

“The greater danger for most of us is not that our aim is too high and we miss it, but that it is too low and we reach it.” – Michelangelo

“To make contact with Divine in food, man should eat everything with gratitude and Love”. -
The Master Beinsa Douno

Control Your Weight*
ETI Educational Program
Chapter #13

1. Introduction

Suggesting that Earth’s biological organisms possess an energetic structure, leads us to the conclusion that humans can only be healthy if their energy-biological matrix is in a state of dynamic balance. We hypothesize that the primary reason for the imbalance originates on an energetic level, subsequently influencing on the physical aspect. Assuming this holds true, we can now try to bridge the current scientific physiological and pathological knowledge with the advances, including the paradigm of energetic healing via the ETI approach.

Each chapter of ETI’s Educational Program addresses several topics: (1) to provide healthcare professional scientifically substantiated and captivating insights into physiology, which are often difficult to find in regular physiology textbooks; (2) to present current scientifically validated nutritional and herbal approaches to support the body during pathological conditions; (3) to offer and explain ETI’s specific energy formulas designed to address and potentially eliminate the energetic factors that contribute to illness.

Storing energy in the form of fat within the adipose tissue has played a crucial role in the survival and reproductive success of individuals. It is plausible that genetic mutations promoting efficient energy storage and metabolism provided an advantage for survival during periods of food shortage. However, the current interplay between readily accessible energy-dense foods and decreased physical activity tends to make these genes less adaptable. As a result, weight gain is likely a complex, polygenic condition shaped by the interaction of genetic and environmental factors.

In this chapter of ETI's Educational Program, we will explore how psychological, cultural, and epigenetic factors significantly contribute to the metabolic processes leading to weight gain. We will also highlight how ETI's energetic formulas and their combinations can potentially address many of these complex behaviors and challenges. The subsequent sections will be outlined below:

- Exploring the Physiology of the Human Metabolic Process
- Key Pathways for Regulating Physiological Energy Equilibrium
- Brain and Food Intake Regulation
- Brain Reward System and Food Consumption
- Psychological Problems Related to Weight Loss
- Strategies for Weight Control Supported by Research Findings

- Nutritional Support for Weight Regulation
- Herbs to Promote Weight Loss
- ETI's Solution for Weight Management and Related Challenges.

2. Exploring the Physiology of the Human Metabolic Process

Weight gain arises from an ongoing disruption in the body's energy balance. To effectively address weight gain and obesity comprehensively, it's crucial to have an understanding of how the human body produces energy.

We often use the word "energy" in every day talk, like saying "I'm lacking energy today" or observing "There's a lively energy in the air." What exactly defines energy? Where do we obtain the energy to enable our motions? How do we utilize this energy?

Here's the simplest way to understand these complex pathways. Our body needs energy to work, just like a car needs fuel. The main energy source is a molecule called ATP. Like many other animals, humans produce ATP using three distinct metabolic energy pathways. These pathways involve a series of enzyme-driven chemical reactions: the phosphagen system, glycolysis, and the aerobic system. The specific pathway a person primarily relies on for ATP production depends on their immediate energy requirements and the amount required. However, ATP production does not solely center on a single energy system. Instead, it results from a harmonized interplay of all energy systems, each contributing to varying extents (Table 1).

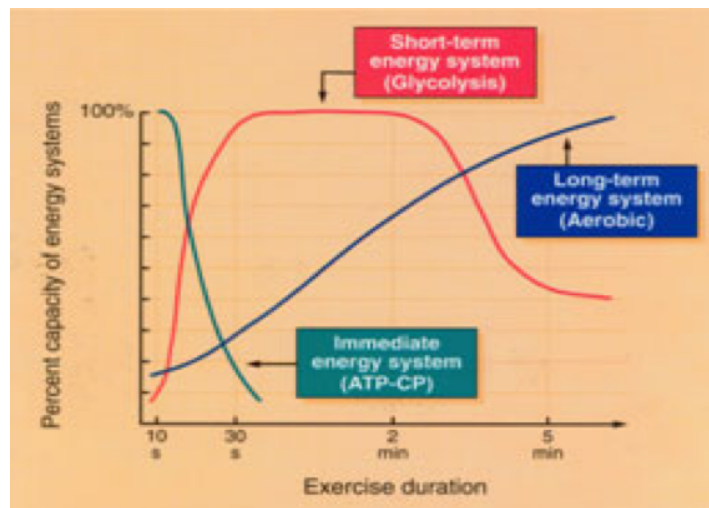


Table 1. From www.nutritionish.com

2.1. Phosphagen System

During brief and intense physical activities, muscles require a significant surge of energy, leading to an increased need for ATP. The phosphagen system, also referred to as the ATP-CP system, emerges as the fastest mechanism for replenishing ATP. In this process, skeletal muscles store creatine phosphate (CP), which contributes a phosphate group to ADP, resulting in the creation of ATP: $ADP + CP = ATP + C$. Importantly, this process doesn't involve the utilization of

carbohydrates or fats; instead, the renewal of ATP relies solely on stored CP. Because it doesn't rely on oxygen for ATP regeneration, this process is classified as anaerobic. Serving as the quickest pathway for ATP renewal, the phosphagen system is the primary metabolic energy route involved in high-intensity exercises lasting for approximately 10 seconds ⁽¹⁾.

2.2. Glycolysis

Glycolysis plays a central role as the primary energy system employed in high-intensity exercises lasting from 30 seconds to approximately 2 minutes. It ranks as the second-fastest method for replenishing ATP. Within the glycolytic pathway, carbohydrates sourced from either blood glucose or muscle glycogen undergo a series of chemical changes, ultimately leading to the production of pyruvate. Initially, glycogen is broken down into glucose through glycogenolysis.

With each glucose molecule undergoing glycolysis and converting into pyruvate, two usable ATP molecules are produced ⁽²⁾. As a result, while the energy yield from this process is relatively moderate, its key benefit lies in the rapid delivery of energy. Once pyruvate is produced, it follows one of two pathways: conversion into lactate or transformation into an intermediary metabolic compound known as acetyl coenzyme A (acetyl-CoA).

On the other hand, when muscles have a sufficient supply of oxygen, pyruvate, through acetyl-Co, enters the mitochondria, where it participates in aerobic metabolism.

2.3. Aerobic System

The majority of cellular energy in the body is generated through metabolic processes that take place in the presence of oxygen ⁽³⁻⁴⁾. This energy production takes place within the mitochondria, driven by the aerobic system. The aerobic system consists of components such as the Krebs cycle (also known as the citric acid cycle) and the electron transport chain, which utilize blood glucose, glycogen, and fat as fuel sources to generate ATP.

When carbohydrates serve as the energy source, glucose and glycogen undergo glycolysis to produce pyruvate. Pyruvate is then converted into acetyl-CoA, which enters the Krebs cycle. In this cycle, electrons are generated and subsequently transported through the electron transport chain. This complex process, known as oxidative phosphorylation, leads to the production of ATP and water ⁽⁵⁾.

The complete oxidation of glucose, achieved through the sequential stages of glycolysis, the Krebs cycle, and the electron transport chain, results in the production of 36 ATP molecules for each individual glucose molecule that is broken down ⁽⁵⁾. The aerobic system generates 18 times more ATP per glucose molecule than anaerobic glycolysis.

Fat is the main fuel source for the aerobic system and is primarily stores as triglycerides in adipose tissue under the skin within skeletal muscles. It represents the body's largest energy reservoir. When fat is utilized, triglycerides undergo an initial breakdown into free fatty acids and glycerol, a process called lipolysis. These free fatty acids, composed of a long chain of carbon atoms, are

transported to muscle mitochondria, where the carbon atoms are used to produce acetyl-CoA through a process called beta-oxidation.

One acetyl-CoA is produced, fat metabolism mirrors that of carbohydrate metabolism. Acetyl-CoA enters the Krebs cycle, and the ensuing electrons are transported to the electron transport chain, leading to the generation of ATP and water. Notably, the oxidation of released fatty acids produces significantly more ATP molecules compared to the oxidation of glucose or glycogen. As an illustration, the oxidation of the fatty acid palmitate yields a total of 129 ATP molecules ⁽²⁾.

Recent research has revealed a connection between mitochondrial dynamics, nutrient availability, and energy expenditure, influencing certain cellular adaptations related to bioenergetics. Scientific studies have shown that when cells are deprived of nutrients, their mitochondria increase ATP production per unit of nutrient consumed. On the other hand, during nutrient excess, mitochondria can contribute to wasting energy as heat through a process called mitochondrial proton leakage ⁽⁶⁾.

The data above suggests that our bodies adapt to changes in energy supply and demand by modifying the efficiency and capacity of ATP synthesis. Persistent shifts in mitochondrial dynamics, such as those occurring in prolonged positive energy imbalances often associated with obesity, can ultimately result in dysfunctional mitochondria, a characteristic feature of metabolic disorders ⁽⁷⁻⁸⁾.

3. Key Pathways for Regulating Physiological Energy Equilibrium

Obesity has become a rapidly increasing global health concern in recent decades, particularly in developed countries ⁽⁹⁾. The brain, especially the hypothalamus, plays a key role in regulating food intake by sensing metabolic signals from peripheral organs and adjusting feeding behaviors accordingly. To accomplish these important roles, the hypothalamus communicates with other brain areas, such as the brainstem and reward-related limbic pathways. The adipocyte-derived hormone leptin and pancreatic β -cell-derived insulin inform adiposity to the hypothalamus ⁽¹¹⁾. Gut hormones such as cholecystokinin, peptide YY, pancreatic polypeptide, glucagon-like peptide 1, and oxyntomodulin relay satiety signals to the brain, while ghrelin sends hunger signals ⁽¹¹⁾ (Table 2).

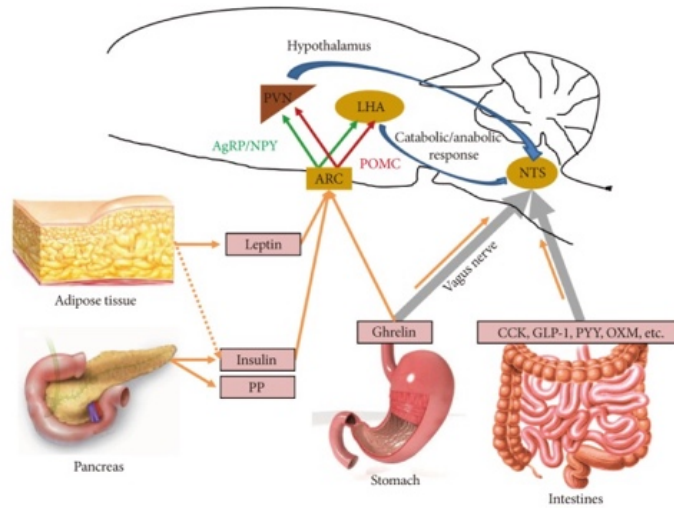


Table 2. From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530708>

For more detailed information of the functions of central and peripheral signals, as well as hormones in the weight control system, please refer to Appendix #1 titled "Peripheral Adiposity Signals and GI Hormones."

Scientific research supports the idea that establishing and maintaining a healthy physiological energy balance depends on the complex interaction of circadian rhythms, sleep-wake regulation, and dietary practices. When these systems function in harmony, they contribute to the effective control of energy intake and expenditure, a foundation of overall health and well-being. Disruptions within these interconnected components have the potential to trigger energy imbalances, leading to health risks, including fluctuations in body weight, metabolic irregularities, and disruptions in sleep patterns⁽¹⁴⁾. Let's briefly discover how these components work together:

3.1. Circadian Rhythmicity

The circadian rhythm is an internal biological clock that regulates various physiological processes over a 24-hour cycle⁽¹²⁾ (Table 3).

