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Hormones, Peptides and Neurotransmitters, Effects on Appetite Regulation and their Relationship to Obesity: Systematic Review

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KEYWORDS
Obesity, appetite, hypothalamus, gut hormones, physical exercise, food intake, Oxytocin

ABSTRACT

Background: Appetite regulation is a highly synchronized process that depends on the interaction of multiple hormones and neurotransmitters. These hormones are secreted by different parts of the body modifying hunger, satiety, and gastrointestinal motility, which affect appetite. The two primary mechanisms regulating appetite involve central nervous system regulators and peripheral regulators. More over hypothalamus has a major impact on appetite regulation.

Aim: to go over current research on how hormones, peptides, and neurotransmitters affect how we eat and how obesity is related to these effects.

Method: Studies published in English from 2000 to August 2022 that discussed appetite hormones, regulation and their connection to obesity were included in this systematic review. Research articles with free full-text, reviews, systematic reviews, meta-analyses, clinical trials, and randomized controlled trials were included. This systemic review was obtained from PubMed/Medline, Scopus, Google Scholar, and Hinari sources using an electronic web-based search approach. Subject headings (e.g., MeSh in PubMed/MEDLINE) were used as search terms for every database. The search was made more narrowly and more broadly using Boolean operators like (AND, OR).

Result: 510 studies were accessed and screened from different databases. 216 publications were evaluated after titles, abstracts, and duplicates were eliminated from the data; 90 of these met the requirements for full-text studies, accessibility and having critical information. All told, 90 studies were taken into account for this systematic review.

Conclusion: In healthy people, eating is tightly controlled by a homeostatic and hedonic controller by initiating the desire to eat or stop eating when required energy is obtained from external sources. Obesity can result from the dysregulation of this system.

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Methods

Eligibility criteria

This systematic review included studies published in English from 2000 to August 2022 that discussed the regulation of appetite hormones and their connection to obesity. Free full-text studies, clinical trials, randomized controlled trials, systematic reviews, meta-analyses, and review articles were included. Studies were obtained from PubMed/Medline, Scopus, Google Scholar, and Hinari databases using an electronic web-based search approach. Subject headings (e.g. MeSh in MEDLINE/PubMed) and words in free text were used as search terms for each database. The search was narrower and wider using Boolean operators such as (AND, OR).

The Literature Search Strategy:

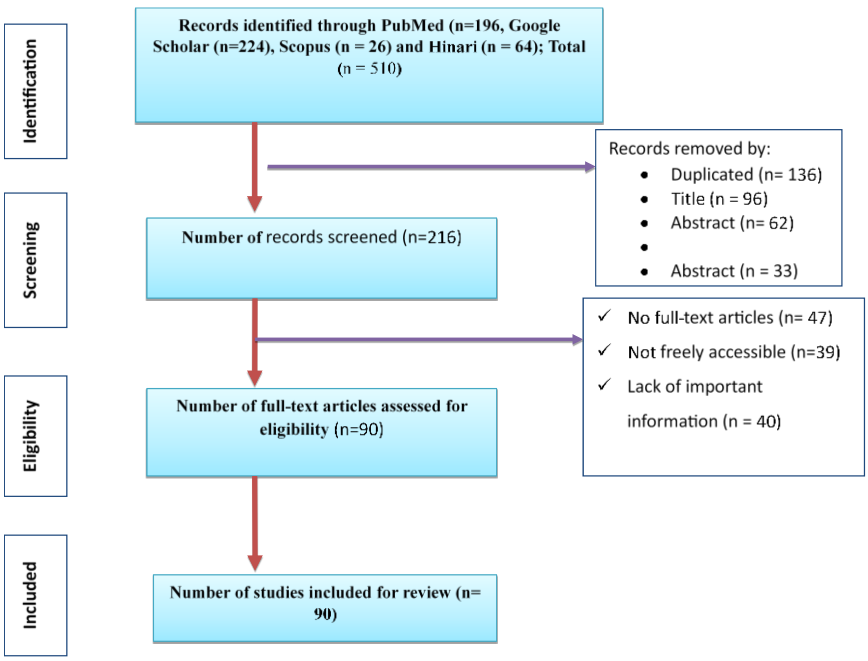
Finding both published and unpublished studies is the goal of the literature search strategies used. The reviewed studies were found on PubMed/Medline, Scopus, and Google Scholar using an electronic web-based search approach. Subject headings (such as MeSh in MEDLINE/PubMed) and words in free text for the idea of "Obesity," "Hypothalamus," "AgRP/POMC," "appetite," "pathogenesis," "food intake," and "brainstem," the following search terms were used. "Endocannabinoids," "endogenous opioid system," "cholecystokinin," "intestinal peptide PYY3-36," "melanocortins," "α-MSH," "Neurotensin," "corticotropin releasing hormone," "neuropeptide Y," "orexins," "galanin," "melanin concentrating hormone," "endocannabinoids," "Obestatin," "Ghrelin," and "Glucagon-like peptide-1," "peptide YY," "gastric inhibitory polypeptide," "Leptin," "adiponectin," "Resistin," "Insulin," "Pancreatic polypeptide," "Amylin," "Oxytocin," "sex hormones," and "physical exercise" were used. The search was made narrower and broader using boolean operators, such as (AND, OR).

