing longevity.

For most of us, the composition and amount of food consumed differ greatly from one meal to the next and from one day to the other. Hence, our combined experience seems to be at disagreement with the hypothesis that food intake is highly

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regulated. There are many variables such as social factors, time of day, emotions, cost, and convenience, which are not biologically regulated, but nonetheless impact energy intake [2].

For this reason, daily energy consumption is variable and differs among individuals, and it is not well associated with daily energy expenditure. Despite short-term mismatches in energy balance (homeostasis), however, most of us try to match energy intake to energy expenditure with great precision by balancing the energy s/he eats during his/her daily meals. This phenomenon reflects an active regulatory process, termed energy homeostasis, which promotes stability in the amount of body energy stored in the form of fat [3].

The central nervous system (CNS) maintains this balance through several brain systems to ensure that there is enough energy available and that the body weight remains stable.

The brainstem receives neural information from the digestive system, while the hypothalamus receives nutritional and hormonal signs from the circulatory system. These systems, then, gather and respond to the facts about the body's nutritious condition. Also, they react with reward and motivation paths which are responsible for the food-seeking conduct [4].

Energy intake and expenditure are two processes which are modulated by the two systems; orexigenic and anorexigenic systems [5]. These are the two main systems in the body which control appetite and body weight. The orexigenic (Appetite-producing) system [6] helps to increase or keep body weight. It does this by increasing the feeling of hunger and the desire to food consumption, and also by decreasing energy spending so that the added fat is stored. The aim of this system is to make sure that the body has an adequate energy reserve [7].

The anorexigenic (Appetite-suppressing) system works to maintain or reduce body weight. It does this by increasing the body's energy spending and reducing the desire to food consumption, which aids in burning fat and reducing its storage. The aim of this system is to prevent unnecessary weight gain. The key difference between the two systems is that the first pushes the body to store energy and gain weight, while the second seeks to burn energy and lose weight [6].

Previous studies have indicated that one of the main causes of obesity is associated to changes in eating behaviors. As daily consumption of highly palatable and caloric foods has become a habit for many individuals, it has led to the development the obesity [7,8].

Evidence suggests that foods high in fat and sugar, which are highly rewarding, not only satisfy a physiological need, but also activate dopamine pathways, promoting the inclination to consume them repeatedly even in the absence of real hunger. This chronic stimulation weakens central satiety control mechanisms and leads to an imbalance in appetite-associated hormonal systems [3,8].

The significance of the study is present insights into the neurophysiological mechanisms responsible for regulating food intake, especially the complex interaction between hormonal and neural signals. This study is critical for understanding how unhealthy foods patterns and weight gain can damage the homeostatic control of appetite and satiety. By exploring these pathways, the study may contribute to a better understanding of obesity pathogenesis and support the development of more effective interventions targeting both the central and peripheral systems involved in eating behavior.

Therefore, this review focuses on (a) the central mechanisms by which the brain regulates food intake with a focus on the integration of neural and hormonal functions in maintaining homeostasis, (b) the impact of highly palatable foods on neural circuits, especially through the activation of the brain's reward system and hypothalamic pathways, (c) the role of key metabolic hormones, leptin, ghrelin and insulin in regulating food intake and explaining the changes that occur in the context of obesity.

2. Food classification and health impacts

Food is any material containing basic nutrients consumed to keep up life processes involving energy production, growth, repair, and regulation of body functions. Food consists of macronutrients (carbohydrates, proteins, and fats) and micronutrients (vitamins and minerals), and can be consumed through eating or drinking. It is digested and metabolized to deliver the elements essential to maintain health and life [9].

Consuming a wide variety of healthy foods throughout a person's life helps maintain good health and protect against diet related no-communicable diseases such as diabetes, heart disease, stroke, and cancer [10].

Foods are generally classified into “healthy and unhealthy categories” based on their nutritional composition and physiological impact on the body.

A healthy food is nutrient-dense, and it is rich in essential vitamins, minerals, fiber, and beneficial macronutrients. Eating healthy foods can help maintain the energy in high levels throughout the day and curb unexpected blood glucose decreases

or increases. Also, staying hydrated is another major part of the equation. This happens by drinking large amounts of water throughout the day, not only when you are really thirsty. It also helps the person to stay active, and it can prevent feelings of lethargy or fogginess [11].

In contrast, unhealthy food often lacks high nutritional values; it either has very low or devoid of nutritional values. Thus, unhealthy food is a food rich in calories and very poor in essential nutrients, and it also contains ingredients that may be harmful to health such as added sugars, saturated and trans fats, a very high percentage of sodium, preservatives, additives, refined carbohydrates among other things [12].

Nowadays, delicious foods are preferred and admired by a very wide range of individuals, in addition to being rewarding in terms of taste. Soda, fried chicken, potato chips, sugar sweetened beverages, egg and sausage sandwiches, cake, sweets, French fries, pizza, etc. are just examples of these types of food. All these foods are available around us, yet they encourage obesity and increase the risk of chronic diseases such as cardiovascular diseases and type 2 diabetes [13].

This classification of foods serves as a fundamental framework for understanding the role of diet in healthy and unhealthy conditions.

Many studies have examined the physiological and metabolic impacts of unhealthy foods. For instance, Cloetens and his colleagues [12] have shown that diets rich in saturated fats and simple sugars lead to impaired insulin sensitivity and increased chronic low-grade inflammation.

Their study shows that these types of food cause changes in the gut microbiota, negatively impacting the digestive and endocrine functions. Excessive consumption of such foods also promotes visceral fat storage and disrupts the regulation of hormones associated with hunger and satiety, such as leptin and ghrelin. These combined effects contribute to the development of insulin resistance, obesity, and metabolic disorders [13].

3. Highly palatable foods and the reward system

If food consumption which provides energy substrates for metabolism was just controlled via homeostatic mechanisms, food eating would directly be a reply to a physiological need, and the large number of individuals would regard their body mass as typical. However, appetite organization in humans is more complicated because it is also driven by agents beyond physiological needs [14].

Currently, one of the important reasons that push people to eat a lot of food without a physiological need can be attributed to the changes that have occurred in foods. The daily consumption of the majority of people has become associated with foods that are very tasty and have high calories.

Therefore, highly palatable foods have become a behavior that has led many persons to develop obesity. The results of recent studies that have used the highly palatable foods as an experimental model of obesity, indicated that animals exposed to these foods became obese and exhibited significant changes in endocrine markers, lipid profiles and over eating (hyperphagia) [15].

Highly palatable foods and their associated cues disrupt appetite regulation and stimulate reward pathways in the brain, leading to increased food seeking and consumption. The reward pathway plays an influential role in what we choose to eat so that the individuals prefer sweet or salty foods with high energy densities and refuse the bitter or acidic foods [16].