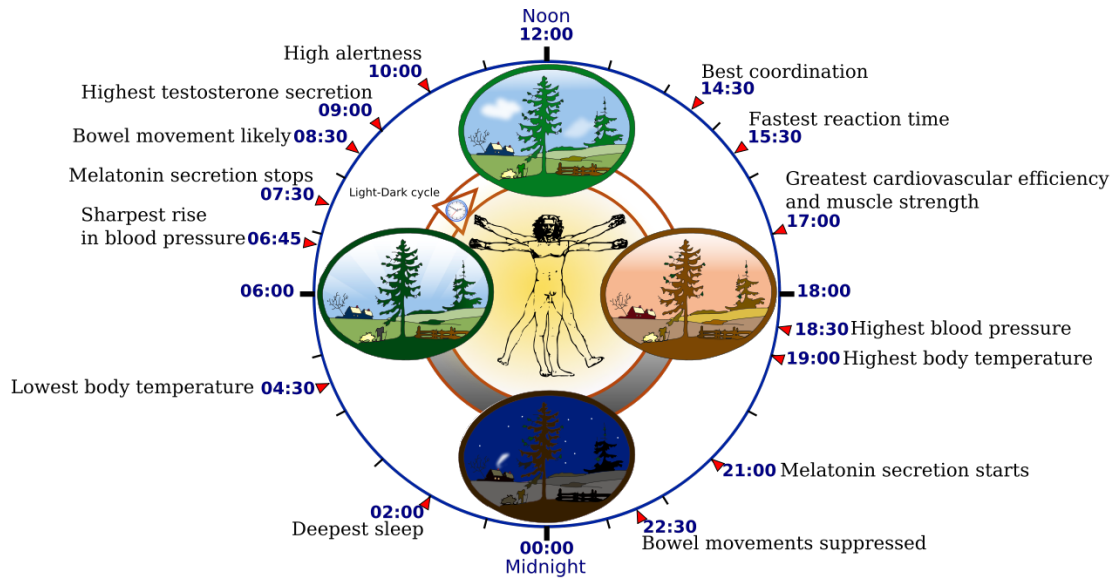


Table 3. From <https://www.thekuproject.com/how-to-understand-and-take-advantage-of-the-circadian-rhythm/>

It is influenced by external signals, primarily the light-dark cycle. Key aspects of circadian rhythmicity include:

- *Body Temperature:* The body's temperature rises and falls in a predictable pattern throughout the day, which can influence metabolic processes ⁽¹³⁾.
- *Hormone Release:* Hormones like cortisol, melatonin, and growth hormone follow a circadian pattern of secretion, which can influence metabolism, appetite, and energy regulation ⁽¹⁴⁾. Glucocorticoids can affect our food preferences by triggering cravings for "comfort foods." This occurs because insulin appears to diminish our brain's responsiveness to rewards, prompting us to seek more gratifying foods to achieve the same pleasurable sensation. This increased calorie intake could be our body's strategy to cope with the elevated energy demands of a stressed mind, allocating more glucose to support our cognitive functions ⁽¹⁵⁾. Surprisingly, indulging in these irresistibly delicious foods can trigger a negative feedback loop on the hypothalamic-pituitary-adrenal (HPA) axis, effectively inhibiting its activity. Consequently, this implies that even the consumption of comfort foods, including junk food or stress-induced ice cream intake, might paradoxically relieve stress symptoms ⁽¹⁶⁾.
- *Gene Expression:* Many genes involved in metabolic processes exhibit circadian patterns, affecting how the body processes nutrients and energy ⁽¹⁷⁾. This rhythmic gene expression is found throughout the central nervous system and can be regulated both by dependent on- and independent of- the master biological clock regulator, the suprachiasmatic nucleus (SCN) ⁽¹⁸⁾. The 24-hour cycles of the mesolimbic dopamine system and the suprachiasmatic nucleus directly shape the activity of these brain regions. When dopamine levels follow their natural rhythm, it directly impacts the function of both the mesolimbic dopamine system and the suprachiasmatic nucleus. Imagine it as a finely synchronized orchestra ⁽¹⁹⁻²¹⁾.

3.2. Sleep-Wake Regulation

Sleep is a critical component of energy balance and overall health. The regulation of sleep-wake cycles is closely intertwined with circadian rhythms. Key points include:

- *Sleep Phases:* Sleep consists of various phases, including REM (rapid eye movement) and non-REM sleep ⁽²²⁾. These phases play different roles in energy conservation, memory consolidation, and hormonal regulation.
- *Appetite and Hunger Hormones:* Sleep duration and quality can influence the levels of hormones like leptin and ghrelin, which control appetite and hunger. Disrupted sleep patterns can lead to overeating or reduced satiety ⁽²³⁾.
- *Energy Conservation:* During sleep, the body's metabolic rate decreases, conserving energy. However, sleep deprivation can disrupt this balance and lead to increased energy intake ⁽²⁴⁾.

3.3. Feeding

Proper feeding behaviors are essential for maintaining energy balance ⁽²⁵⁾. Key factors include:

- *Meal Timing:* Eating at regular intervals can help synchronize feeding patterns with circadian rhythms. Irregular eating times can disrupt the body's internal clock and lead to metabolic disturbances.
- *Nutrient Intake:* The types and quantities of nutrients consumed play a significant role in energy balance. Balanced diets that provide adequate energy without excess are crucial.
- *Portion Control:* Eating appropriate portion sizes can help prevent overconsumption of calories, contributing to energy balance.
- *Snacking:* Snacking habits can affect overall energy intake. Mindful snacking can be a part of a healthy diet, but excessive or unplanned snacking can disrupt energy balance.

3.4. Interplay of Circadian, Sleep, and Feeding Centers within the Hypothalamus

The neuronal connections linking circadian, sleep, and feeding centers in the hypothalamus play are pivotal in regulating various physiological processes, including our sleep-wake cycle, hunger and eating behavior, and the overall circadian rhythm ⁽²⁶⁻²⁹⁾. Let's break down these connections and their functions:

- *Hypothalamus:* The hypothalamus, a small yet crucial brain region, functions as a central command center for numerous autonomic processes, such as temperature regulation, thirst, hunger, and circadian rhythms. Within the hypothalamus, multiple discrete nuclei or groups of neurons exist, with each nucleus dedicated to overseeing particular functions ⁽³⁰⁾.
- *Circadian Center:* The central center of our circadian system, primarily located within a region of the hypothalamus known as the suprachiasmatic nucleus (SCN), plays a pivotal role in orchestrating our circadian rhythms. These rhythms consist of approximately 24-hour cycles that manage our sleep-wake patterns, hormone secretion, and various other physiological functions. The SCN receives input from specialized light-sensitive cells in

the retina, aiding in the alignment of our internal biological clocks with the external day-night cycle ⁽³¹⁾.

- *Sleep Center:* The sleep center, located in the hypothalamus and involving various nuclei such as the ventrolateral preoptic nucleus (VLPO), plays a crucial role in promoting sleep ⁽³²⁾. Neurons in the sleep center release neurotransmitters like GABA (gamma-aminobutyric acid) and adenosine, which inhibit wakefulness-promoting regions of the brain and encourage the transition from wakefulness to sleep ⁽³³⁻³⁴⁾.
- *Feeding Center:* The feeding center, which includes nuclei like the arcuate nucleus (ARC) and the lateral hypothalamus (LH), regulates appetite, hunger, and feeding behavior. Different groups of neurons within this center release neuropeptides like neuropeptide Y (NPY) and agouti-related peptide (AgRP) to stimulate hunger, while others release proopiomelanocortin (POMC) to suppress appetite ⁽³⁵⁾.

Let's discuss the connections between these centers:

- *Circadian-Sleep Connection:* The SCN in the circadian center is closely connected to the sleep center. The SCN not only regulates the timing of sleep-wake transitions but also influences the release of hormones like melatonin, which promote sleep. It sends signals to the sleep center to help synchronize our sleep patterns with the natural day-night cycle ⁽³⁶⁾.
- *Circadian-Feeding Connection:* The circadian center also communicates with the feeding center. It helps establish circadian rhythms in hunger and eating behavior, ensuring that our bodies are prepared for nourishment at the appropriate times of the day. Disruptions in these rhythms can lead to irregular eating habits and metabolic issues ⁽³⁷⁾.
- *Sleep-Feeding Connection:* The sleep center and feeding center have complex interactions. Sleep deprivation can disrupt the balance of hunger-regulating hormones, potentially leading to increased appetite and overeating ⁽³⁸⁾. Conversely, eating too close to bedtime can affect sleep quality due to digestive processes and the release of insulin and other hormones.

These interconnected pathways and centers in the hypothalamus illustrate how our sleep, circadian rhythms, and feeding behavior are closely integrated and regulated. Disruptions in any of these systems can have significant consequences for our overall health and well-being, including increased risk of sleep disorders, obesity, and metabolic disorders.

4. Brain and Food Intake Regulation

The brain plays a crucial role in regulating various bodily functions, including metabolism and weight regulation. While the brain itself does not directly cause weight loss or gain, it influences behaviors, hormones, and processes that can impact body weight ⁽³⁹⁻⁴¹⁾.

As we described before, the brain controls hunger and satiety signals through a complex interplay of hormones and neurotransmitters. Different regions of the brain, such as the hypothalamus, regulate appetite and help maintain energy balance. Imbalances in these systems can lead to increased or decreased appetite, potentially affecting weight ⁽⁴⁰⁻⁴³⁾.

The hypothalamus also produces various neuropeptides that influence appetite. For example, neuropeptide Y (NPY) stimulates hunger, while pro-opiomelanocortin (POMC) suppresses appetite. Imbalances in the production or response to these neuropeptides can contribute to changes in appetite and body weight ⁽⁴⁴⁻⁴⁵⁾ (Table 4).

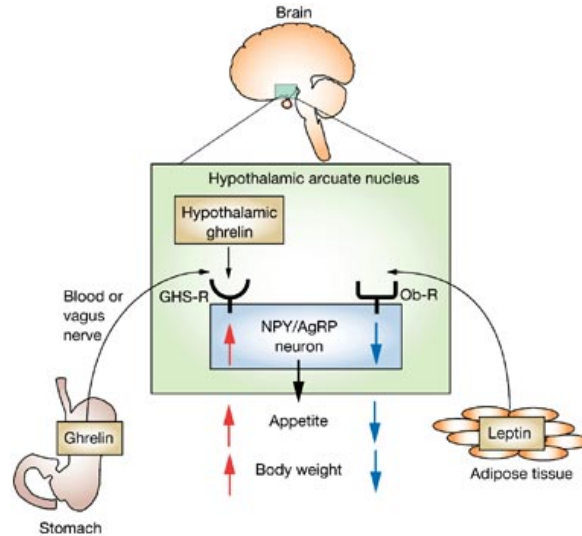


Table 4. From www.precisionnutrition.com

The brain's reward system, primarily involving the neurotransmitter dopamine, plays a role in regulating food intake. When we consume highly tasty foods, dopamine is released, providing a pleasurable sensation and reinforcing the desire to eat. This can lead to overeating or the consumption of calorie-dense foods, potentially contributing to weight gain ⁽⁴⁶⁻⁴⁸⁾.

The brain's limbic system, involved in emotions and motivation, can influence eating behaviors. Emotional factors, such as stress, depression, or anxiety, may trigger overeating or comfort eating, which can contribute to weight gain.