Study selection

To remove duplicates and view appropriate abstracts and titles, all the articles were imported into EndNote X7 For data management purposes, studies that qualified the criteria with full text were imported into Mendeley Reference Manager Version 2.51.0.

Result

510 studies were accessed in different databases. After eliminating titles, abstracts, and duplicates from the data, 216 publications were evaluated. Of the 216 articles included, 90 met the requirements for full-text studies, were publicly available, and had critical information. Overall, 90 studies were taken into account in this systematic review.



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Review Output

In this Systematic review we targeted to present advancement of information on the effect of neurotransmitters, peptides hormones on appetite regulation and their connection to obesity. The epidemiology and pathogenesis of obesity; the role hypothalamus, brainstem, midbrain, gut, pancreas, adipocyte, oxytocin hormone, sex hormones and physical exercise on appetite control were reviewed.

Review Output

In this systematic review, we aim to present advances in information on the effects of neurotransmitters and peptide hormones on appetite regulation and their connection to obesity. We reviewed the epidemiology and pathogenesis of obesity, including the role of the hypothalamus, brainstem, midbrain, gut, pancreas, adipocytes, oxytocin hormone, sex hormones, and physical exercise on appetite control.

In table 1 and 2, we tried to tabulate recently studied research articles done on Humans and Animals to show the effect of hormone and peptides on appetite and obesity.

Table 1. recent studies on Human model's

Autor	Research Design	Study participant Male/female	Age	BMI	Result
(2019)(15)	Experimental	40 Type 2 Diabetic and obese patients of both sex	18-75 Years	30kg/m^2	Participants having elevated BMI, glycemia and TG prior to aGLP-1 therapy showed good response after aGLP-1 therapy. Fasting ghrelin and GLP-1 level were elevated in participants with BMI loss ≥5 but ghrelin levels were decreased in post nutritional states.
(2019)(16)	Cross-sectional	55 intact females	10-45 years		Mean oxytocin level were1011.2 ± 52.3pg/ml in fasting state, while at 30 and 60minutes post meal, there was significant reduction with p value of 0.001 and 0.003. The level of Oxytocin was reduced in the starting to midfollicular phase of menstrual cycle with a significant p value and higher in younger females (P = 0.002).
(2021)(17)	A Randomized controlled trial	N= 8 for each trial	21.8 ± 2.1	21.8± 1.4 kg/m^2	Food intake and impulse to eat was elevated after moderate intensity (MI) exercise than high intensity (HI) exercise The willingness to eat was higher in HI than MI subsequent to exercise and immediately after meal.. Plasma insulin was higher after meal in SD than MI and higher in MI than HI. Plasma ghrelin was higher in SD compared with MI and HI subsequent to meal.
(2022)(18)	Case control study	N=42	18-48 years	25≤BMI<40	The study pointed out that there is a positive correlation between insulin and RMR, but there is a negative correlation between ghrelin and RMR. From the collected questioner the desire to eat and starvation have positive correlation with RMR, but not significant correlation with leptin and RMR. The study pointed out that there exists inverse correlation between the level of ghrelin hormone and RMR (P-value=0.027), while there is a positive correlation between insulin hormone level and RMR P-value=0.001), leptin levels and RMR were not significantly correlated.
(2022)(19)	Experimental	N=24, 12 men and 12 women	18-35 years		During the time of food deprivation both sexes had equal desire to eat and ghrelin level. But following eating women reach the highest level of fullness before men (p=0.007). following meal, Ghrelin inhibition was higher in women (p=0.041)

(2022)(15)	Case control	N= 200	12.8 ± 3.6 years		There is no significant difference between overweight and non-overweight in case of protein, fat and roughage diets. The cases had less liking for predicted meals having elevated sucrose and complex carbohydrates. FT4 is a strong marker of food that carry saturated and polyunsaturated fatty acid and protein diets but is having inverse association with roughage diets. exclusively found in obese adolescents.