The reward pathway is composed of the amygdala (AMG), ventral-tegmental area (VTA), prefrontal cortex (PFC) and nucleus accumbens (NAc), since it is stimulated by the overeating of palatable foods. However, it leads to the secretion of dopamine which controls the motivational states of wanting or craving these foods; once overstimulated, the pathway becomes primed to request more of those special stimuli (Fig. 1).

Therefore, as humans, our brains are programmed to seek out behaviors or activities that trigger the release of dopamine in our reward system. For example, when a person does something pleasurable, the brain produces a large amount of dopamine, which creates a feeling of pleasure and thus stimulates the desire to repeat the experience to get the same feeling. Similarly, fast foods and sweets are addictive; they provide a temporary feeling of pleasure that makes you want to relive the experience again [17].

4. Obesity: the mechanisms of its development

In most people, body weight remains stable, and an individual can maintain this weight for many years by keeping the energy balance. This means that the amount of energy consumed is equal to the amount of energy burnt. However, when the energy homeostasis gets disturbed, this would lead to sustained weight issues. If the amount of energy consumed is more than the energy burnt, the body will store the excess as fat, leading to weight gain. On the other hand, if the amount of energy burnt is

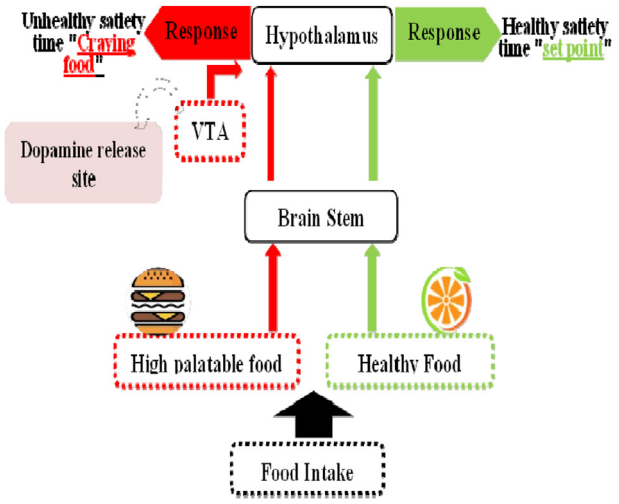

Fig. 1. ***Signaling of food consumption in the brain.*** *The signaling pathway stimulated by high palatable foods is shown in red arrows (on the left), which is associated with stimulating the reward system and it increases the release of dopamine without an effective stopping mechanism. In contrast, the signaling stimulated by healthy foods is shown in green arrows (on the right). Regulatory signals are activated, which leads to the cessation of eating via satiety centers. The figure reflects the contrast in neural and hormonal responses between the two species and their potential impact on overeating and obesity (Designed By researcher).*

larger than the energy consumed, the body will burn the stored fat for energy, leading to weight loss [18].

Obesity is a medical condition characterized by excessive accumulation of fat in the body, which increases the risk of developing numerous conditions such as cardiovascular diseases, type 2 diabetes, osteoarthritis, hypertension, and even some kinds of cancer. Also, metabolic syndrome is linked with obesity; it involves some conditions such as hyperinsulinemia, insulin resistance, dyslipidemia, and hypertension; each with risk factors directly related with both types 2 diabetes and cardiovascular diseases (CVD) [19].

Obesity is one of the prominent health challenges in the current time as its rates are constantly rising in the world. This is attributed to numerous intertwined factors including lifestyle changes, increased reliance on processed foods, lack of physical activity, and genetic factors [20].

An unhealthy diet is one of the most prominent contributors to overweight and obesity. This happens when an imbalance between the energy (Calories) consuming and the energy (Calories) burning occurs, with an increase in the energy consumed because of the increasing intake of foods rich in energy particularly foods that are high in fat and sugar such as Hyper-palatable foods (HPF). This leads to the excess energy being stored as fat in the body. This is accompanied with a decrease in physical activity because of the sedentary nature of numerous types of jobs, increasing urbanization, as well as changing modes of transportation. This leads to a decrease in calories burning, which also causes weight gain [21].

The hyper-palatable foods (HPF) which are rich in fat and sugar, are considered more attractive to a very large number of people because they are converted very quickly into energy, so their consumption over long periods can be compared to drug addiction because both lead to the stimulation of the reward system in the brain [22].

Ease access to HPFs (for example their wide availability and cheap price), as well as, their signal (Like the smell, the taste and even the color and shape) represent important sources of the stimulation that may lead to unnecessary consumption of food and participate to the increase of obesity.

HPFs encourage more and more of their consumption through increasing each of the hedonic components and motivation of the reward system. In obese cases, high food consumption may reflect an allostatic move in the set-point, described by either an increased hedonic requirement or an increased motivation to compensate for a deficit in the reward system. Then overeating begins due to the increased need for pleasure, yet with more exposure, the hedonic value of the HPF is reduced, leading to an increased motivation for eating [23].

However, the biological regulation of food selection and consumption is mediated by an interaction between energy balance and complex neural circuits in the hypothalamus. Generally, cues produced in the intestine tract and processed by the sensory receptors in central brain structures could spur or inhibit energy expenditure [24] (Fig. 2).

5. Central control of eating behavior

Homeostasis happens through a never-ending conversation that takes place between the brain and the rest of the body. The body's energy balance (Homeostasis) is finely regulated by a complex system that includes reciprocal communication between the brain and the peripheral organs (such as the liver, adipose tissue, kidney, intestines, and pancreas) [25].

Purnell and Roux mentioned that one of most important structures included in this regulation is the hypothalamus (HT); a small part (about an almond in size) of the brain and a very important part of the central nervous system which lies in the forebrain. Despite its small size, it possesses a key role in controlling numerous biological functions [26].

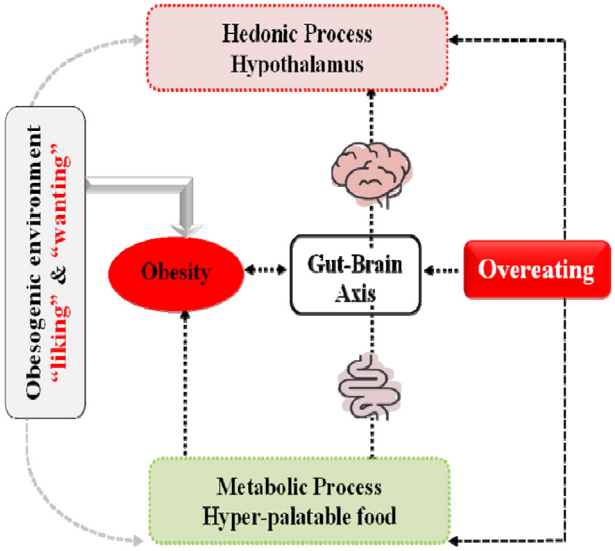

*Fig. 2. **A schematic diagram illustrating the hedonic systems work in the obesogenic food environment.** The diagram shows how an environment rich in highly palatable foods can overstimulate the hedonic system, leading to hedonic overeating, a contributing factor to the development of obesity. Over time, obesity itself may lead to a disruption in the sensitivity of the hedonic system and the efficiency of metabolic processes, impairing normal compensatory responses to food intake and contributing to the persistence of overeating. This disruption is exacerbated by a negative feedback loop that promotes the development of obesity and increases the risk of metabolic disorders (Researcher's design).*

The hypothalamus (HT) is a major brain center, having a net of neuronal mechanisms responsible for many important functions including. The main function is to maintain homeostasis (controls feeding) by integrating peripheral humoral signals that influence food intake and energy expenditure with neural signals from the brainstem and higher cortical centers. Other functions include thermoregulation, fluid equilibrium, circadian rhythm, stress response, conative and social behaviors, growth and reproduction, among other things [27].