Let's research in more detail about how the brain's limbic system, which is involved in emotions and motivation, can influence eating behaviors, particularly in relation to emotional factors:

- *Stress and Overeating:* When we experience stress, the brain's response involves the release of stress hormones like cortisol. Cortisol can increase appetite and motivate us to seek out comfort or high-calorie foods. This can lead to a behavior known as stress eating or emotional eating, where individuals turn to food for emotional comfort or to cope with stress. Over time, excessive calorie intake from stress eating can contribute to weight gain ⁽⁴⁹⁾.
- *Emotional Factors and Reward Pathways:* The limbic system is interconnected with the brain's reward system, which involves the release of dopamine. In response to pleasurable stimuli, including certain foods, dopamine is released, creating feelings of reward and reinforcing the behavior. This can lead to a cycle of seeking comfort through food in response to emotional distress, as the brain associates eating with positive emotions ^(46, 51).

- *Depression and Appetite:* Depression can have a significant impact on appetite regulation. Some individuals with depression may experience a loss of appetite, leading to weight loss. However, others may experience an increase in appetite, particularly for calorie-dense foods. This can result in weight gain and the development of unhealthy eating habits ⁽⁵²⁾.
- *Anxiety and Overeating:* Anxiety can trigger overeating or mindless eating in some individuals. The limbic system can be involved in the heightened arousal and emotional response associated with anxiety. In an attempt to soothe or distract themselves from anxious thoughts and feelings, individuals may turn to food as a coping mechanism ⁽⁵³⁻⁵⁵⁾.

Here are some key points about how food can affect the brain's reward system:



From <https://aprilhansen2000.com/overeating-cycle/>

- *Tastiness and Cravings:* Pleasant foods, which are often high in sugar, fat, or salt, can activate the brain's reward system more intensely. These foods can trigger cravings and lead to overeating. The combination of taste, texture, and sensory pleasure associated with palatable foods can make them particularly rewarding and reinforce the desire to consume them ⁽⁵⁶⁾.
- *Training and Food-Related Signals:* The brain's reward system can become trained to associate certain cues with food rewards. For example, the sight or smell of food, the sound of a package being opened, or the environment in which food is typically consumed can trigger dopamine release and increase the desire to eat. This conditioning can contribute to habitual eating behaviors, even in the absence of true hunger ⁽⁵⁷⁾.
- *Food Addiction:* Some researchers have proposed that certain highly tasty foods, particularly those high in sugar and fat, can have addictive properties and lead to behaviors resembling addiction. In individuals susceptible to food addiction, the brain's reward system may become dysregulated, leading to compulsive overeating and difficulty in controlling food intake ⁽⁵⁸⁻⁶⁰⁾.
- *Individual Variations:* It's important to note that individual differences exist in how the brain's reward system responds to food. Factors such as genetics, early life experiences, and environmental influences can all contribute to variations in food preferences, cravings, and the brain's response to reward ^(57, 61).

The brain communicates with other organs, such as the thyroid gland and adrenal glands, to regulate metabolism and hormonal balance. Hormonal imbalances, such as hypothyroidism ⁽⁶²⁻⁶⁴⁾ or polycystic ovary syndrome (PCOS) ⁽⁶⁵⁾, can affect weight. To support your thyroid through dietary changes, refer to Appendix #3.

Also, the brain influences motivation, energy levels, and motor control, which can impact physical activity. Regular exercise is an essential component of weight management and overall well-being ⁽⁶⁶⁾. Example of physical exercise is provided in Appendix #4.

5. Brain Reward System and Food Consumption

The brain's reward system, also known as the mesolimbic system, a complex network of neural circuits and structures, plays a crucial role in reinforcing behaviors and experiences that are pleasurable and beneficial for survival, such as eating, exercising, and forming social bonds ⁽⁶⁷⁾. However, it can also be vulnerable to manipulation by substances like drugs, which can lead to addiction ⁽⁶⁸⁾.

When an individual engages in reward-related activities, this system becomes activated, releasing of varied neurotransmitters where dopamine plays a critical role in mediating the reward value of food, drink, sex, social interaction, and substance abuse ⁽⁶⁹⁾. The dopaminergic pathway mostly involved in reward is formed by projections of midbrain dopamine neurons of the ventral tegmental area (VTA) to the striatum, prefrontal cortex, amygdala, hippocampus, and many other structures of the limbic system. When rewarding stimuli are experienced, the dopaminergic mesolimbic system is activated which causes the release of dopamine to the targeted nuclei ⁽⁷⁰⁾ (Table 5).

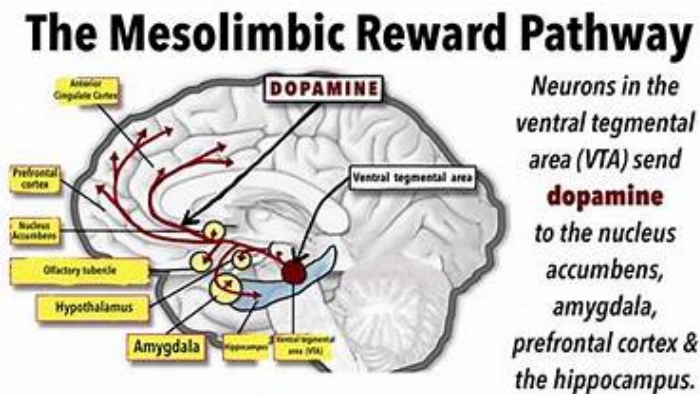


Table 5. From <https://drconley.org/articles/how-opioids-change-your-brain>

The reward system determines the degree of a stimulus and signals whether it is to be avoided or approached, as well as assigning the priority of one stimulus over another. Substances of abuse, whether prohibited (e.g., cocaine, heroin, etc.) or legal (e.g., alcohol, nicotine, etc.), takeover the mesolimbic system by present a reward without a recognizable biological function. However, the pleasure and reward linked to initial substance use are then lost by their abuse, which leads to a vicious circle of addiction ⁽⁶⁸⁾.

The interaction between the metabolic center and reward center in the brain is crucial for regulating eating behavior and body weight ⁽⁶⁷⁾. In normal-weight individuals, these centers work in *harmony* to maintain a balanced energy intake. In overweight individuals, *dysregulation* of these centers can lead to overeating and contribute to the development and maintenance of obesity ⁽⁷¹⁻⁷²⁾. Let's break down this interaction in both scenarios:

Normal-weight individuals:

- *Metabolic Center (Hypothalamus, Brain Stem)*: It receives signals from the body about hunger, fullness, and energy expenditure. When energy stores are low (e.g., after a period of fasting), the metabolic center stimulates hunger and reduces energy expenditure to encourage food intake and replenishment of energy stores ⁽⁷³⁾.
- *Reward Center (VTA, Nucleus Accumbens, Forebrain)*: The reward center, which includes the ventral tegmental area (VTA), nucleus accumbens (NA), and various forebrain regions, is responsible for processing the pleasurable and rewarding aspects of eating ⁽⁶⁷⁾. It releases dopamine, a neurotransmitter associated with pleasure and reward, in response to food consumption, making eating an enjoyable experience ^(69,74).

Interaction in normal-weight individuals: In individuals with a healthy weight, the metabolic center and reward center work in harmony. When the metabolic center signals hunger, it engages the reward center to motivate food-seeking behavior. After eating, the reward center provides a sense of satisfaction and pleasure, reinforcing the consumption of a balanced amount of food. This balance helps maintain a stable body weight ^(67,71-73).

Overweight individuals:

- *Metabolic Center (Hypothalamus, Brain Stem)*: In overweight individuals, the metabolic center may become dysregulated. This can result from factors like genetic predisposition, hormonal imbalances, or chronic overeating. As a result, the signals related to hunger and fullness may not function properly. Some overweight individuals may have a heightened sensitivity to food signals, which can lead to overeating ^(67,72).
- *Reward Center (VTA, Nucleus Accumbens, Forebrain)*: The reward center in overweight individuals can also undergo changes. Over time, regular consumption of highly appealing, calorie-rich foods can result in a reduced sensitivity of the reward system ⁽⁷²⁾. This means that individuals may require more food or find it harder to experience the same level of pleasure from eating, which can drive overeating.

Interaction in overweight individuals: In overweight individuals, there is often a *disconnect* between the metabolic center and reward center ⁽⁷²⁾. Dysregulated metabolic signals can lead to excessive food intake, while changes in the reward system can make it harder for them to control their eating behavior.

6. Psychological Problems Related to Weight Loss

Psychological problems related to weight loss can be complex and vary from person to person. Many individuals struggle with their weight and may experience emotional and psychological challenges throughout their weight loss journey. Let's look into some typical psychological issues that people encounter when trying to lose weight with paying a special attention to the stress-related data:

- *Body Image Issues:* People often have distorted body image perceptions, which can lead to dissatisfaction with their bodies even after significant weight loss. This can result in low self-esteem and poor self-image ⁽⁷⁵⁾.
- *Eating Disorders:* Engaging in extreme dieting or severely restrictive eating habits can potentially trigger eating disorders like anorexia nervosa, bulimia nervosa, or binge-eating disorder, which may result in significant physical and psychological consequences. For additional information, please go to the Appendix 2 for more details
- *Depression and Anxiety:* Trying to lose weight can be really tough. The pressure to shed those pounds, the fear of not reaching your goals, and the expectations from society can make things even harder. On top of that, your mood can also be influenced by the hormonal changes that happen when you're on a weight loss journey ⁽⁷⁶⁾.
- *Emotional Eating:* Some people use food as a coping mechanism for stress, anxiety, or other emotional issues ⁽⁷⁷⁻⁷⁸⁾. Addressing these emotional triggers is crucial for successful and sustainable weight loss. Moreover, adults with a combination of shorter night sleep duration and emotional eating may be particularly vulnerable to weight gain ⁽⁷⁸⁾.



From <https://www.myhealthexplained.com/diabetes-information/diabetes-articles/when-our-food-choice-isnt-just-about-food>

- *Stress:* Trying to balance a weight loss regimen with daily life responsibilities can lead to stress and feelings of overwhelm.

Right after a stressful event occurs, the body initiates a response mediated by corticotropin-releasing hormone (CRH), which suppresses food intake. CRH is released into the arcuate nucleus

of the hypothalamus (ARC) to inhibit neuropeptide Y (NPY)/agouti-related peptide (AGRP) neurons there⁽⁷⁹⁾. This population of cells is normally responsible for stimulating feeding behavior and suppressing energy expenditure; thus, CRH released after acute stress inhibits appetite⁽⁷⁹⁻⁸⁰⁾. This redirection of the body's resources away from the immediate need to seek and consume food is intended to prioritize fight, flight, or withdrawal responses to address the stressful situation. In the hours following this initial response, there is a subsequent increase in hunger and eating behavior, mediated by glucocorticoids.

However, when it comes to persistent psychological stress, continuously elevated glucocorticoid levels can result in long-term stimulation of eating behavior and excessive weight gain. Stress, in particular, can boost the inclination to consume high-calorie and "pleasurable" foods by affecting central reward pathways. The activation of this circuitry can also interact with the hypothalamic-pituitary-adrenal (HPA) axis to dampen its further activation⁽⁸¹⁾.

In the hours to days following the start of a continuous stressful event, like an infection or grief, there is an increase in glucocorticoid levels in the bloodstream. These glucocorticoids, when present in the body, boost the activity of lipoprotein lipase in adipose tissue, resulting in an increase in fat storage⁽⁸²⁾. This effect is particularly pronounced in visceral fat, where lipoprotein lipase activity is naturally higher⁽⁸³⁾.

Another mechanism by which glucocorticoids can influence appetite during stress is via its interaction with ghrelin. Ghrelin is a peptide derived principally from the gut. It is released as a signal of hunger or just prior to the usual meal time to stimulate feeding⁽⁸⁴⁾. Chronic or severe stress resulting in elevated glucocorticoid secretion will also lead to elevated circulating ghrelin levels, culminating in increased ghrelin-mediated stimulation of NPY/AGRP and increased food intake⁽⁸⁵⁾.

7. Strategies for Weight Control Supported by Research Findings



Below, we will provide some research-backed facts to further assist you in designing a personalized approach to managing your weight.