Table 2 recent studies on Animal model's

Autor's	Design	Study animals	age	Result
(2004)(20)	Experimental	Male rat n=12 per group.Food intake weighted at 2, 4,8 and 24 hr post T3 injection.	7-8 weeks	Meal intake increased substantially by 140% 2 hr after subcutaneous T3 injection (4.5 nmol/kg) ($P< 0.05$). Lower dose had no effect. 24 hr post injection had no stimulatory effect. There was no effect seen on plasma leptin level post 2hr T3 injection
(2016)(21)	Experimental	Male rat n= 70		Intra VTA injection of orexin A significantly increased sucrose intake ($p<0.01$), increased first meal size ($p<0.05$). Bilateral intra VTA injection of orexin A receptor antagonist (SB334867) suppresses sucrose intake after 30 minute ($p<0.05$).
(2017)(2)	Experimental	Male mice are used n≥5 for each trial at least 5 trial, for expression n=5 for single trial	7-9 week at time of surgery 16-20 week after experiment	Denial of meal or optogenetic enhancement of AgRP neurons stimulate the feeding and resists the food inhibitory effects of amylin, CCK, and LiCl, but not LPS.. Photostimulation of AgRP neurons can also enhance meal intake by reducing the Fos expression in PBN CGRP neurons at the time of chemogenetic-mediated activation.
(2019)(22)	Experimental	Male Sprague Dawley rat divided into two groups (n=9 well feed, n=13 food deprived).	12 weeks Average weight 400g	Administration of intraperitoneal OT injection after 22h and 2h of fasting, no significant change is seen, but in the case of 2h fasting rat undergoing C-Fos immunohistochemistry, change is observed from the feeding center of hypothalamic nuclei except ARC, VMH, and DMH ($p= 0.001$).
(2021)(23)	Experimental	24 female rats. 8 served as control for locomotor activity. 16 were divided into two groups. 8 for oxytocin injection and 8 as control for 12 days.		i.p high dose OT injection were significantly decrease eating, weight and visceral fat, and also reduce serum TG and LDL-cholesterol level, but does not affect liver, kidney and movement activity.

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Epidemiology of Obesity

Obesity is a cause for a variety of non-transmitted diseases and is considered a real health threat across the world. Obesity is manifested by inharmony between food consumption and energy consumption at any age. Obesity is categorized by body mass index (BMI) as overweight (BMI = 25.0–29.9 kg/m2) or obese (BMI 30.0 kg/m2). According to the Center for Disease Control (CDC), in 2022, the prevalence of obesity was 41.5% in the age group of >60 years, 44.3% in the age group of 40–59 years, and 39.8% in the age interval of 20–39 years (15–18). Obese patients are at major risk for more than one illness simultaneously, such as heart problems, elevated lipid profiles, increased blood glucose levels, diseases of the alimentary canal, connective and muscular diseases, respiratory issues, and psychiatric problems, all of which directly affect routine activities and ultimately succumb to death(19,20). Consumption of energy-dense food and feeding habit culture, excess alcohol consumption, confectionaries, sugars, soft drinks, and fats are highly correlated with chronic diseases and increase the occurrence of obesity (21). In 2016, the World Health Organization (WHO) reported that 75% of the world population suffers from obesity and overweight, of which 1.9 billion are adults and around 400 million are children and teenagers(22). Obese children have a high propensity for lung problems, bone disintegration, high blood pressure, impaired insulin sensitivity, psychological issues, and a high risk of premature death and disability in adulthood(23).