The central control mechanism of eating food is an extremely complex process dependent on humoral and neural signs that reach the HT in the brain. This mechanism serves as a long loop that includes numerous linked processes which are:

- Hormonal signs come from various organs of the body to HT, including signals from ghrelin (which catalyzes the hunger) and leptin (which reduces appetite and promotes the fullness) [28].
- Nerve paths come from several organs and zones of the nervous system to HT, and transmit input about the body's situation in terms of energy and nutritional requirements.
- Obligatory processing: when the hormonal and nervous signals reach HT, this information is processed in particular HT circuits to be explained, then a suitable response is determined [29].
- Following processing the information, HT forwards descending nerve commands by vagus nerve and spinal cord into the peripheral nervous system. These commands act through impacting the several body organs to control energy intake according to the body's necessities [30].

The hypothalamus organ has four key sub-zones, namely, anterior, tubular, posterior and lateral zones, each of which contains clusters of specialized nerve nuclei that work together to perform numerous diverse physiological functions. These areas are linked to the autonomic nervous system and aid in controlling several vital processes in the body over complex connections between nerve and hormonal signs (Fig. 3) [31].

The anterior (Preoptic) area is located in the anterior part of the HT, and it contains the nerve nuclei which are; the preoptic nuclei, the paraventricular nuclei (PVN), the anteroventral periventricular nuclei, the supra-optic nuclei and the suprachiasmatic nuclei. The medial area is located in the middle of the HT, and it contains the dorsomedial nuclei, the ventromedial nuclei, and the arcuate nuclei (ARC). The lateral area contains the lateral nucleus. The posterior area is located at the back of the HT, and it contains the posterior nucleus and the mammillary bodies [32].

Especially within the HT, the ARC nucleus is important for controlling the eating behavior and metabolic processes. The ARC lies close to the median eminence (ME). Since the ME acts to transfer the peripheral hormonal and nutritional cues and then their sensing through the ARC nerve cells, the ARC integrates these cues from the bloodstream with the neuronal information to create a suitable response [33].

The ARC possesses two functionally opposed types of nerve cells, namely, the appetite stimulating neurons that promote hunger and expressed neuropeptide Y (NPY) and agouti related peptide (AgRP), and appetite suppressing neurons that promote satiety and expressed proopiomelanocortin (POMC).

The PVN regulates the endocrine and autonomic reactions by information from ARC, whereby it releases a hormone that impacts the feeding behavior. The VMH is also known as the "satiety center". Therefore, any destruction in this area leads to overeating (hyperphagia). However, the LHA is also known the "hunger center", yet it acts to stimulate feeding [34].

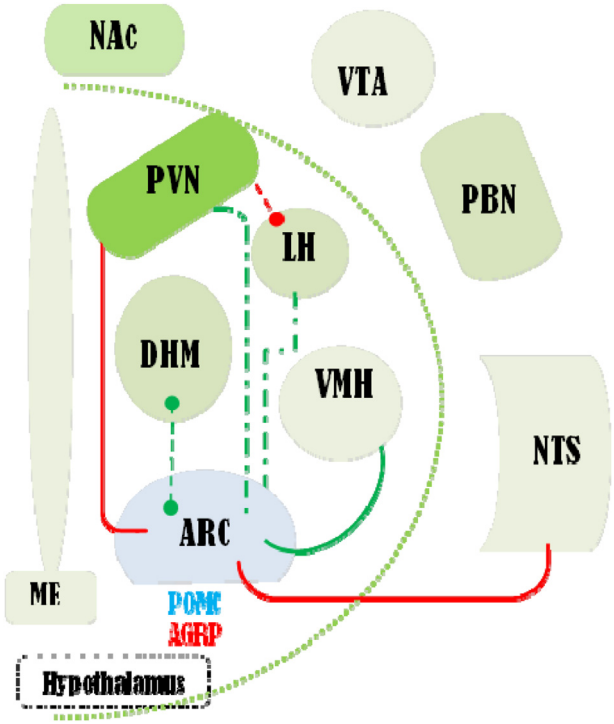

Fig. 3. ***Summary hypothalamus nuclei for appetite balance.*** *The hypothalamic nuclei are involved in regulating food intake through a complex network of neural and hormonal signals. The ARC regulates appetite via POMC cells and their stimulatory AGRP, and sends signals to PVH and VMN to regulate satiety and hunger. LH is activated by hunger, while the NTS is involved in satiety responses. Hormonal factors such as leptin and insulin influence these nuclei, stimulating satiety via POMC and inhibiting appetite via AGRP. TME also plays a role in linking hormonal and neural signals, while PBN contributes to the transmission of satiety signals via the NTS. NAc interacts with reward pathways in the brain, enhancing feelings of satisfaction with eating through its influence on the VTA.* ***Abbreviations:*** **PVH: paraventricular, LH: lateral hypothalamic area, NTS: nucleus of the solitary tract, ARC: arcuate nucleus, NAc: The nucleus accumbens, VTA: ventral tegmental area, NTS: nucleus of solitary tract, VMN: ventromedial nucleus, DHM: dorsomedial hypothalamic, PBN: parabrachial nucleus, ME: median eminence, POMC: pro-opiomelanocortin, AGRP: agouti-related peptide, ME: median eminence (Designed by researcher).*

6. Neuroendocrine control of homeostasis

The human body uses energy to run all biological functions. This energy comes from food intake, which is an organized vital process coordinated by a complex regulatory system, i.e. the hunger and satiety system. This system includes:

1- The central (the hypothalamus) organ.
2- Peripheral (the gastrointestinal tract, adipose tissue) organs [35].

Energy homeostasis is dependent on the balance between food intake and energy expenditure, and is regulated by:

- The endocrine system.
- The metabolic process.
- The hunger and satiety system.

All of these systems are mainly organized through HT centers at the brain level. By a complex neuro circuitry, appetite is regulated, and is defined as the motivational drive to obtain food by merging a diversity of interceptive cues to measure the nutritional state and then direct suitable levels for seeking foods [36].