7.1. The significance of meal timing, not just food choice

Enhancing the feeding-fasting cycle, which supports a strong circadian clock in peripheral organs, leads to positive effects on health⁽⁸⁶⁾. To illustrate, regular mice subjected to a high-fat diet only during their typical awake hours, exhibited a more noticeable rhythmic expression of circadian clock genes. This regimen also helped them resist obesity, metabolic issues, and liver damage, in contrast to mice allowed to eat freely⁽⁸⁷⁾.

7.2. Sleep is an appropriate therapeutic target for treatment and prevention of obesity and diabetes

Accumulating evidence highlights the significance of maintaining a consistent sleep schedule in regulating metabolism and preventing the onset of metabolic syndrome ⁽⁸⁸⁻⁸⁹⁾. Sleep disruption's metabolic consequences seem to affect both the brain and peripheral organs, highlighting its role in weight management and overall health ⁽⁹⁰⁻⁹¹⁾.

7.3. Enhancing your gut microbiome contributes to the maintenance of body weight

Numerous studies have established a strong connection between the composition of gut microbiota and particular metabolic disorders linked to obesity ⁽⁹⁴⁻⁹⁷⁾.

7.4. Prolonged exposure to stress can lead to overweight and obesity

Stress disturbs cognitive functions like executive function and self-regulation, impacting behavior in various ways. It can lead to overeating, causing the consumption of calorie-rich, fatty, or sugary foods ⁽⁹⁸⁾. Stress also reduces physical activity ⁽⁹⁹⁾ and sleep duration ⁽¹⁰⁰⁾. Additionally, stress initiates physiological changes in the hypothalamic-pituitary-adrenal axis ⁽¹⁰¹⁾, influences reward processing in the brain ⁽¹⁰²⁾, and potentially affects the gut microbiome ⁽¹⁰³⁾. This stress response can trigger the production of biochemical hormones and peptides such as leptin, ghrelin, and neuropeptide Y ⁽¹⁰⁴⁻¹⁰⁵⁾.

7.5. Hydration plays a significant role in weight loss and weight management

Dehydration can sometimes be confused with hunger. When you're not adequately hydrated, your body may send signals that you interpret as hunger when you're actually thirsty. This can lead to unnecessary calorie consumption. Staying well-hydrated can help you distinguish between true hunger and thirst, potentially reducing your overall calorie intake ⁽¹⁰⁶⁻¹⁰⁷⁾.

7.6. Enjoy physical activities as a tool for weight management

Engaging in physical activity plays a fundamental role in regulating energy expenditure, making it a basis for maintaining a healthy energy equilibrium and managing body weight ⁽¹⁰⁹⁻¹¹⁰⁾. Many programs recommend at least 30 minutes of daily physical activity, highlighting that extra exercise can offer even more substantial health benefits and improved weight management. One such exercise program is detailed in Appendix #4.

7.7. Intermittent fasting - time-restricted eating

Intermittent fasting involves cycling between periods of eating and fasting, and it has gained popularity for its potential health benefits, including weight loss and improved metabolic health.

For example, there is a growing body of evidence suggesting that adopting a 6-hour eating window followed by 18 hours fasting period can initiate a metabolic shift from relying on glucose for energy to utilizing ketones. This transition is associated with enhanced stress resilience, extended lifespan, and a reduced risk of various diseases, such as cancer and obesity ⁽¹¹¹⁻¹¹⁴⁾.

During the process of eating, our body utilizes carbohydrates as its primary energy source. Any excess carbohydrates, if not immediately required, are either stored in the liver as glycogen or transformed into fat. After we've completed our daily meals, our body initially relies on the glucose derived from recently consumed carbohydrates for energy for a few hours. Subsequently, it starts utilizing stored carbohydrates, or glycogen, stored in the liver. This glycogen reserve typically sustains us for several hours, depleting roughly eight hours after our last meal, at which point our body initiates the utilization of stored fat for energy. *Notes that in the moment we ingest food again — even if it's just coffee with a bit of sugar and milk — we switch back into the other mode and start burning carbohydrates and storing glycogen and fat.*

When you shorten your eating window and extend your fasting window, you're essentially increasing the amount of time your body spends in a fasted state. During this fasted state, several metabolic changes occur:

- **Insulin Levels Drop:** When you eat, especially foods high in carbohydrates, your body releases insulin to help process the incoming glucose (sugar) from the food. Extended fasting periods lead to lower insulin levels, which can make it easier for your body to access stored fat for energy ⁽¹¹⁵⁾.
- **Glycogen Depletion:** Your body stores glucose in the form of glycogen in the liver and muscles. During fasting, your body depletes its glycogen stores, and once these stores are used up, your body begins to break down fat for energy ⁽¹¹⁶⁾.
- **Increased Fat Oxidation:** As your glycogen stores are depleted, your body turns to stored fat as its primary energy source. This is when you're in a state of fat-burning or "ketosis." Fatty acids are released from fat cells and transported to the liver to be converted into ketones, which can be used by the body and brain as an energy source ⁽¹¹⁷⁻¹¹⁸⁾.
- **Appetite Regulation:** Some people find that intermittent fasting helps regulate their appetite. When you're in a fasted state, hunger hormones like ghrelin may decrease, potentially making it easier to control your calorie intake during the eating window ⁽¹¹⁹⁾.

8. Nutrition Support to Weight Regulation

- **5-HTP:** 5-HTP serves as the building block for serotonin, a neurotransmitter linked to functions like sleep, mood regulation, movement, appetite, and anxiety. By influencing serotonin levels in the brain, 5-HTP might potentially modulate eating patterns and contribute to weight loss among individuals dealing with obesity ⁽¹²⁰⁾.
Precautions: Refrain from use if you have an allergy to 5-HTP. Exercise caution if there is a history of psychological disorders. It's recommended to avoid 5-HTP during pregnancy or while breastfeeding.
- **DHEA:** DHEA, which stands for dehydroepiandrosterone, is a hormone manufactured by the adrenal glands. The majority of human studies exploring the influence of DHEA on weight or fat loss corroborate its utilization for this specific goal ⁽¹²¹⁻¹²²⁾.
Precautions: Avoid from usage if you have an allergy to DHEA. If there is a history of seizures, it is advisable to avoid its use. Exercise caution if you have adrenal or thyroid disorders. Additionally, be cautious if you are taking anticoagulants, medications, herbs, or supplements intended for diabetes, heart conditions, seizures, or stroke management.

Discontinue use two weeks prior to and right after surgical, dental, or diagnostic procedures involving bleeding risks. DHEA should be avoided during pregnancy or while breastfeeding.

- **Calcium:** Calcium is the most abundant mineral in the human body. Calcium is needed for muscle contraction, blood vessel contraction and expansion, the release of hormones and enzymes, and nervous system signaling. Diets with higher calcium density (high levels of calcium per total calories) have been associated with a reduced incidence of being overweight or obese in several studies ⁽¹²³⁾.

Precautions: Refrain from usage if you have an allergy or heightened sensitivity to calcium or lactose. Ingesting high oral doses may lead to the formation of kidney stones. Avoid if there are elevated levels of calcium in the blood or urine, excessive parathyroid hormone, bone tumors, digitalis toxicity, ventricular fibrillation (irregular heart ventricle contractions), kidney stones, kidney disease, or sarcoidosis. Exercise caution if you have achlorhydria (absence of gastric hydrochloric acid) or arrhythmia (irregular heartbeat). Calcium seems to pose no significant risks for pregnant or breastfeeding women.

- **Vitamin A (retinol):** Vitamin A is a type of fat-soluble vitamin that originates from two primary sources: retinoids and carotenoids. Retinoids are present in animal-derived sources such as livers, kidneys, eggs, and dairy products. Meanwhile, carotenoids are abundant in plant-based sources like dark or yellow vegetables. There's a suggestion that daily vitamin A could potentially contribute to weight loss ⁽¹²⁴⁾.

Precautions: Refrain from use if you have an allergy or heightened sensitivity to vitamin A. Be aware that excessive dosages of vitamin A can lead to toxicity. Exercise caution if you have liver disease or a history of alcoholism. Smokers who consume alcohol and beta-carotene may face an elevated risk of lung cancer or heart disease. When taken at recommended doses, vitamin A seems to pose no significant risks for pregnant women. However, its use while breastfeeding should be approached cautiously, as the potential benefits or risks to nursing infants are not definitively established.

9. Herbs for Promoting Weight Loss

- **Damiana:** Damiana (*Turnera diffusa*) is a plant native to Central and South America, and it has been used traditionally as a natural remedy for a variety of purposes, including as an aphrodisiac, mood enhancer, and for its potential to support weight loss ⁽¹²⁵⁾. However, it's important to note that scientific evidence supporting the use of damiana specifically for weight loss is limited. The potential mechanisms through which damiana might be associated with weight loss are not well-established, but some advocates suggest that it may help indirectly by improving mood and reducing stress and anxiety, which can lead to overeating or emotional eating in some individuals. Additionally, it has been suggested that damiana may have mild diuretic properties, which could potentially lead to temporary weight loss due to water loss, but this is not a sustainable or healthy method for losing weight.

Precautions: Use cautiously with a history of breast cancer. Avoid with Alzheimer's disease or Parkinson's disease. Use cautiously with psychiatric disorders. Use cautiously if taking medications that alter blood sugar levels.

- **Green tea:** Green tea is derived from the dried leaves of the evergreen shrub known as *Camellia sinensis*. It has a rich history, with its origins dating back approximately 5,000

years in China. Various small-scale human studies have explored the utilization of green tea extract capsules to enable weight loss or weight maintenance among both overweight and average-weight individuals ⁽¹²⁶⁻¹²⁷⁾.

Precautions: Avoid if allergic or hypersensitive to caffeine or tannin. Use cautiously with diabetes or liver disease.

- **Guarana:** Guarana (*Paullinia cupana*) originates from South America and possesses stimulating properties when consumed orally. It offers a stimulant effect similar to that of caffeine and is commonly employed for purposes such as boosting energy, aiding in weight loss ⁽¹²⁸⁾, and as an ingredient in soft drinks.

Precautions: Avoid from using guarana if you have allergies to guarana caffeine, tannins, or related species within the Sapindaceae family. Avoid consumption if you have high blood pressure, psychological or psychiatric conditions, liver ailments, or irregular heart rhythms. Be caution when using guarana if you have breast conditions, impaired kidney function, diabetes, a pre-existing mitral valve prolapse, iron deficiency, gastric or duodenal ulcers, bleeding disorders, glaucoma, or are at risk for osteoporosis. Avoid guarana if you are pregnant or breastfeeding.

- **Psyllium:** Psyllium comes from the husks of the seeds of *Plantago ovata*. The reviewed evidence seems to show that psyllium may improve blood sugar and lipid levels ⁽¹²⁹⁻¹³⁰⁾, which has been associated with obesity.

Precautions: Prescription drugs should be taken one hour before or two hours after psyllium. Use cautiously if pregnant or breastfeeding.

- **Bladderwrack:** Bladderwrack (*Fucus vesiculosus*) is a form of marine seaweed or algae with a long history of use in traditional medicine and herbal therapies. It comprises a range of compounds, notably iodine, which is vital for the thyroid gland's optimal operation. The thyroid gland is pivotal in overseeing metabolism ⁽¹³¹⁾, leading to some individuals investigating the possible use of bladderwrack for weight management owing to its iodine content and its potential influence on thyroid function.

Precautions: Avoid with a history of thyroid disease, bleeding, acne, kidney disease, blood clots, nerve disorders, high blood pressure, stroke, or diabetes. Avoid if pregnant or breastfeeding.