Hypothalamic control of appetite

Fuel expenditure and feeding control signals are highly integrated in the hypothalamus of the brain. In addition to integrating and generating coordinated feedback for metabolic signals, central neural input, hormonal signals, nutritional input, and input from peripheral circulation, the hypothalamus is involved in coordinating the activity of the arcuate nucleus (ARC), which encloses Agouti-Related Proteins and Neuropeptide Y, which induces appetite and Pro-Opiomelanocortin and Cocaine- and Amphetamine-Regulated Transcript that suppresses appetite. Arcuate nuclei lesions result in obesity and overweight (24–27). The dorsomedial nucleus, paraventricular nucleus, ventromedial nucleus, lateral hypothalamic area, and arcuate nucleus are the five hypothalamic nuclei that regulate food intake and energy expenditure [28]. By receiving neural input from the lateral hypothalamic area and paraventricular nucleus, the arcuate nucleus suppresses feeding activity by activating corticotropin-releasing hormone and oxytocin(29). Once activated by ghrelin, NPY and AgRP are involved in initiating the center of eating, whereas hormones that release α-MSH stimulate fullness, which is triggered by POMC (30).

Pro-opiomelanocortin (POMC)

POMC, which consists of 241 amino acid residues, activates melanocortin peptides such as ACTH and α, β, and γ-melanocyte-stimulating hormone (MSH) through the action of MC1 R through MC5 R receptors that suppress food intake. Obesity may result from the pathogenic action of POMCs and MC4 receptor mutation (31–33).

Neurotensin (NT)

Neurotensin (NT) is a 13-amino acid peptide found throughout the brain and the gastrointestinal tract (GIT). It suppresses food intake by activating neurotensin receptors 1,2, and 3. They are also involved in thermoregulation, modulation of dopaminergic transmission, and pituitary hormone secretion (34,35).

Corticotropin-releasing hormone (CRH)

The paraventricular nucleus generates corticotropin-releasing hormone that suppresses food intake. Corticotropin Releasing Hormone administration decreases gastric emptying and stomach acid secretion while increasing colonic motility, leading to emptying of the bowels (36). The medial parvocellular paraventricular nucleus of the hypothalamus, which regulates acute hunger, releases CRH in response to stress. Type 1 CRH and typ2 CRH information to the ARC of the hypothalamus inhibits NPY/AgRP neuron secretion, which activates food intake(37).

Neuropeptide Y (NPY)

A 36-amino acid peptide known as NPY is highly abundant in the central nervous system (CNS), paraventricular nucleus, and outside the CNS, mainly in GIT. NPY has 70% homology with peptide YY (PYY) and 50% homology with the pancreatic polypeptide. NPY is activated by neuropeptide 1 and neuropeptide 5 receptors to modulate food intake, increase appetite, and stimulate eating, which is a key activity in controlling appetite and energy homeostasis (38,39).

Agouti-related peptides (AgRP)

AgRP is a neuropeptide produced in the brain by AgRP/NPY neurons. The gene encodes 132 amino acid peptides that resemble agouti. It is an essential melanocortin signaling regulator. AgRP neurons are found in the hypothalamus and co-exhibit both neuropeptide Y and the neurotransmitter gamma-aminobutyric acid. It is a potent orexigenic peptide that increases appetite when injected centrally. AgRP works to suppress metabolism and energy expenditure while increasing appetite (40)

Orexins

Orexin A/hypocretin 1 and Orexin B/hypocretin 2 are peptide hormones. (OX A/Hcrtr1) is composed of 33 amino acids with two intrachain disulfide bonds and (OX B/Hcrtr2) is composed of 28 amino acids and is activated by both Orexin/hypocretin-1 and Orexin/hypocretin-2 receptors. These hormones were first discovered to control hunger centers; however, they are now involved in feeding behavior management and sleep/wakefulness cycle modulators(41). Orexin A activity is highly amplified by the orexin/hypocretin-1 receptor, but the Orixin 2 receptor has equal affinity for both neuropeptides (42). Orexins stimulate orexin neurons, which act as monoamine and Ach neurotransmitters in the CNS to sustain a prolonged, coherent awake period. Moreover, orexins play a role in drug addiction mechanisms and reward systems(43). Studies have revealed that orexin-A increases appetite by lowering the behaviorally normal satiety center(44).