The phases of the food intake cycle include hunger and satiety.

The need to eat, also known as hunger, is characterized by an uneasy feeling of emptiness in the abdomen, while the feeling of fullness which leads to the end of a meal is referred to as satiety.

In order to prevent overeating and regulate it, the body works to activate a set of the peripheral satiety signs (i.e. the metabolic, hormones and nervous signs), which in turn spread the brain centers (primarily HT, brain stem and reward stations) over the blood circulation, and thus, they facilitate communication between the central nervous system and the gastrointestinal tract [37].

Along with the quantity, the structure and the calories amount of meal also play a significant role in estimating satiety (fullness). By neural (vagal afferences) and hormonal signs, the beginning and end of a meal are controlled, and this signal of reception and integration occurs in the central nervous system (CNS), particularly in the hypothalamus.

The brain has the capacity to receive and process a wide variety of signals that indicate the nutritional status and energy level of the organism, and thus produce the proper reactions in terms of food intake, energy expenditure, and metabolic activity [38].

The central nervous system is informed of the nutritional status of the body in order to regulate food intake through HT which receives signs from periphery as metabolic and endocrine nervous motivations.

The nutrients act to stimulate the production and secretion of hormones from the gut, pancreas, and adipose tissue. These hormones' cues are sent from the vagus nerve to the brainstem and hypothalamus, then, in the brain, peripheral signs are combined in the brainstem and HT which is involved in regulating energy metabolism [39].

Most peripheral signs can act directly on various hypothalamic nuclei. So, they induce the satiety center which is attributed to the ventromedial nucleus (VMN), or the hunger center which is attributed to the lateral hypothalamic area (LH) in order to promote appetite or satiety.

For example, hunger (which is a lack of internal energy) is expressed through hormonal signals such as ghrelin. The mechanism of action of the ghrelin activates NPY/AgRP neurons in the hypothalamic arcuate nucleus (ARC) in order to stimulate the hunger feeling. On the other hand, satiety peptides, including glucagon like peptide-1 (GLP-1), stimulate satiety through prompting POMC/CART neurons in the hypothalamic arcuate nucleus (ARC) and prevent hunger by inhibiting NPY/AgRP neurons [40].

Also, adiposity cues such as leptin and insulin act on neurons in HT, which in turn transmits cues to nerve cells to control satiety and hunger (Fig. 4). Leptin regulates energy balance and inhibits food intake through its action of inhibiting orexigenic peptides such as NPY and AgRP, while promoting anorexigenic peptides such as POMC and CART.

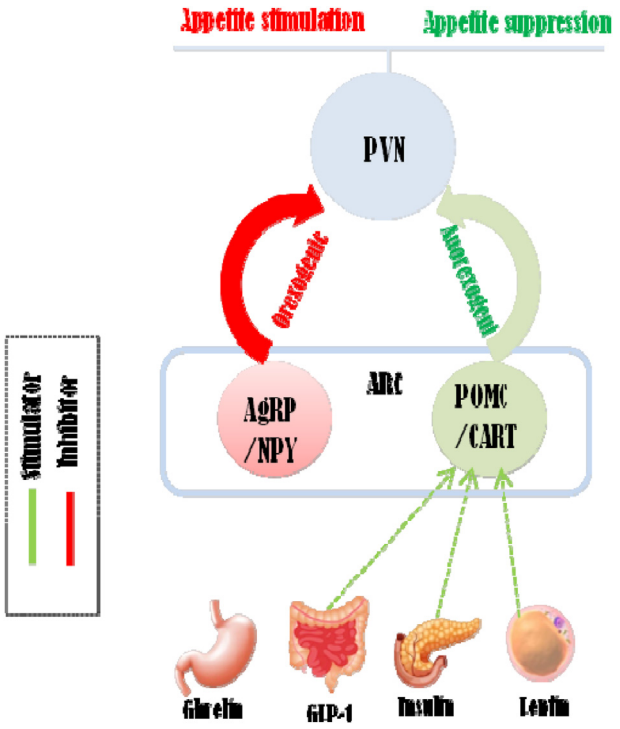

*Fig. 4. A schematic diagram illustrating the hormones pathways involved in appetite regulation. GLP-1 (From small intestine), leptin (from adipose tissue) and insulin (from the pancreas) stimulate POMC/CART neurons and inhibit NPY/AgRP neurons, resulting in appetite suppression, while, ghrelin (from the stomach) activates NPY/AgRP neurons, promoting food intake. The ARC communicates with other hypothalamic nuclei such as the PVH to modulate the feeding behavior. Red arrows indicate stimulatory effects, while green arrows represent inhibitory actions. **Abbreviations:** **ARC:** Arcuate Nucleus of the Hypothalamus, **POMC:** Pro-opiomelanocortin, **AGRP:** Agouti-Related Peptide, **NPY:** Neuropeptide Y, **CART:** Cocaine- and Amphetamine-Regulated Transcript, **PVN:** Paraventricular Nucleus of the Hypothalamus.*

Also, anorexigenic (Inhibit appetite) and orexigenic (Stimulate appetite) signs from nucleus tractus solitarius (NTS) of hindbrain impact hypothalamic neurons, which are effected by peripheral signs working on vagal afferents. In individuals, the energy balance regulation involves not only the expert of various HT areas like: ARC, DMN and PVN, but also other brain areas participate in this regulation [41].

The process of regulating food eating and understanding pleasure from food consumption can be classified into many stages that happen within the brain. During food intake, numerous sensory organs in the mouth and other digestive tract parts send out sensory signs about food characteristics like taste, structure and smell, then, these signs are first explained in specific zones of the brain, such as mesencephalon bridge and thalamus, which are responsible for processing main sensory inputs [42].

After that, the input stored via these principal zones interact with higher brain zones namely, the amygdala and the prefrontal cortex. These zones are in control of more complex tasks, combine cognitive and emotional information (i.e. they assess the pleasant or unpleasant food) and then store this input for future use [43]. For instance, when an individual intakes a certain food and gains an enjoyable experience, these higher brain zones register this experience, thus impact if the individual desires to consume that food again [44].

Nevertheless, despite the value of these neural circuits in controlling food consumption, the central regulation of food intake is not enough to keep a steady body weight over time. This is true because additional agents like dietary habits, the environment and psychological factors, also impact eating food decisions [45].

7. Regulation of feeding in short term way

Hunger and satiety are controlled in the short term way by many cues sent via the gut to the brain depending on the situation of the digestive tract. In the fasting state, when the stomach is empty, the stretch sends signals through the nerves to the brain stem, giving a sign that the body is feeling hungry [46]. Also, the stomach produces and secretes a ghrelin hormone, which plays a main role in activating the feeling of hunger [47]. It is termed the "hunger hormone" which stimulates appetite, rises food intake and stimulates fat storage. It circulates in the bloodstream and works at the hypothalamus mainly the arcuate nucleus, where it stimulates the secretion of the orexigenic peptides NPY and AgRP (which stimulate food intake). Also, ghrelin

has been shown to work on areas of the brain shared in reward processing like the amygdala [48].