- **Spirulina:** Spirulina is a type of cyanobacteria, often referred to as blue-green algae, that grows in both saltwater and freshwater environments. Spirulina is highly nutritious and is often considered a superfood. It is rich in protein, vitamins (such as B vitamins and vitamin K), minerals (including iron and magnesium), and various antioxidants like beta-carotene and phycoerythrin. It's also a source of essential fatty acids, primarily gamma-linolenic acid (GLA). This nutrient profile makes spirulina a valuable addition to a balanced diet. *Weight Loss:* While spirulina is a nutrient-dense food, it's not a magic solution for weight loss on its own. Spirulina can be part of a balanced and low-calorie diet, providing essential nutrients while helping to curb hunger due to its protein and fiber content ⁽¹³²⁻¹³³⁾. *Appetite Suppression:* Spirulina's high protein and fiber content may help some people feel fuller for longer, which could potentially reduce overall calorie intake. However, its appetite-suppressing effects are not as significant as pharmaceutical appetite suppressants. Additionally, individual responses to spirulina can vary.

Precautions: Avoid if allergic or hypersensitive to spirulina or blue-green algae. Avoid with phenylketonuria. Avoid if pregnant or breastfeeding.

- **Hoodia:** Hoodia (*Hoodia gordonii*) is a tasty plant native to the dry regions of Southern Africa, primarily found in countries like South Africa, Namibia, and Botswana. The traditional use of Hoodia by indigenous San Bushmen in Southern Africa is often cited as the basis for its appetite-suppressing properties. These indigenous people have reportedly used Hoodia for centuries to reduce hunger and thirst during long hunting trips in the desert. They would chew on the plant to stave off hunger. It has gained attention in recent years due to claims that it can act as an appetite suppressant and aid in weight reduction ⁽¹³⁴⁾. However, it's essential to approach these claims with caution, as there is limited scientific evidence to support these claims.
Precautions: the safety and efficacy of Hoodia as a dietary supplement have not been thoroughly researched or confirmed. Additionally, the sale of Hoodia supplements has been associated with fraudulent and mislabeled products in the past.
- **Coleus:** *Coleus (Coleus forskohlii)* Coleus extract showed a substantial effect on weight loss and was safe and effective in reducing body fat in overweight/obese people ⁽¹³⁵⁻¹³⁶⁾. *Coleus forskohlii* formulation appears to be well tolerated in daily oral doses up to 500 mg, and deserves further investigation for its efficacy as a long-term anti-obesity intervention.
Precautions: while coleus supplements are generally considered safe for most people when taken at recommended dosages, there can be side effects, especially when consumed in excessive amounts or for extended periods. Some individuals may experience digestive problems such as diarrhea, loose stools, or an upset stomach when taking coleus supplements. If you already have low blood pressure or are taking medications to lower blood pressure, coleus supplements may cause your blood pressure to drop further, leading to dizziness or fainting. Coleus may interact with certain medications, including anticoagulants and antiplatelet drugs. The active compound in coleus, may influence thyroid hormone production, potentially leading to imbalances in thyroid function.

10. ETI's Solution for Weight Management and Related Challenges

We recommend using our energetic formulas and formulations for a significant reason: they enable you to create a more nourishing approach that promotes well-being in both our physical bodies and our emotional and mental states.

A lot of people turn to food as a way to cope with stress, emotions, or trauma. This pattern can create a cycle of emotional eating, resulting in increased weight gain, which can further exacerbate psychological distress. This is where our formulations can make a significant difference. Below, you'll find details about our new weight stabilizer formula as well as various formula combinations designed to challenge different aspects of weight management effectively.

10.1. Appetite Suppressant Formula

Description:

The purpose of this formula is to stimulate the body's energy, encouraging cells to enhance their metabolism and promoting equilibrium in the energetic signals that control hunger and fullness. In doing so, we aim to energetically support a healthy eating pattern grounded in a more balanced interplay between the human metabolic and reward systems.

This formula helps us in getting back to a healthy eating routine, something that has become challenging in today's world. It encourages us to eat when we're hungry and to refrain from eating when we're not. Moreover, it also helps of not overeating, both physically and in terms of our emotional and mental well-being.

Key Features from the energetic point of influence:

- Balancing the effects of hunger signals from both the brain and the digestive system, whether it's during or after a chosen diet or fasting period.
- Encouraging a more positive approach to eating behaviors by positively affecting emotional factors like stress, depression, or anxiety.
- Enhancing communication between the Metabolic and Reward Centers in the brain for better coordination.
- Reducing cravings that may be influenced by genetics, early life experiences, and social and environmental factors.
- After two weeks of taking 10-15 drops three times a day, you may begin to experience a new ability to identify the foods that work best for you.
- It is improving your thoughts and emotions when it concerns food preferences.

Dosage:

Mix 10-15 drops of the formula with 2-4 oz. of water. Consume this mixture either before eating or between meals whenever you experience food cravings signals for a duration of two to three weeks.

Side Effects: No side effects expected within the recommended dosage.

10.2. Increase the brain-body communication in reducing the signals of food cravings

Description:

The formulation has the potential of restoring regular energy signaling in the brain's centers responsible for regulating food intake. It can possibly help diminish cravings during dieting or whenever you intend to cut down on food intake. Additionally, it may assist in harmonizing the signaling between the metabolic and reward centers.

Formulation and Dosage:

Combined dosage of Hypothalamus Support (15 drops), Appetite Suppressant (5 drops) and GI Aid (5 drops) in 2-4 oz. of water. Drink 2-3 times per day 10-15 minutes before food intake for two-three weeks.

Side Effects: No side effects, if used with the recommended dosages.

10.3. Potential support for individuals with anorexia nervosa

Description:

This formulation could potentially assist individuals suffering from anorexia nervosa, who often experience an intense fear of gaining weight and a distorted body image.

Formulation and Dosage:

Combined dosage of Oxytocin (5 drops), Master Brain (5 drops) and Rejuvenation (2-3 drops) in 2-4 oz. of water. Drink 2-3 times per day 10-15 minutes before food intake for two-three weeks.

Side Effects: No side effects, if used with the recommended dosages.

10.4. Assistance for individuals dealing with binge-eating disorder

Description:

It may aid individuals in reducing their tendency to frequently consume large amounts of food in a short period and regain a sense of increased control during these episodes.

Formulation and Dosage:

Combined dosage of Appetite Suppressant (5 drops), Master Brain (5 drops) and Balance (2-3 drops) in 2-4 oz. of water. Drink 2-3 times per day 10-15 minutes before food intake for two-three weeks.

Side Effects: No side effects, if used with the recommended dosages.

10.5. Support in managing anxiety related to eating due to past traumatic experiences

Description:

This formulation could offer support for handling emotional upsets, unsettling memories, or feelings of concern around food intake.

Formulation and Dosage:

Combined dosage of Stress Relief (5 drops), Adrenal Support (5 drops) and Hypothalamus Support (2-3 drops) in 2-4 oz. of water. Drink 2-3 times per day 10-15 minutes before food intake for two-three weeks.

Side Effects: No side effects, if used with the recommended dosages

10.6. Boost GI functions and enhance metabolic rate

Description:

This formulation could potentially be beneficial for individuals with compromised GI functions and a sluggish metabolism.

Formulation and Dosage:

Combined dosage of Thyroid formula (10 drops), Circulatory formula (3 drops) and Adaptogen (2 drops) in 2-4 oz. of water. Drink 2-3 times per day 10-15 minutes before food intake for two-three weeks.

Side Effects: No side effects, if used with the recommended dosages.

Precautions: This is an active energy pattern; avoid intaking it within 3 hours of your bedtime.

Appendixes:

Appendix #1. Peripheral Adiposity Signals and GI Hormones

- Leptin

Leptin is synthesized within white adipocytes and is subsequently released into the systemic circulation. Plasma concentrations of leptin rise in proportion to the amount of body fat, making it a valuable biomarker for measuring adiposity. Circulating leptin gains access to the brain by crossing both the blood-brain barrier (BBB) and the blood-cerebrospinal fluid (CSF) barriers through receptor-mediated mechanisms.

Leptin receptors are abundantly present in the neurons of the hypothalamus, particularly in the arcuate nucleus (ARC). Leptin primarily binds to the leptin receptors known as Ob-Rb on ARC neurons. This binding event triggers the activation of Janus kinase 2 (JAK2)-STAT3 signaling while inhibiting the activity of AMP-activated protein kinase (AMPK).

Also, the activation of leptin signaling in the hypothalamus results in an increase in the neuronal activity of proopiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) neurons. Simultaneously, it decreases the activity of neuropeptide Y (NPY) and agouti-related protein (AgRP) neurons. These combined effects lead to a reduction in food intake and an increase in energy expenditure.

Leptin is additionally synthesized within the gastric epithelium, where it plays a role in enhancing local signals of satiation from the gut, including cholecystokinin (CCK). Also, leptin has an influence on the perception thresholds for sweet tastes on the tongue.

The majority of obese individual's exhibit heightened levels of leptin in their bloodstream, suggesting the presence of leptin resistance rather than a shortage of leptin. Furthermore, administering leptin treatment to obese individuals has demonstrated ineffectiveness. One potential explanation for leptin resistance is a decrease in the transport of leptin to the brain, possibly because the leptin transporters at the blood-brain barrier (BBB) become saturated.

- Insulin

Insulin is quickly released by pancreatic β -cells in response to a meal and is subsequently transported to the brain. Fasting levels of plasma insulin exhibit a strong positive correlation with body fat mass. Consequently, insulin is regarded as a secondary indicator of adiposity. Within the central nervous system (CNS), insulin receptors are prominently expressed in hypothalamic nuclei, including the arcuate nucleus (ARC), dorsomedial nucleus (DMN), and paraventricular nucleus (PVN) – well-known regions involved in the regulation of feeding behavior.

Similar to leptin, insulin binds to insulin receptors located on ARC neurons. This binding event triggers the activation of proopiomelanocortin (POMC) neurons and the inhibition of neuropeptide Y (NPY) and agouti-related protein (AgRP) neurons through the insulin receptor substrate (IRS)-2, as well as the phosphatidylinositol-3-kinase (PI3K)-Akt-FoxO1 signaling pathway. These

collective outcomes enable insulin to convey an anorexigenic signal to the brain, leading to a reduction in appetite.

GI Hormones

The gastrointestinal (GI) tract is recognized as the body's largest endocrine organ. Beyond its primary role in digestion and nutrient absorption, the gut also plays a significant role in governing energy balance, particularly in the short-term regulation of food consumption.

- *Cholecystokinin (CCK)*

Cholecystokinin (CCK) stands out as the gut hormone with the anorexigenic properties. It is released by enteroendocrine cells of the I-type located in the duodenum and small intestine. After secretion, CCK travels to the intestinal lamina propria, where it binds to CCK receptors situated on vagus nerve terminals. This interaction conveys signals of satiety to the hypothalamus via a relay through the brainstem and the pontine parabrachial nucleus.

- *Pancreatic polypeptide (PP)*

The consumption of a meal triggers the secretion of pancreatic polypeptide (PP) from PP cells within the pancreatic islets, and this process is mediated by the vagus nerve. The increase in circulating PP levels after a meal is directly related to the calorie content of the meal and can persist for as long as six hours. Studies have demonstrated lower plasma PP levels in individuals who are obese.

- *Peptide tyrosine-tyrosine (PYY)*

Post-meal, peptide YY (PYY) is released by L cells located in the ileum, colon, and rectum. Circulating PYY then binds to the Y2 receptor found on the presynaptic terminals of hypothalamic neurons responsible for producing neuropeptide Y (NPY) and agouti-related protein (AgRP). This binding event leads to the deactivation of NPY/AgRP neurons and the beginning of reduced appetite.

Studies have shown that individuals who are overweight exhibit lower levels of plasma PYY compared to those who are lean. Consequently, it has been proposed that diminished PYY secretion during the postprandial period may play a role in the development of obesity.