Galanin (Gal)

Galanin is a 29-amino acid peptide secreted from the locus coeruleus, dorsal raphe nucleus, rostral ventrolateral medulla, as well as the gut and spinal cord Galanin, which is administered intraventricularly or through the hypothalamus, stimulates feeding in satiated rats(45). Gralanin influences energy balance, neuropathic pain, alcohol consumption, impaired insulin activity, and controls pituitary hormone secretion(46). To date, three different types of galanin receptors (GalR1, GalR2, and GalR3) have been discovered by molecular cloning techniques (47,48). Studies have shown that galanin plays a role in feeding and body weight regulation(49).

Melanin Concentrating Hormone (MCH) Level

The lateral hypothalamus synthesizes this 19-amino-acid peptide, which binds to MCH-R1 and MCH-R2 receptor types. MCH neurons have cannabinoid CB1 receptors and OX1-R receptors that are directly connected to orexin neurons. The hippocampus and amygdala are two regions of the human brain that express MCH-R2, whereas MCH-R1 is extensively dispersed throughout the brain. Overexpression of MCH causes obesity and insulin resistance, whereas central MCH injection increases appetite. MCH has the same potency as orexins but less potent than NPY. Food restrictions have an impact on MCH. Although MCH is not a glucose-sensitive hormone, its secretion is influenced by fasting and inhibited by leptin(50).

Endocannabinoids (ECS)

Arachidonic acid synthesizes eicosanoid compounds known as endocannabinoids. It stimulates eating and digestion behaviors by acting on cannabinoid1 receptors in the brain(51). CB1 modulators are involved in the motor control of breast-feeding activity after delivery, suggesting that endocannabinoids are present in the developing brain of infants. Therefore, it is involved in the regulation of appetite and energy expenditure.

Role of the brainstem in food intake:

The brainstem is part of the central nervous system that controls and integrates feeding and fuel balance. The brainstem receives vagal satiety input from the gut and sends it to the brain through the nucleus Tractus Solitaires. As a result, it is considered as a link between peripheral, hypothalamic nuclei, and dorsal vagal complex for the management of food intake and energy metabolism(52,53). Brain derived neurotrophic factor (BDNF), pro-glucagon, tyrosine hydroxylase (TH), CART, GABA, NPY, and other neuropeptides that modulate appetite are among the diverse populations of neurons that make up the brainstem in food regulation. In addition, these neurons have different biophysical and neurochemical characteristics(54). The caudal brainstem has an in-tier connection with ARC, PVN, and LHA areas of the hypothalamus. Feeding behavior adjusted by the short-term feedback mechanism derived from gut and

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gustation When CCK is activated from the gut, it sends vagal afferent signals to NTS to activate the brainstem and hypothalamus(55). The ventral tigmental area (VTA) affects how much food is valued by modifying stress response pathways originating from the lateral hypothalamus that control dopamine signaling in the nucleus accumbens as well as reward signals. Additionally, VTA is sensitive to peripheral appetitive hormone levels of ghrelin, leptin, and insulin and influences food-seeking behaviors by modifying food reward value (59). It has been reported that appetite is influenced by endogenous Orexin 1 receptor and external infused Orexin A, which is activated by VTA(56).

Gut hormones in appetite regulation

The digestive system secretes and releases peptide hormones that have physiological and regulatory effects on eating behavior.

Cholecystokinin (CCK)

Pro-CCK, a CCK precursor consisting of 115 amino acids, is the source of CCK. Most CCK is synthesized in the gut, particularly in the duodenum and jejunum; however, it is widely spared in both the CNS and gut. The first gut peptide to regulate appetite is CCK, which controls appetite by activating CCK A and CCK B receptors. CCK-5, CCK-8, CCK-22, CCK-33, CCK-39, CCK-58, and CCK-83 are among the recently discovered bioactive CCK peptides based on the number of amino acids (57,58).

Intestinal peptide YY3–36 (PYY3–36)

Peptide YY 3-36 is one of the most popular gastrointestinal peptides in the GI system. Dipeptidyl peptidase IV enzyme converts PYY to PYY3-36. Fat triggers the release of PYY peptide; however, intravenously administered lipids have little impact on the release of PYY in the circulation. On the other hand, administration of single dosage PYY3–36 decreases hunger and food consumption by 30%(59). Y1, Y2, Y3, Y4, and Y5 of the neuropeptide Y receptor family are involved in modulating and activating PYY. The Y2 receptor has great affinity to PYY3–36 and triggers central regulation of food intake and energy balance in addition to secretory and motor functions(60).