Ghrelin links to its receptors in the ARC of the HT and activates AgRP/NPY nerve cells which forward cues to the body to promote hunger and lead to food consumption, slow metabolic processes, and stimulate fat storage in preparation for times of food scarcity [49].

In obesity, there appears to be resistance to ghrelin signaling, leading to impaired appetite regulation. The relationship between ghrelin and obesity is complex. While ghrelin contributes to the regulation of hunger and satiety, altered responsiveness in obesity can lead to difficulty managing weight [50].

When eating food, once it begins to fill up the stomach, the stomach forwards signs to the brain stem, notifying a feeling of fullness because of stomach expansion, which decreases the feeling of hunger [51]. The ghrelin production is stopped, which reduces the stimulation of the hunger [52]. At the same time, the gut secretes many hormones and peptides, such as Cholecystokinin (CKK), glucan like peptide-1 (GLP-1), and peptide YY (PYY). All these peptides act on various zones of the brain involving HT where they contribute to decrease appetite, and promote increase energy expenditure [53].

In this mechanism, the brain receives specific signs about the state of the gut and energy levels, which assist it to control the eating behavior and achieve energy balance in the short term [54].

8. Regulation of feeding in long term way

In the regulation of feeding in the long term way, the body depends on hormonal signs that reflect the quantity of fat stored. The low body fat amount promotes feeding and energy keeping, while the high body fat amount reduces appetite and stimulates energy expenditure. The two principal hormones in this mechanism are leptin and insulin, each of which impacts HT in the brain [55].

Insulin is released from the pancreas into the blood after eating when blood sugar levels increase. In addition to its main role in controlling the levels of blood sugar, insulin impacts appetite via sending signals to the brain [56].

Insulin can enter the brain by being transferred across the blood-brain barrier (BBB) through particular transporters, and it usually enters specific areas of the brain including the hippocampus, striatum, hypothalamus, amygdala, pons, cerebellum, frontal cortices and parietal [57].

Insulin receptors are mostly expressed in the brain, particularly in the hypothalamic nuclei, including the ARC, DMN, and PVN, all of which have a key role in controlling food intake [58].

Leptin is produced by the adipose tissue in a process based on insulin. The quantity of leptin in the blood is proportional to the body fat amount. When the levels of fat are high, leptin also increases and sends cues to the brain that the body has enough stored energy. So, it exerts its anorexigenic impact via the ARC. Within the ARC, there are two principal groups of neurons that carry leptin receptors, namely, POMC/CART neurons and AGRP/NPY neurons [59].

Leptin inhibits its NPY/AgRP neurons that are responsible for rising the appetite. At the same time, it promotes POMC/CART neurons that are responsible for decreasing the appetite and rising energy expenditure. This controlling mechanism aids to keep the energy balance and avert weight gain via prohibiting overconsumption of food and rising calorie expenditure [58,60].

Leptin and insulin interconnect in the brain to regulate food consumption and energy spending. When there are sufficient fat stores, the high levels of leptin act together with high levels of insulin to activate the centers of satiety in HT nuclei to decrease feelings of hunger. In contrast, the low levels of fat lead to reduced levels of leptin, leading to feelings of hunger and a crave to eat food [61].

8.1. Leptin resistance

Obese persons possess raised levels of leptin in their blood proportional to their body fat mass (adipose tissues), but the raised levels of leptin do not act to decrease food intake. So, they lead to gain weight and cause obesity [61].

In simple terms, the inability of high levels of leptin to suppress appetite and reduce weight in obese individuals suggests a relative resistance to the effects of leptin in stimulating weight loss in these individuals.

Many agents participate to decrease the signaling of leptin, but the contribution of each agent differs from person to another. These factors include genetics, lifestyle, changes in cellular signaling, among others [61].

In obesity that occurs because of following a diet with high energy, the person takes in a lot of saturated fatty acids (SFA). These SFAs can travel across BBB and reach a particular zone, namely, HT, which regulates the appetite and satiety. In this area, the SFAs prompt an inflammatory response in the neurons there. This inflammation causes stress on these neurons and weakens their capability to respond to the leptin. Therefore, these neurons

become unable to receive signals from leptin effectively, and this is known as leptin resistance [62].

In spite of the high levels of leptin in the blood as a result of fat accumulation, the brain cannot interpret this as a satiety signal due to leptin resistance. This occurs as a result of a defect in the long form of the leptin receptor (Ob-Rb) in HT. HT is responsible for activating the Janus Kinase 2/Signal Transducer and Activator of Transcription 3 pathway (JAK2/STAT3 which Transmits leptin signals from receptors in the brain to regulate appetite and energy balance).

With obesity, the expression of the Suppressor of Cytokine Signaling 3 (SOCS3) increases, which suppresses the signal and increases the feeling of hunger. This leads to continued eating without feeling satisfied, resulting in weight gain and worsening obesity [63].

8.2. Insulin resistance

Insulin resistance and obesity are increasingly prevalent health conditions worldwide, with obesity being one of the major factors contributing to the improvement of insulin resistance.

Physiologically, insulin resistance is defined as a state characterized by incapability of some types of tissues to response to normal levels of insulin. This causes blood sugar levels to rise, and the pancreas has to secrete more insulin to try to control these levels. In the long run, this situation can stress the pancreas and increase the risk of developing type 2 diabetes and metabolic syndrome [64].

It is worth noting that insulin plays a fundamental role in regulating blood sugar levels, such as inhibiting high blood sugar levels, preventing fat breakdown, increasing glucose absorption into cells, and stimulating the synthesis of both glycogen and proteins. All of the above roles are not observed in insulin-resistant tissues.

Obesity, especially central obesity (excess fat around the abdomen), is a major factor contributing to the development of insulin resistance. Excess fat releases hormones and inflammatory factors that negatively affect the effectiveness of insulin. In fact, people who have overweight are more likely to develop insulin resistance than those of normal weight, a condition that is exacerbated by a sedentary lifestyle and overeating [65].

Insufficient leptin signaling in HT, which is produced via either reduced availability of leptin for delivering HT (Leptinopenia case), or limited leptin passing across BBB (Hyperleptinemia case in obese persons), is mainly responsible for stimulating hyperglycemia (high blood glucose) and hyperinsulinemia (high blood insulin) [66].

9. Conclusion

Obesity is a main public health problem affecting an important proportion of children and adults worldwide. It is associated with increased mortality rates and a higher risk of numerous diseases including chronic inflammation, cardiovascular diseases, and type 2 diabetes. This study explains the biological mechanisms which prefer unhealthy foods, with a specific focus on hypothalamus, a main brain region implicated in controlling food intake. Understanding how the neural circuits affect nutritional choices might offer visions into obesity prevention and intervention strategies.