- *GLP-1*

GLP-1, derived from the proglucagon precursor peptide, is synthesized within the L cells situated in the ileum and colon. Following secretion, GLP-1 enters the systemic circulation but has a short lifespan, typically lasting only about 1 to 2 minutes.

GLP-1 exerts its appetite-suppressing effects through the GLP-1 receptor (GLP-1R), which is broadly distributed throughout the brain, gastrointestinal tract, and pancreas.

- *Oxyntomodulin (OXM)*

OXM, derived from the preproglucagon molecule, is produced concurrently with GLP-1 in the intestinal L cells. The potential appetite-regulating effects of OXM, certainly present, are currently less well-defined and remain unclear.

- *Ghrelin*

Ghrelin stands out among gut hormones as it possesses an orexigenic effect, stimulating appetite. When administered either centrally or peripherally, ghrelin prompts increased food intake and leads to weight gain. Additionally, plasma ghrelin levels surge during periods of fasting, solidifying its role as a natural hunger hormone.

Furthermore, the levels of plasma ghrelin exhibit a circadian rhythm, with a notable increase before each meal followed by a rapid decline after eating. This pattern supports the idea that ghrelin plays a role in initiating meals. The current consensus is that fluctuations in plasma ghrelin levels may represent a compensatory response to alterations in energy metabolism.

Appendix # 2. Eating Disorders

Eating disorders include complex mental health conditions characterized by unconventional eating habits and thought patterns centered on food, body weight, and body image. These disorders often lead to physical, emotional, and social consequences and can be life-threatening when left unattended. Several types of eating disorders include:

- *Anorexia Nervosa*: Individuals afflicted by anorexia nervosa experience an overwhelming dread of weight gain and a skewed perception of their own body. They frequently engage in food restriction, extreme dieting, and sometimes excessive exercise, which can result in profound weight loss, malnutrition, and a spectrum of both physical and psychological health issues.
- *Bulimia Nervosa*: People suffering from bulimia nervosa often participate in episodes of excessive eating, designated binge eating, which are subsequently followed by compensatory actions such as vomiting, using laxatives, or engaging in excessive exercise. This repetitive cycle of bingeing and eliminating can inflict damage on the body, particularly the digestive system.
- *Binge-Eating Disorder*: This condition entails recurring episodes of binge eating, without the compensatory actions observed in bulimia. Individuals with binge-eating disorder frequently consume substantial amounts of food within a brief timeframe and experience a sense of diminished control during these episodes.
- *Avoidant/Restrictive Food Intake Disorder (ARFID)*: ARFID is defined by selective eating or the avoidance of certain foods, often restricting from sensory sensitivities, fear of choking, or a general disinterest in particular food items. Unlike anorexia, which is primarily motivated by the interest of weight loss, ARFID is distinguished by these unique factors that shape an individual's eating habits and choices. Individuals with ARFID may find certain textures, tastes, or smells of foods to be overwhelming or unpleasant, leading them to limit their dietary choices. Others might experience anxiety

around eating due to the fear of choking or a traumatic past experience. These factors can significantly impact their ability to maintain a balanced and varied diet, potentially affecting their overall health and nutrition.

- *Other Specified Feeding or Eating Disorder (OSFED)*. OSFED is a comprehensive category encompassing eating disorders that exhibit disordered eating behaviors and thought patterns but do not precisely align with the specific diagnostic criteria for anorexia nervosa, bulimia nervosa, or binge-eating disorder. OSFED serves as a vital catch-all classification within the realm of eating disorders, acknowledging the diversity and complexity of these conditions. OSFED acknowledges that eating disorders can manifest differently across individuals, reflecting the unique interplay of psychological, emotional, and sociocultural factors.

Appendix #3. Diet Modification to Improve Thyroid Health

Here are some dietary modifications that may be beneficial for thyroid health:

- *Balanced Diet*: A balanced diet that provides a mix of macronutrients (carbohydrates, proteins, and fats) and micronutrients (vitamins and minerals) is essential for overall health, including thyroid health.
- *Limit Sugar and Processed Foods*: High sugar and highly processed foods can contribute to inflammation and hormonal imbalances, potentially affecting thyroid function.
- Some foods contain compounds known as *goitrogens* that can interfere with thyroid function. Cooking these foods can help reduce their goitrogenic effects. Examples of goitrogenic foods include cruciferous vegetables (broccoli, cauliflower, cabbage) and soy products.
- *Iodine* is a crucial component for thyroid hormone production. Ensuring you have an adequate intake of iodine is important, but excessive intake can also be harmful. Foods rich in iodine include iodized salt, seafood (such as fish and seaweed), and dairy products.
- *Tyrosine* is an amino acid that's a building block for thyroid hormones. Foods like lean meats, dairy products, eggs, and legumes contain tyrosine.
- *Selenium* is another important mineral for thyroid function and helps convert the inactive thyroid hormone (T4) into the active form (T3). Foods rich in selenium include Brazil nuts, tuna, sardines, eggs, and whole grains.
- *Zinc* is involved in thyroid hormone production and helps regulate the body's response to thyroid hormones. You can find zinc in foods like lean meats, nuts, seeds, and whole grains.
- *Antioxidant-Rich Foods*: Antioxidants help protect the thyroid gland from damage caused by oxidative stress. Include a variety of colorful fruits and vegetables in your diet, such as berries, spinach, kale, and bell peppers.
- *Hydration*: Staying adequately hydrated supports overall bodily functions, including the thyroid.
- *Gluten Sensitivity*: Some individuals with thyroid disorders may also have sensitivities to gluten. If you suspect gluten intolerance, consider discussing this with a healthcare professional.

- Incorporate vitamin *A-rich foods and Omega-3 fatty acids* into your diet as they play a significant role in enhancing gene transcription associated with thyroid function. Consider switching to spring water for drinking and cooking to avoid the potential thyroid function reduction linked to the inclusion of artificial fluoride in tap water. If dealing with autoimmune thyroid issues or hypothyroidism, you might find benefit trying a food elimination diet. This could involve the exclusion of gluten and cow dairy from your meals.
- Include *carotenoid-rich foods* in your diet, such as squash, carrots, mangoes, and sweet potatoes.

Appendix #4. Exercise Program

It is good to discovering physical activities that bring you joy and fit good into your daily routine. This could be activities such as commuting to work on foot or by bicycle, engaging in dance, tending to your garden, or indulging in a beloved sport.

Here are 10-minute breathing and active movement routines that can be effortlessly incorporated into your daily routine. During this exercise session, your body experiences a revitalization, igniting a sense of warmth and activity throughout your entire being. These exercises have been endorsed through 20 years of practice by individuals worldwide.

1. Begin by positioning yourself with your feet separated comfortably. Allow your arms to hang down, keeping your palms open and directed backward. Swiftly sweep your arms backward while breathing in through your nostrils, simultaneously tilting your chin upwards slightly. During the arms' backward motion, exhale. Perform this sequence 10 to 25 times consecutively.
2. Position yourself with a comfortable stance and your feet separated. Extend your right arm vertically upwards. Lower the elevated arm and seamlessly lift the opposite arm in one fluid motion. Inhale through your nostrils as each arm ascends, and exhale as they transition positions. Perform this sequence 10 to 25 times continuously.
3. Stand with your feet separated. Elevate your right arm while situating your left arm in front of your stomach, palm facing upward. Swing the elevated arm to the left, switching the arrangement of the arms. Inhale through your nostrils as each arm reaches the highest point, and exhale during the midpoint of the motion. Repeat this pattern 10 to 25 times
4. Position yourself with your feet spread wider than your shoulders. Hinge forward at the waist and stretch one arm behind you and the other arm forward. Initiate a circular arm motion akin to a swimmer's stroke, breathing in through your nostrils as you extend one arm forward, and exhaling at the midpoint of the movement. Perform this sequence 10 to 25 times.
5. Stand with your feet separated. Bend slightly and lift your right arm, simultaneously raising your left leg. Alternate between elevating and lowering the opposite arm and leg in a

coordinated manner. Breathe in through your nostrils as you initiate the movement, and exhale at the midpoint of the motion. Repeat this sequence 10 to 25 times.

6. Position yourself with your feet separated. Maintain a straight back and allow your arms to hang in a relaxed manner. Sway your upper body from left to right, inhaling as you lean towards the left and exhaling as you return to the center. Perform this movement for a total of 10 repetitions.
7. Stand with your feet separated. Extend both arms out to your sides and maintain the position. Alternate lifting your legs while extending your heels forward. Perform this sequence 10 to 25 times.
8. Position your left knee onto the ground and stretch your right leg sideways, making contact with the floor. Position your arms to provide support for your body, ensuring they are at shoulder width. Elevate your extended leg while inhaling through your nostrils. Exhale as you gently lower the leg without allowing it to touch the floor. Repeat this action 10 to 25 times. Then, switch legs and replicate the process with your left leg.
9. Start by positioning your knees on the ground, about hip-width apart. Support your body using your arms, ensuring they are at shoulder-width distance. Now, extend your right leg straight back, allowing it to rise slightly as you take a gentle inhale through your nose. Give this movement a go for 10 to 25 repetitions. Then, switch over to the other leg and repeat the same process with your left leg.

References

1. Elington W.R. Evolution and physiological roles of phosphagen systems. *Annu Rev Physiol.* 2001;63:289-325.
2. Brooks George A. The Science and Translation of Lactate Shuttle Theory *Cell Metabolism*. Exercise Physiology Laboratory, Department of Integrative Biology, University of California, Berkeley, Berkeley, CA 94720, USA*Correspondence: gbrooks@berkeley.edu.
3. Hochachka P.W., Gunga H.C. & Kirsch K. (1998). Our ancestral physiological phenotype: an adaptation for hypoxia tolerance and for endurance performance. *Proceedings National Academy of Science* 95. 1998;1915–20.
4. Hochachka P.W. & Monge, C. Evolution of human hypoxia tolerance physiology. *Adv. Exp. Med. Biol.* 2000;475:25–43.
5. Robergs R.A. & Roberts S. *Exercise Physiology: Exercise, performance, and clinical applications*. 1997. St Louis, MO: Mosby.
6. Liesa M. & Shrihai O.S. Mitochondrial dynamics in the regulation of nutrient utilization and energy expenditure. *Cell Metabolism*. 2013;17(4):491–506.
7. Jheng H.F., Huang S.H., Kuo H.M., Hughes M.W. & Tsai Y.S. Molecular insight and pharmacological approaches targeting mitochondrial dynamics in skeletal muscle during obesity. *Annals of the New York Academy of Sciences*. 2015;1350:82–94.