Ghrelin

The 28-amino acid peptide hormone ghrelin is known. Ghrelin is a type 1a endogenous ligand that stimulates the secretion of the growth hormone receptor. GIT is the primary site of ghrelin secretion; however, other organs, such as the pituitary, jejunum, hypothalamus, duodenum, lung, colon, heart, pancreas, and kidney, are involved in ghrelin secretion (61 In the hypothalamus, especially in the arcuate nucleus and hindbrain, AgRP/NPY synthesis is stimulated by ghrelin, which increases feeding. Ghrelin-expressing neurons modulate orexigenic neurons (NPY/AgRP) and anorexigenic neurons (POMC/CART)(62). Fasting increases the expression of ghrelin in the stomach and blood, which affects food intake and consequently body weight (63).

Obestatin

Obestatin, a 23-amino acid peptide with a glycine residue on its C-terminus, was recently extracted from the stomach of rats in both active and inactive forms. It quickly binds to an orphan G protein-coupled receptor (GPR39), but it is highly degraded and does not easily cross the blood-brain barrier. Obestatin affects the pancreas, fatty tissues, cardiovascular system, and gastrointestinal tract. According to previous reports, it can lower body weight, limit food intake, decrease appetite, and slow down jejunal motility. In addition, a recent study focusing primarily on animal research showed that obestatin reduces thirst, promotes sleep, and/or enhances memory (64).

Oxyntomodulin (OXM)

Oxyntomodulin, a 37-amino acid peptide, is secreted after proglucagon translation in intestinal cells. It's named after the fact that it inhibits the stomach oxyntic glands. Nutrient intake triggers PYY and oxyntomodulin secretion from specialized enteroendocrine L cells of the intestinal tract(65). In rodents, central injection of OXM decreases eating and weight gain(66). This hormone is a dual agonist; the glucagon receptor is thought to mediate the effect of OXM on weight loss, whereas the GLP-1 receptor mediates its anorectic effect. When OXM or GLP-1 is taken externally, it stimulates satiety and increases high energy consumption (67).

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Gastric inhibitory protein (GIP)
Gastric inhibitory peptide (GIP) is a 42-amino acid polypeptide (GIP) secreted by endocrine K-cells found in the upper small intestinal epithelium, duodenum, and jejunum. Following a meal, the pancreatic β-cells release insulin in a glucose-dependent manner due to the secretion of GIP. Consumption of fat and glucose is a major factor in GIP production. GIP contributes to obesity by encouraging the storage of fat and glucose [69]. The intestine secretes two main incretin hormones GIP and GLP-1. Glucagon-like peptide-1 (GLP-1) acts by binding with the GIP receptor (GIPR), whereas glucagon-like peptide-1 (GLP-1) acts by binding with the GLP-1 receptor (GLP-1R) to enhance its effects(70).

Oxytocin levels in food intake (OT)
Parvo and magnocellular neurons of PVN and supraoptic nucleus (SON) both produce oxytocin(71). It is a neuropeptide with nine amino acids. This neuropeptide is mainly injected intravenously in order to stimulate uterine contractions and cause labor. In addition, an increase in endogenous oxytocin leads to a reduction in anxiety, stopping feeding, and limiting meal size(72). Oxytocin administered centrally and peripherally reduces food consumption. Activation of the endogenous OT system is linked to feeding cessation(73). OT also resulted in increased energy expenditure and weight loss in diet-induced obese rodents and primates(74). Patients with diabetes have low levels of oxytocin and high levels of insulin, blood glucose, and glycosylated hemoglobin, as well as a high homeostatic model assessment of insulin resistance(75). Pancreatic α and β islet cells have oxytocin receptors [76]. It has been shown that centrally secreted oxytocin is useful in maintaining body weight, metabolism and appetite. According to research findings, oxytocin is effective in combating obesity(77).

Thyroid hormone levels and food intake:
A well-established activity of thyroid hormone is involved in metabolism. Hyperthyroidism in humans and rodents results in activation of the feeding center but induces leanness as compared to normal thyroid gland function(78). Triiodothyronine (T3) affects body weight, thermogenesis, lipolysis and cholesterol consumption, as well as regulating consumption and fuel balance(79). In the hypothalamus, the thyroid hormone T3 is directly stimulated by feeding. Peripheral T3 administration doubled food intake over two hours in rats fed at-well(80). Serum T4 and T3 levels decrease in both humans and rodents when fasting occurs. However, the way in which T4 reacts to starvation depends on the species. The plasma T4 concentration in humans is unaffected by starvation, but the plasma T3 concentration in rats and pigs decreases(81). Thyroid dysfunction has clinically significant effects on appetite and body weight. Weight gain and decreased basal energy expenditure is a typical outcome of hypothyroidism. Conversely, hyperthyroidism lowers body weight and increases energy expenditure. In rodents, the central administration of TSH and TRH resulted in a decrease in feeding(6). Obesity and overweight strongly affect thyroid hormone levels in the circulation (82).