Ethics information

None: because this review did not involve any samples (human or animals), and thus, it was not necessary to get ethical approval in accordance with institutional and national guidelines.

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Conflicts of interest

The authors declare that they have no competing interests.

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References

[1] J.M. Jurek, A. Maruda, The role of emotional eating as relief mechanism from psychological distress and its impact on overall wellbeing, Debates em Psiquiatria 14 (14) (2024) 1–23, https://doi.org/10.25118/2763-9037.2024.v14.1268.

[2] L. Wenhua, N. Dongsheng Tang, L. Qin, Z. Zhu, Multimodal neuroimaging of obesity: from structural-functional mechanisms to precision interventions, Brain Sci. 5 (2025) 446, https://doi.org/10.3390/brainsci15050446.

[3] J.R. Speakman, J.M. de Jong, S. Sinha, K.R. Westerterp, Y. Yamada, H. Sagayama, P.N. Ainslie, L.J. Anderson, L. Arab, K. Bedu-Addo, S. Blanc, Total daily energy expenditure has declined over the past three decades due to declining basal expenditure, not reduced activity expenditure, Nat. Metab. 4 (2023) 579–588, https://doi.org/10.1038/s42255-023-00782-2.

[4] S. Esposito, M. Bonaccio, E. Ruggiero, S. Costanzo, A. Di Castelnuovo, A. Gialluisi, V. Esposito, G. Innocenzi, S. Paolini, C. Cerletti, M.B. Donati, Food processing and risk of central nervous system tumours: a preliminary case–control analysis from the MEditerranean DIet in relation to CancEr of brAin (MEDICEA) study, Clin. Nutr. 2 (2023) 93–101, https://doi.org/10.1016/j.clnu.2022.11.016.

[5] R. Rajesh Kumar, B. Bromage, J. De Neve, A. Barik, Lifestyle risk factors for overweight and obesity among rural Indian adults: a community-based prospective cohort study, J. Nutr. Sci. 14 (2025) 18, https://doi.org/10.1017/jns.2025.4.
[6] J. Song, S.Y. Choi, Arcuate nucleus of the hypothalamus: anatomy, physiology, and diseases, Exp. Neurobiol. 6 (2023) 371–386, https://doi.org/10.5607/en23040.
[7] H.W. Gan, M. Cerbone, M.T. Dattani, Appetite-and weight-regulating neuroendocrine circuitry in hypothalamic obesity, Endocr. Rev. 3 (2024) 309–342, https://doi.org/10.1210/endrev/bnad033.
[8] Q. Wu, J. Chen, T. Hua, J. Cai, Alpha-melanocyte-stimulating hormone-mediated appetite regulation in the central nervous system, Neuroendocrinol. 9 (2023) 885–904, https://doi.org/10.1159/000530804.
[9] I. Ramasamy, Physiological appetite regulation and bariatric surgery, J. Clin. Med. 5 (2024) 1347, https://doi.org/10.3390/jcm13051347.
[10] S.S. Daundasekara, K.R. Arlinghaus, C.A. Johnston, Quality of life: the primary goal of lifestyle intervention, Am. J. Lifestyle Med. 3 (2020) 267–270, https://doi.org/10.1177/1559827620907309.
[11] M.M. Shams-White, T.E. Pannucci, J.L. Lerman, K.A. Herrick, M. Zimmer, K.M. Mathieu, E.E. Stoody, J. Reedy, Healthy eating index-2020: review and update process to reflect the dietary guidelines for Americans, 2020-2025, J. Acad. Nutr. Diet. 9 (2023) 1280–1288, https://doi.org/10.1016/j.jand.2023.05.015.
[12] L. Cloetens, L. Ellegård, Energy–a scoping review for the Nordic Nutrition Recommendations 2023 project, Food Nutr. Res. 67 (2023) 10–29219, https://doi.org/10.29219/fnr.v67.10233.
[13] M.S.H. Khan, S.Q.A. Kim, R.C. Ross, F. Corpodean, R.A. Spann, D.A. Albarado, S.O. Fernandez-Kim, B. Clarke, H.R. Berthoud, H. Münzberg, D.H. McDougal, D. H, FGF21 acts in the brain to drive macronutrient-specific changes in behavioral motivation and brain reward signaling, Mol. Metabol. 91 (2025) 102068, https://doi.org/10.1016/j.molmet.2024.102068.
[14] G. Corsetti, E. Pasini, T.M. Scarabelli, C. Romano, A. Singh, C.C. Scarabelli, F.S. Dioguardi, Importance of energy, dietary protein sources, and amino acid composition in the regulation of metabolism: an indissoluble dynamic combination for life, Nutrients 15 (2024) 2417, https://doi.org/10.3390/nu16152417.
[15] Y. Feng, Y. Chen, X. Wu, J. Chen, Q. Zhou, B. Liu, L. Zhang, C. Yi, Interplay of energy metabolism and autophagy, Autophagy 2 (2024) 4–14, https://doi.org/10.1080/15548627.2023.2247300.
[16] C.R. Ferrario, H. Münzberg-Gruening, L. Rinaman, J.N. Betley, S.L. Borgland, M. Dus, D.A. Fadool, K.F. Medler, G.J. Morton, D.A. Sandoval, C.B. de La Serre, Obesity-and diet-induced plasticity in systems that control eating and energy balance, Obesity 8 (2024) 1425–1440, https://doi.org/10.1002/oby.24060.
[17] V. Calcaterra, H. Cena, V. Rossi, S. Santero, A. Bianchi, G. Zuccotti, Ultra-processed food, reward system and childhood obesity, Children 5 (2023) 804, https://doi.org/10.3390/children10050804.