8. Paradies G., Paradies V., Ruggiero F.M. & Petrosillo G. Oxidative stress, cardiolipin and mitochondrial dysfunction in nonalcoholic fatty liver disease. *World Journal of Gastroenterology*. 2014;20(39):14205–18.
9. Agha M, Agha R. The rising prevalence of obesity: part A: impact on public health. *Int J Surg Oncol (N Y)*. 2017; (7): e17.
10. Niswender K.D. & Schwartz M.W. Insulin and leptin revisited: adiposity signals with overlapping physiological and intracellular signaling capabilities. *Front Neuroendocrinol*. 2003;24(1):1-10.
11. Wren A.M. Gut and hormones and obesity. *Front Horm Res*. 2008;36:165-81.
12. Vitaterna M.H., Takahashi J.S. & Turek F.W. Overview of circadian rhythms. *Alcohol Res Health*. 2001;25(2):85-93.
13. Garami A. & Székely M. Body temperature: Its regulation in framework of energy balance. *Temperature*. 2014;1(1):28-9.
14. Hirotsu C., Tufik S, Andersen ML. Interactions between sleep, stress, and metabolism: From physiological to pathological conditions. *Sleep Sci*. 2015;8(3):143-52.
15. Peters A., Kubera B., Hubold C. & Langemann D. The selfish brain: stress and eating behavior. *Front. Neurosci*. 2011;5:74.
16. Foster M. T., Warne J. P., Ginsberg A. B., Horneman H. F., Pecoraro N. C., Akana S. F., et al. (2009). Palatable foods, stress, and energy stores sculpt corticotropin-releasing factor, adrenocorticotropin, and corticosterone concentrations after restraint. *Endocrinology*. 2009;150 2325–33.
17. Vitaterna M.H., Shimomura K. & Jiang P. Genetics of Circadian Rhythms. *Neurol Clin*. 2019;37(3):487-504.
18. Panda S. Circadian physiology of metabolism. *Science*. 2016;354(6315):1008-15.
19. Scheer F.A., Morris C.J. & Shea S.A. The internal circadian clock increases hunger and appetite in the evening independent of food intake and other behaviors. *Obesity (Silver Spring)*. 2013;21(3):421-3.
20. Greco C.M. & Sassone-Corsi P. Circadian blueprint of metabolic pathways in the brain. *Nat Rev Neurosci*. 2019;20(2):71-82.
21. Jauch-Chara K. & Oltmanns K.M. Obesity – a neuropsychological disease? Systematic review and neuropsychological model. *Prog Neurobiol*. 2014;114:84–101.
22. Peever J. & Fuller P.M. Neuroscience: A Distributed Neural Network Controls REM Sleep. *Curr Biol*. 2016;26(1):34-5.
23. Rogers E.M, Banks N.F. & Jenkins NDM. The effects of sleep disruption on metabolism, hunger, and satiety, and the influence of psychosocial stress and exercise: A narrative review. *Diabetes Metab Res Rev*. 2023:e3667.
24. Medic G., Wille M. & Hemels M.E. Short- and long-term health consequences of sleep disruption. *Nat Sci Sleep*. 2017;9:151-61.
25. Fu O., Minokoshi Y. & Nakajima K.I. Recent Advances in Neural Circuits for Taste Perception in Hunger. *Front Neural Circuits*. 2021;15:609824.
26. Shukla C. & Basheer R. Metabolic signals in sleep regulation: recent insights. *Nat Sci Sleep*. 2016;8:9-20.
27. Van Drunen R. & Eckel-Mahan K. Circadian Rhythms of the Hypothalamus: From Function to Physiology. *Clocks Sleep*. 2021;3(1):189-226.
28. Masri S. & Sassone-Corsi P. The circadian clock: a framework linking metabolism, epigenetics and neuronal function. *Nat Rev Neurosci*. 2013;14(1):69-75.

29. Nowak N., Rawleigh A. & Brown S.A. Circadian Clocks, Sleep, and Metabolism. *Adv Exp Med Biol.* 2021;1344:21-42.
30. Biran J., Tahor M., Wircer E. & Levkowitz G. Role of developmental factors in hypothalamic function. *Front Neuroanat.* 2015;9:47.
31. Welsh D.K., Takahashi J.S. & Kay S.A. Suprachiasmatic nucleus: cell autonomy and network properties. *Annu Rev Physiol.* 2010;72:551-77.
32. Chou T.C., Bjorkum A.A., Gaus S.E., Lu J., Scammell T.E. & Saper C.B. Afferents to the ventrolateral preoptic nucleus. *J Neurosci.* 2002;22(3):977-90.
33. Siegel J.M. The neurotransmitters of sleep. *J Clin Psychiatry.* 2004;65 (16):4-7.
34. Gottesmann C. GABA mechanisms and sleep. *Neuroscience.* 2002;111(2):231-39.
35. Yu J.H. & Kim M.S. Molecular mechanisms of appetite regulation. *Diabetes Metab J.* 2012;36(6):391-98.
36. Blume C., Garbazza C. & Spitschan M. Effects of light on human circadian rhythms, sleep and mood. *Somnologie.* 2019;23(3):147-56.
37. Pickel L. & Sung H.K. Feeding Rhythms and the Circadian Regulation of Metabolism. *Front Nutr.* 2020;7:39.
38. Foster R.G. Sleep, circadian rhythms and health. *Interface Focus.* 2020;10(3):20190098.
39. Farr O.M., Li C.R. & Mantzoros C.S. Central nervous system regulation of eating: Insights from human brain imaging. *Metabolism.* 2016;65(5):699-713.
40. Rui L. Brain regulation of energy balance and body weight. *Endocr Metab Disord.* 2013;14(4):387-407.
41. Faulconbridge L.F. & Hayes M.R. Regulation of energy balance and body weight by the brain: a distributed system prone to disruption. *Psychiatr Clin North Am.* 2011;34(4):733-45.
42. Klok M.D., Jakobsdottir S. & Drent M.L. The role of leptin and ghrelin in the regulation of food intake and body weight in humans: a review. *Obes Rev.* 2007;8(1):21-34.
43. Obradovic M., Sudar-Milovanovic E., Soskic S., Essack M., Arya S, Stewart A.J., Gojobori T. & Isenovic E.R. Leptin and Obesity: Role and Clinical Implication. *Front Endocrinol.* 2021; 12:585887.
44. Vohra M.S., Benschoula K., Serpell C.J. & Hwa W.E. AgRP/NPY and POMC neurons in the arcuate nucleus and their potential role in treatment of obesity. *Eur J Pharmacol.* 2022;915:174611.
45. Sohn J.W. Network of hypothalamic neurons that control appetite. *BMB.* 2015;48(4):229-33.
46. Lewis R.G., Florio E., Punzo D. & Borrelli E. The Brain's Reward System in Health and Disease. *Adv Exp Med Biol.* 2021;1344:57-69.
47. Arias-Carrion O., Stamelou M., Murillo-Rodríguez E., Menendez-Gonzalez M. & Peppel E. Dopaminergic reward system: a short integrative review. *Int Arch Med.* 2010;3:24.
48. Chau BKH., Jarvis H., Law C.K. & Chong T.T. Dopamine and reward: a view from the prefrontal cortex. *Behav Pharmacol.* 2018;29(7):569-83.
49. Razzoli M., Pearson C., Crow S. & Bartolomucci A. Stress, overeating, and obesity: Insights from human studies and preclinical models. *Neurosci Biobehav Rev.* 2017; 76 (Pt A):154-62.
50. Frank G.W., Shott M.E. & DeGuzman M.C. The Neurobiology of Eating Disorders. *Child Adolesc Psychiatr Clin N Am.* 2019;28(4):629-40.

51. Koob G.F. & Volkow N.D. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry*. 2016;3(8):760-73.
52. Simmons W.K., Burrows K., Avery J.A., Kerr K.L., Bodurka J., Savage C.R. & Drevets W.C. Depression-Related Increases and Decreases in Appetite: Dissociable Patterns of Aberrant Activity in Reward and Interoceptive Neurocircuitry. *Am J Psychiatry*. 2016;173(4):418-28.
53. Rosenbaum D.L. & White K.S. The Role of Anxiety in Binge Eating Behavior: A Critical Examination of Theory and Empirical Literature. *Health Psychol Res*. 2013;1(2):e19.
54. Konttinen H. Emotional eating and obesity in adults: the role of depression, sleep and genes. *Proc Nutr Soc*. 2020;79(3):283-89.
55. Singh M. Mood, food, and obesity. *Front Psychol*. 2014;5:925.
56. Ikeda A., Miyamoto J.J., Usui N., Taira M. & Moriyama K. Chewing Stimulation Reduces Appetite Ratings and Attentional Bias toward Visual Food Stimuli in Healthy-Weight Individuals. *Front Psychol*. 2018;9:99.
57. Alonso-Alonso M., Woods S.C., Pelchat M., Grigson P.S., Stice E., Farooqi S., Khoo C.S., Mattes R.D. & Beauchamp G.K. Food reward system: current perspectives and future research needs. *Nutr Rev*. 2015;73(5):296-307.
58. Gordon E.L., Ariel-Donges A.H., Bauman V. & Merlo L.J. What Is the Evidence for "Food Addiction?" A Systematic Review. *Nutrients*. 2018;10(4):477.
59. Leigh S.J. & Morris M.J. The role of reward circuitry and food addiction in the obesity epidemic: An update. *Biol Psychol*. 2018;131:31-42.
60. Adams R.C., Sedgmond J., Maizey L., Chambers C.D. & Lawrence N.S. Food Addiction: Implications for the Diagnosis and Treatment of Overeating. *Nutrients*. 2019;11(9):2086.
61. Ziauddeen H., Alonso-Alonso M., Hill J.O., Kelley M. & Khan N.A. Obesity and the neurocognitive basis of food reward and the control of intake. *Adv Nutr*. 2015;6(4):474-86.
62. Alqahtani H.A., Almagsoodi A.A., Alshamrani N.D., Almalki T.J. & Sumaili A.M. Common Electrolyte and Metabolic Abnormalities Among Thyroid Patients. *Cureus*. 2021;13(5).
63. Mullur R., Liu Y.Y. & Brent G.A. Thyroid hormone regulation of metabolism. *Physiol Rev*. 2014;94(2):355-82.
64. McAninch E.A. & Bianco A.C. Thyroid hormone signaling in energy homeostasis and energy metabolism. *Ann N Y Acad Sci*. 2014;1311:77-87.
65. Moran L.J., Lombard C.B., Lim S., Noakes M. & Teede H.J. Polycystic ovary syndrome and weight management. *Womens Health*. 2010;6(2):271-83.
66. Kirwan J.P., Sacks J. & Nieuwoudt S. The essential role of exercise in the management of type 2 diabetes. *Cleve Clin J Med*. 2017;84(7(1):15-21.
67. Ahima R.S. & Antwi D.A. Brain regulation of appetite and satiety. *Endocrinol Metab Clin North Am*. 2008;37(4):811-23.
68. Volkow N.D., Koob G.F. & McLellan A.T. Neurobiologic advances from the brain disease model of addiction. *N Engl J Med*. 2016;374:363-71.
69. Hernandez L. & Hoebel B.G. Food reward and cocaine increase extracellular dopamine in the nucleus accumbens as measured by microdialysis. *Life Sci*. 1988;42:1705-12.
70. Cameron C.M., Wightman R.M. & Carelli R.M. Dynamics of rapid dopamine release in the nucleus accumbens during goal-directed behaviors for cocaine versus natural rewards. *Neuropharmacology*. 2014; 86:319-28.