Effect of sex hormones on appetite and body weight
Tight maintenance of feeding and fuel catabolism is affected by estrogen, progesterone, and androgen hormone. In the majority of animals, including humans, food consumption and reproductive processes are closely related (83). During the menstrual cycle in women, eating patterns also change. During the peri-ovulatory period, which is generally defined as the four days preceding the surge of LH, women consume the least amount of food each day (83). According to research, progesterone stimulates appetite while oestrogens suppress it. Women eat more during the luteal phase when progesterone levels increase and less during the periovulatory phase when oestrogen levels are higher. In addition, postmenopausal women generally gain weight because they eat more because their oestrogen reserves are depleted. Treatment with oestrogens may stop this increase in eating(84). According to animal studies, the effect of ghrelin on food intake may vary depending on sex. Research indicates that ghrelin significantly increases feeding in male and untreated ovariectomized female rats compared to healthy and estradiol-treated ovariectomized female rats. Estrdiol suppresses the activity of ghrelin, which plays a significant role in feeding, but ghrelin levels are higher in females than in males to induce eating(85).

Effect of physical exercise on appetite
Physical exercise has the potential to modulate appetite control by enhancing satiety signaling, modifying

hedonic responses and food choice(86). According to recently published research, physical exercise may enhance the coupling between feeding and fuel expenditure as well as increase postprandial satiety and hunger during fasting(87). According to a randomized cross-over design study, low- to moderate-intensity, brief physical activity increases appetite in the post-exercise period. Following high-intensity exercise, less food was consumed (88). Strengthening post-meal satiety and desire to eat are affected by chronic exercise. Depending on the intensity and duration of exercise, a negative energy balance occurs during exercise, which has a significant impact on hunger and food intake. Ghrelin, leptin, and obestatin are the three main hormones that can explain how exercise affects hunger and eating(89).

Conclusion

The regulation of eating and fuel expenditure is well-regulated in healthy individuals, with peptidergic regulators mainly triggering the desire to start eating or stop eating once the required amount of energy is obtained from external sources. Obesity causes a variety of non-transmitted diseases and is considered a real health threat worldwide. The fundamental pathophysiology of obesity consists in controlling cellular processes, physical activity and/or appetite by upregulating or downregulating calorie consumption. The homeostasis pathway regulates energy balance by increasing the desire to eat when stored energy is depleted. On the other hand, hedonic or reward-based regulation can override the homeostatic pathway during times of relative energy abundance by increasing the desire to consume highly palatable food. These two complementary drivers control how much food is consumed. The brainstem and hypothalamus play a key role in appetite regulation. The hypothalamus receives, interprets, and integrates sensory information (hormones, nutrients, and neuronal signals) coming from the brainstem and periphery. Feedback is sent through the efferent neuron to a specific effector area to control feeding and fuel expenditure. The gut synthesizes and secretes a large number of peptides. It is now clear that, in spite of their long-standing role in the regulation of gastrointestinal activity, they also have physiological effects on eating behavior. The secretion of resistin, adiponectin, and leptin plays a significant role in food intake. Increased levels of insulin in the brain are thought to trigger a net catabolic response, which in turn affects regulatory mechanisms that control food intake. It is thought that insulin is a satiety hormone. Oxytocin administered centrally and peripherally reduces food intake and activation of the endogenous OT system, which is linked to the cessation of feeding. In rodents, central injections of TSH and TRH resulted in decreased food intake, whereas central injections of T3 resulted in increased food intake. The sex hormones progesterone, oestrogen, and androgens also influence the complex regulation of hunger, eating, and energy metabolism. Strengthening the sensitivity of the physiological satiety signaling system, altering hedonic responses to food, and influencing macronutrient preferences or food choices may modulate appetite control.

No conflict of interest

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