[18] D.J. Baer, M. Dalton, J. Blundell, G. Finlayson, F.B. Hu, Nuts, energy balance and body weight, Nutrients 5 (2023) 1162, https://doi.org/10.3390/nu15051162.
[19] S. Nutter, L.A. Eggerichs, T.S. Nagpal, X. Ramos Salas, C. Chin Chea, S. Saiful, J. Ralston, O. Barata-Cavalcanti, C. Batz, L.A. Baur, S. Birney, Changing the global obesity narrative to recognize and reduce weight stigma: a position statement from the World Obesity Federation, Obes Rev. 1 (2024) 13642, https://doi.org/10.1111/obr.13642.
[20] C. Boutari, C.S. Mantzoros, A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on, Metabolism 133 (2022) 155217, https://doi.org/10.1016/j.metabol.2022.155217.
[21] I. Lingvay, R.V. Cohen, C.W. le Roux, P. Sumithran, Obesity in adults, Lancet 10456 (2024) 972–987, https://doi.org/10.1016/S0140-6736(24)01210-8.
[22] N. Shinozaki, K. Murakami, S. Masayasu, S. Sasaki, Highly processed food consumption and its association with anthropometric, sociodemographic, and behavioral characteristics in a nationwide sample of 2742 Japanese adults: an analysis based on 8-day weighed dietary records, Nutrients 5 (2023) 1295, https://doi.org/10.3390/nu15051295.
[23] C.A. Sutton, M. Stratton, A.M. L'Insalata, T.L. Fazzino, Ultraprocessed, hyper-palatable, and high energy density foods: prevalence and distinction across 30 years in the United States, Obesity 1 (2024) 166–175, https://doi.org/10.1002/oby.23897.
[24] T.L. Fazzino, K.L. Kong, A new paradigm for investigating the etiology of obesity in early childhood: exposure to added sugars and hyper-palatable foods in infancy and dysregulation of food reinforcement processes, Obes. Rev. 2 (2023) 1–24, https://doi.org/10.1111/obr.13526.
[25] F. Díaz-Castro, E. Morselli, M. Claret, Interplay between the brain and adipose tissue: a metabolic conversation, EMBO Rep. 12 (2024) 5277–5293, https://doi.org/10.1038/s44319-024-00321-4.
[26] J.Q. Purnell, C.W. le Roux, Hypothalamic control of body fat mass by food intake: the key to understanding why obesity should be treated as a disease, Diabetes, Obes. Metabol. 26 (2024) 3–12, https://doi.org/10.1111/dom.15478.
[27] J.A. Rusch, B.T. Layden, L.R. Dugas, Signalling cognition: the gut microbiota and hypothalamic-pituitary-adrenal axis, Front. Endocrinol. 14 (2023) 1130689, https://doi.org/10.3389/fendo.2023.1130689.
[28] P. Toh, J.L. Nicholson, A.M. Vetter, M.J. Berry, D.J. Torres, Selenium in bodily homeostasis: hypothalamus, hormones, and highways of communication, Int. J. Mol. Sci. 23 (2022) 15445, https://doi.org/10.3390/ijms232315445.
[29] D. Grassi, M. Marraudino, L.M. García-Segura, G.C. Panzica, The hypothalamic paraventricular nucleus as a central hub for the estrogenic modulation of neuroendocrine function and behavior, Front. Neuroendocrinol. 65 (2022) 100974, https://doi.org/10.1016/j.yfrne.2021.100974.
[30] M.N. Lord, E.E. Noble, Hypothalamic cannabinoid signaling: consequences for eating behavior, Pharmacol. Res. Perspect. 5 (2024) 1251, https://doi.org/10.1002/prp2.1251.
[31] M. Iovino, T. Messana, S. Marucci, D. Triggiani, V.A. Giagulli, E. Guastamacchia, G. Piazzolla, G. De Pergola, G. Lisco, V. Triggiani, The neurohypophyseal hormone oxytocin and eating behaviors: a narrative review, Hormones 1 (2024) 15–23, https://doi.org/10.1007/s42000-023-00505-y.
[32] M. Arcon, The interplay between hypothalamic and brainstem nuclei in homeostatic control of energy balance, Behav. Brain Res. 480 (2025) 115398, https://doi.org/10.1016/j.bbr.2024.115398.
[33] G.S. Clarke, A.J. Page, S. Eldeghaidy, The gut–brain axis in appetite, satiety, food intake, and eating behavior: insights from animal models and human studies, Pharmacol. Res. Perspect. 5 (2024) 70027, https://doi.org/10.1002/prp2.70027.
[34] A. Lachance, J. Daoust, M. Pelletier, A. Caron, A.C. Carpentier, L. Biertho, J. Maranzano, A. Tchernof, M. Dadar, A. Michaud, Changes in hypothalamic subunits volume and their association with metabolic parameters and gastrointestinal appetite-regulating hormones following bariatric surgery, medRxiv 31 (2024) 2024–2028, https://doi.org/10.1101/2024.08.30.24312638.
[35] S.E. Racine, V. Trolio, E.A.E. Miller, A. Mehak, E. Bicaker, S. Wilson, D. Stephen Benning, Testing a reward-processing model of negative urgency in women with and without binge eating, Clin. Psychol. Sci. 2 (2025) 407–424, https://doi.org/10.1177/21677026241267996.
[36] M. Romaní-Pérez, R. Líebana-García, A. Flor-Duro, D. Bonillo-Jiménez, C. Bullich-Vilarrubias, M. Olivares, Y. Sanz, Obesity and the gut microbiota: implications of neuroendocrine and immune signaling, FEBS J. 6 (2024) 1397–1420, https://doi.org/10.1111/febs.17249.