71. Broberger C. Brain regulation of food intake and appetite: molecules and networks. *J Intern Med.* 2005;258(4):301-27.
72. Higgs S., Spetter M.S., Thomas J.M., Rotshtein P., Lee M., Hallschmid M. & Dourish C.T. Interactions between metabolic, reward and cognitive processes in appetite control: Implications for novel weight management therapies. *J Psychopharmacol.* 2017;31(11):1460-74.
73. Ahima R.S. & Antwi DA. Brain regulation of appetite and satiety. *Endocrinol Metab Clin North Am.* 2008;37(4):811-23.
74. Cai J. & Tong Q. Anatomy and Function of Ventral Tegmental Area Glutamate Neurons. *Front Neural Circuits.* 2022;16: 867053.
75. Jiménez-Limas K., Miranda-Barrera V.A., Muñoz-Díaz K.F., Novales-Huidobro S.R. & Chico-Barba G. Body Dissatisfaction, Distorted Body Image and Disordered Eating Behaviors in University Students: An Analysis from 2017-2022. *Int J Environ Res Public Health.* 2022;19(18):11482.
76. Memon A.N., Gowda A.S., Rallabhandi B., Bidika E., Fayyaz H., Salib M. & Cancarevic I. Have Our Attempts to Curb Obesity Done More Harm Than Good? *Cureus.* 2020;12(9).
77. Konttinen H. Emotional eating and obesity in adults: the role of depression, sleep and genes. *Proc Nutr Soc.* 2020;79(3):283-89.
78. Konttinen H., van Strien T., Mannisto S., Jousilahti P. & Haukkala A. Depression, emotional eating and long-term weight changes: a population-based prospective study. *Int J Behav Nutr Phys Act.* 2019;16(1):28.
79. Sapolsky R. M., Romero L. M. & Munck A. U. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr. Rev.* 2000;21 55–89.
80. Heinrichs S. C. & Richard D. The role of corticotropin-releasing factor and urocortin in the modulation of ingestive behavior. *Neuropeptides.* 1999;33: 350–59.
81. Richard D., Lin Q. & Timofeeva E. The corticotropin-releasing factor family of peptides and CRF receptors: their roles in the regulation of energy balance. *Eur. J. Pharmacol.* 2002;440:189–97.
82. Bjorntorp P. The regulation of adipose tissue distribution in humans. *Int. J. Obes. Relat. Metab. Disord.* 1996;20:291–302.
83. Marin P., Darin N., Amemiya T., Andersson B., Jern S. & Bjorntorp P. (1992b). Cortisol secretion in relation to body fat distribution in obese premenopausal women. *Metabolism.* 1992;41:882–86.
84. Hosoda H., Kojima M. & Kangawa K. Biological, physiological, and pharmacological aspects of ghrelin. *J. Pharmacol. Sci.* 2006;100:398–410.
85. Lutter M., Sakata I., Osborne-Lawrence S., Rovinsky S. A., Anderson J. G., Jung S., et al. The orexigenic hormone ghrelin defends against depressive symptoms of chronic stress. *Nat. Neurosci.* 2008;11:752–53.
86. Chaix A., Zarrinpar A., Miu P. & Panda S. Time-restricted feeding is a preventative and therapeutic intervention against diverse nutritional challenges. *Cell. Metab.* 2014;20:991–1005.
87. Hatori M., et al. Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. *Cell. Metab.* 2012;15:848–60.
88. Chasens E.R., Imes C.C., Kariuki J.K., Luyster F.S., Morris J.L., et al. Sleep and Metabolic Syndrome. *Nurs Clin North Am.* 2021;56(2):203-17.

89. Sharma S, & Kavuru M. Sleep and metabolism: an overview. *Int J Endocrinol.* 2010;270832.
90. Chaput J.P. & Tremblay A. Adequate sleep to improve the treatment of obesity. *CMAJ.* 2012;184(18):1975-76.
91. Kline C.E., Chasens E.R., Bizhanova Z., Sereika S.M., Buysse DJ, et al. The association between sleep health and weight change during a 12-month behavioral weight loss intervention. *Int J Obes.* 2021;45(3):639-49.
92. Papatriantafyllou E., Efthymiou D., Zoumbaneas E., Popescu C.A. & Vassilopoulou E. Sleep Deprivation: Effects on Weight Loss and Weight Loss Maintenance. *Nutrients.* 2022;14(8):1549.
93. Yannakoulia M., Anastasiou C.A., Karfopoulou E., Pehlivanidis A., Panagiotakos D.B., et al. Sleep quality is associated with weight loss maintenance status: the MedWeight study. *Sleep Med.* 2017;34:242-45.
94. Hur K.Y. & Lee M.S. Gut Microbiota and Metabolic Disorders. *Diabetes Metab J.* 2015;39(3):198-203.
95. Fan Y. & Pedersen O. Gut microbiota in human metabolic health and disease. *Nat Rev Microbiol.* 2021;19(1):55-71.
96. Wu J., Wang K., Wang X., Pang Y. & Jiang C. The role of the gut microbiome and its metabolites in metabolic diseases. *Protein Cell.* 2021;12(5):360-73.
97. Yang J.Y. & Kweon M.N. The gut microbiota: a key regulator of metabolic diseases. *BMB Rep.* 2016;49(10):536-41.
98. Razzoli M., Pearson C., Crow S. & Bartolomucci A. Stress, overeating, and obesity: Insights from human studies and preclinical models. *Neurosci Biobehav Rev.* 2017;76(Pt A):154-62.
99. Stults-Kolehmainen M.A. & Sinha R. The effects of stress on physical activity and exercise. *Sports Med.* 2014;44(1):81-121.
100. Nollet M., Wisden W. & Franks N.P. Sleep deprivation and stress: a reciprocal relationship. *Interface Focus.* 2020;10(3):20190092.
101. Leistner C. & Menke A. Hypothalamic-pituitary-adrenal axis and stress. *Handb Clin Neurol.* 2020;175:55-64.
102. Porcelli A.J., Lewis A.H. & Delgado M.R. Acute stress influences neural circuits of reward processing. *Front Neurosci.* 2012;6:157.
103. Konturek P.C., Brzozowski T. & Konturek S.J. Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options. *J Physiol Pharmacol.* 2011;62(6):591-99.
104. Tomiyama A.J. Stress and Obesity. *Annu Rev Psychol.* 2019;70:703-18.
105. Steimer T. The biology of fear- and anxiety-related behaviors. *Dialogues Clin Neurosci.* 2002; (3):231-49.
106. McKiernan F., Houchins J.A. & Mattes RD. Relationships between human thirst, hunger, drinking, and feeding. *Physiol Behav.* 2008;94(5):700-08.
107. McKiernan F., Hollis J.H., McCabe G.P. & Mattes R.D. Thirst-drinking, hunger-eating; tight coupling? *J Am Diet Assoc.* 2009;109(3):486-90.
108. Cox C.E. Role of Physical Activity for Weight Loss and Weight Maintenance. *Diabetes Spectr.* 2017;30(3):157-60.

109. Epstein L.H. & Goldfield G.S. Physical activity in the treatment of childhood overweight and obesity: Current evidence and research issues. *Med. Sci. Sports Exerc.* 1999;31:553–59.
110. Yang Y.J. An Overview of Current Physical Activity Recommendations in Primary Care. *Korean J Fam Med.* 2019;40(3):135-42.
111. Patterson R.E., Laughlin G.A., LaCroix A.Z., Hartman S.J., Natarajan L., et al. Intermittent Fasting and Human Metabolic Health. *J Acad Nutr Diet.* 2015;115(8):1203-12.
112. de Cabo R. & Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. *N Engl J Med.* 2019;381(26):2541-51.
113. Dynka D., Paziewska A. & Kowalczke K. Keto Menu-Effect of Ketogenic Menu and Intermittent Fasting on the Biochemical Markers and Body Composition in a Physically Active Man-A Controlled Case Study. *Foods.* 2023;12(17):3219.
114. Kang S.H., Park Y.S., Ahn S.H. & Kim H.H. Intermittent Fasting: Current Evidence in Clinical Practice. *J Obes Metab Syndr.* 2020;29(2):81-3.
115. Albosta M. & Bakke J. Intermittent fasting: is there a role in the treatment of diabetes? A review of the literature and guide for primary care physicians. *Clin Diabetes Endocrinol.* 2021;7(1):3.
116. Zumida Y., Yahagi N., Takeuchi Y., Nishi M., Shikama A, et al. Glycogen shortage during fasting triggers liver-brain-adipose neurocircuitry to facilitate fat utilization. *Nat Commun.* 2013;4:2316.
117. Kanungo S., Wells K., Tribett T & El-Gharbawy A. Glycogen metabolism and glycogen storage disorders. *Ann Transl Med.* 2018;6(24):474.
118. Murray B, Rosenbloom C. Fundamentals of glycogen metabolism for coaches and athletes. *Nutr Rev.* 2018;76(4):243-59.
119. Pradhan G., Samson S.L. & Sun Y. Ghrelin: much more than a hunger hormone. *Curr Opin Clin Nutr Metab Care.* 2013;16(6):619-24.
120. Hinz M., Stein A. & Uncini T. 5-HTP efficacy and contraindications. *Neuropsychiatr Dis Treat.* 2012; 8:323-28.
121. Klinge C.M., Clark B.J. & Prough R.A. Dehydroepiandrosterone Research: Past, Current, and Future. *Vitam Horm.* 2018;108:1-28.
122. Ostojic S.M., Calleja J. & Jourkesh M. Effects of short-term dehydroepiandrosterone supplementation on body composition in young athletes. *Chin J Physiol.* 2010;53(1):19-25.
123. Kerksick C.M., Roberts M.D., Campbell B.I., Galbreath M.M., Taylor L.W., Wilborn C.D., Lee A., Dove J., Bunn J.W., Rasmussen C.J. & Kreider R.B. Differential Impact of Calcium and Vitamin D on Body Composition Changes in Post-Menopausal Women Following a Restricted Energy Diet and Exercise Program. *Nutrients.* 2020;12(3):713.
124. Gomes C.C., Passos T.S. & Morais A. Vitamin A Status Improvement in Obesity: Findings and Perspectives Using Encapsulation Techniques. *Nutrients.* 2021;13(6):1921.
125. Hoffmann D. Medical herbalism. Healing Arts Press; Rochester, VT: 2003. pp. 483–521.
126. Chacko S.M., Thambi P.T., Kuttan R. & Nishigaki I. Beneficial effects of green tea: a literature review. *Chin Med.* 2010;5:13.

127. Van Baak M.A. & Mariman EM. Dietary strategies for weight loss maintenance. *Nutrients*. 2019;11(8).
128. Bortolin R.C., Vargas A.R., de Miranda Ramos V., Gasparotto J., Chaves P.R., et al. Guarana supplementation attenuated obesity, insulin resistance, and adipokines dysregulation induced by a standardized human Western diet via brown adipose tissue activation. *Phytother Res*. 2019 May;33(5):1394-1403.
129. Anderson J.W., Allgood L.D., Turner J., Oeltgen P.R. & Daggy BP. Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. *Am J Clin Nutr*. 1999;70(4):466-73.
130. Xiao Z., Chen H., Zhang Y., Deng H., Wang K, et al. The effect of psyllium consumption on weight, body mass index, lipid profile, and glucose metabolism in diabetic patients: A systematic review and dose-response meta-analysis of randomized controlled trials. *Phytother Res*. 2020;34(6):1237-47.
131. Paradis M.E., Couture P. & Lamarche B. A randomised crossover placebo-controlled trial investigating the effect of brown seaweed (*Ascophyllum nodosum* and *Fucus vesiculosus*) on postchallenge plasma glucose and insulin levels in men and women. *Appl Physiol Nutr Metab*. 2011;36(6):913-19.
132. DiNicolantonio J.J., Bhat A.G. & O'Keefe J. Effects of spirulina on weight loss and blood lipids: a review. *Open Heart*. 2020;7(1).
133. Karkos P.D., Leong S.C., Karkos C.D., Sivaji N. & Assimakopoulos D.A. Spirulina in clinical practice: evidence-based human applications. *Evid Based Complement Alternat Med*. 2011; 531053.
134. Roza O., Lovász N., Zupkó I., Hohmann J. & Csupor D. Sympathomimetic activity of a *Hoodia gordonii* product: a possible mechanism of cardiovascular side effects. *Biomed Res Int*. 2013;171059.
135. Henderson S., Magu B., Rasmussen C., Lancaster S., Kerksick C., et al. Effects of *coleus forskohlii* supplementation on body composition and hematological profiles in mildly overweight women. *J Int Soc Sports Nutr*. 2005;2(2):54-62.
136. Loftus H.L., Astell K.J., Mathai M.L. & Su XQ. *Coleus forskohlii* Extract Supplementation in Conjunction with a Hypocaloric Diet Reduces the Risk Factors of Metabolic Syndrome in Overweight and Obese Subjects: A Randomized Controlled Trial. *Nutrients*. 2015;7(11):9508-22.

*These statements have not been evaluated by the Food & Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.