[37] M. Zhang, L. Zhu, G. Wu, H. Zhang, X. Wang, X. Qi, The impacts and mechanisms of dietary proteins on glucose homeostasis and food intake: a pivotal role of gut hormones, Crit. Rev. Food Sci. Nutr. 33 (2024) 12744–12758, https://doi.org/10.1080/10408398.2023.2256400.
[38] E. Rodríguez-Vázquez, A. Aranda-Torrecillas, M. López-Sancho, J.M. Castellano, M. Tena-Sempere, Emerging roles of lipid and metabolic sensing in the neuroendocrine control of body weight and reproduction, Front. Endocrinol. 15 (2024) 1454874, https://doi.org/10.3389/fendo.2024.1454874.
[39] B. Zhou, H. Ran, Q. Zhang, H. Chen, F. Han, C. Xu, Q. Zhao, Unveiling the impact of rapeseed meal on feeding behavior and anorexigenic endocrine in litopenaeus vannamei, Animals 4 (2024) 540, https://doi.org/10.3390/ani14040540.
[40] R. Stark, The olfactory bulb: a neuroendocrine spotlight on feeding and metabolism, J. Neuroendocrinol. 6 (2024) 13382, https://doi.org/10.1111/jne.13382.
[41] S.A. Boor, J.D. Meisel, D.H. Kim, Neuroendocrine gene expression coupling of interoceptive bacterial food cues to foraging behavior of C, elegans, Elife 12 (2024) 91120, https://doi.org/10.7554/eLife.91120.
[42] D. Ni, H.E. Smyth, D. Cozzolino, M.J. Gidley, Holistic approach to effects of foods, human physiology, and psychology on food intake and appetite (satiation & satiety), Crit. Rev. Food Sci. Nutr. 12 (2024) 3702–3712, https://doi.org/10.1080/10408398.2022.2134840.
[43] A.J. Dijker, Moderate eating with pleasure and without effort: toward understanding the underlying psychological mechanisms, Health Psychol. Open 2 (2019) 2055102919889883, https://doi.org/10.1177/2055102919889883.
[44] R.J. Stevenson, The psychological basis of hunger and its dysfunctions, Nutr. Rev. 10 (2024) 1444–1454, https://doi.org/10.1093/nutrit/nuad092.
[45] D. Garcia-Burgos, P. Wilhelm, C. Vögele, S. Munsch, Food restriction in anorexia nervosa in the light of modern learning theory: a narrative review, Behav. Sci. 2 (2023) 96, https://doi.org/10.3390/bs13020096.
[46] H.R. Berthoud, V.L. Albaugh, W.L. Neuhuber, Gut-brain communication and obesity: understanding functions of the vagus nerve, J. Clin. Investig. 10 (2021), https://doi.org/10.1172/JCI143770, 17-13.
[47] G.K. Frank, M.E. Shott, J. Stoddard, S. Swindle, T.L. Pryo, Association of brain reward response with body mass index and ventral striatal-hypothalamic circuitry among young women with eating disorders, JAMA Psychiatr. 10 (2021) 1123–1133, https://doi.org/10.1001/jamapsychiatry.2021.1580.
[48] W. Wu, L. Zhu, Z. Dou, Q. Hou, S. Wang, Z. Yuan, B. Li, Ghrelin in focus: dissecting its critical roles in gastrointestinal pathologies and therapies, Curr. Issues Mol. Biol. 1 (2024) 948–964, https://doi.org/10.3390/cimb46010061.
[49] I. Rubinić, M. Kurtov, R. Likić, Novel pharmaceuticals in appetite regulation: exploring emerging gut peptides and their pharmacological prospects, Pharmacol. Res. Perspect. 4 (2024) 1243, https://doi.org/10.1002/prp2.1243.
[50] M. Perello, S.L. Dickson, J.M. Zigman, L. Leggio, Ghrelin Nomenclature Consensus Group, toward a consensus nomenclature for ghrelin, its non-acylated form, liver expressed antimicrobial peptide 2 and growth hormone secretagogue receptor, J. Neuroendocrinol. 1 (2023) 13224, https://doi.org/10.1111/jne.13224.
[51] M. Iovino, T. Messana, G. Lisco, F. Mariano, V.A. Giagulli, E. Guastamacchia, G. De Pergola, V. Triggiani, Neuroendocrine modulation of food intake and eating behavior, Endocr. Metab. Immune Disord. -Drug Targets (Formerly Current Drug Targets-Immune, Endocrine Metab. Disord.) 13 (2022) 1252–1262, https://doi.org/10.2174/1871530322666220127114326.
[52] Z. Guleken, T. Uzbay, Neurobiological and neuropharmacological aspects of food addiction, Neurosci. Biobehav. Rev. 139 (2022) 104760, https://doi.org/10.1016/j.neubiorev.2022.104760.
[53] E. Baranek, C. Heraud, L. Larroquet, A. Surget, A. Lanuque, F. Terrier, S. Skiba-Cassy, R. Jérôme, Long-term regulation of fat sensing in rainbow trout (Oncorhynchus mykiss) fed a vegetable diet from the first feeding: focus on free fatty acid receptors and their signalling, Br. J. Nutr. 1 (2024) 1–6, https://doi.org/10.1017/S0007114523001599.
[54] X. Zhao, Y. Qiu, L. Liang, X. Fu, Interkingdom signaling between gastrointestinal hormones and the gut microbiome, Gut Microbes 1 (2025) 2456592, https://doi.org/10.1080/19490976.2025.2456592.
[55] H.L. Hübner, T. Bartelmeß, Associations of sugar-related food parenting practices and parental feeding styles with prospective dietary behavior of children and adolescents: a systematic review of the literature from 2017 to 2023, Front. Public Health 12 (2024) 1382437, https://doi.org/10.3389/fpubh.2024.1382437.
[56] A.I. Aedh, M.S. Alshahrani, M.A. Huneif, I.F. Pryme, R. Oruch, A glimpse into milestones of insulin resistance and an updated review of its management, Nutrients 4 (2023) 921, https://doi.org/10.3390/nu15040921.
[57] D.A. Wittekind, J. Kratzsch, R. Mergl, R. Baber, K. Wirkner, M.L. Schroeter, A.V. Witte, A. Villringer, M. Kluge, Leptin, but not ghrelin, is associated with food addiction scores in a population-based subject sample, Front. Psychiatr. 14 (2023) 1201, https://doi.org/10.3389/fpsyt.2023.1200021.
[58] A.G. Izquierdo, A.B. Crujeiras, F.F. Casanueva, M.C. Carreira, Leptin, obesity, and leptin resistance: where are we 25 years later? Nutrients 11 (2019) 2704, https://doi.org/10.3390/nu11112704.
[59] G.G. de Assis, E. Murawska-Ciałowicz, Exercise and weight management: the role of leptin—a systematic review and update of clinical data from 2000–2022, J. Clin. Med. 13 (2023) 4490, https://doi.org/10.3390/jcm12134490.
[60] D.A. Wittekind, J. Kratzsch, R. Mergl, R. Baber, K. Wirkner, M.L. Schroeter, A.V. Witte, A. Villringer, M. Kluge, Leptin, but not ghrelin, is associated with food addiction scores in a population-based subject sample, Front. Psychiatr. 14 (2023) 1200021, https://doi.org/10.3389/fpsyt.2023.1200021.
[61] J. Jakubiec, J. Gmitrzuk, Z. Malinka, K. Wiśniewska, A. Jachymek, M. Opatowska, M. Karasiński, Obesity in adults: causes, health consequences, and treatment methods, Quality Sport 17 (2024) 53051, https://doi.org/10.12775/QS.2024.17.53051 (2024) 53051.
[62] C. Sanchez, C. Colson, N. Gautier, P. Noser, J. Salvi, M. Villet, L. Fleuriot, C. Peltier, P. Schlich, F. Brau, A. Sharif, Dietary fatty acid composition drives neuroinflammation and impaired behavior in obesity, Brain Behav. Immun. 117 (2024) 330–346, https://doi.org/10.1016/j.bbi.2024.01.216.
[63] A. Rivas-Domínguez, H. Mohamed-Mohamed, M. Jimenez-Palomares, V. García-Morales, L. Martinez-Lopez, M.L. Orta, J.J. Ramos-Rodriguez, B. Bermudez-Pulgarin, Metabolic disturbance of high-saturated fatty acid diet in cognitive preservation, Int. J. Mol. Sci. 9 (2023) 8042, https://doi.org/10.3390/ijms24098042.
[64] W. Yang, W. Jiang, S. Guo, Regulation of macronutrients in insulin resistance and glucose homeostasis during type 2 diabetes mellitus, Nutrients 21 (2023) 4671, https://doi.org/10.3390/nu15214671.
[65] Y. Yanagisawa, How dietary amino acids and high protein diets influence insulin secretion, Physiol. Rep. 2 (2023) 15577, https://doi.org/10.14814/phy2.15577.
[66] M. Heni, The insulin resistant brain: impact on whole-body metabolism and body fat distribution, Diabetologia 7 (2024) 1181–1191, https://doi.org/10.1007/s00125-024-06104-9.