Postprandial energy metabolism and metabolic syndrome

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Review

Postprandial energy metabolism and metabolic syndrome.

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Abstract: Postprandial studies are essential to understand metabolism functioning after food intake and, the metabolic syndrome is a combination of different cardiovascular risk factors which can endanger human health. Thus, this review aims to describe the relationship between the postprandial metabolism of the organism and its possible connection with metabolic syndrome. An electronic search was performed using the databases "Cercabib", "PubMed", "Scopus" and "Google Academy" and articles published after the 2000's were selected. The data indicate that the postprandial response is linked to the ability to suffer from metabolic syndrome. Alterations in the postprandial metabolism of the organism, adherence to Western diets, decrease in physical activity, etc., they are characteristics that are part of the complex definition of the postprandial state, and it will favor the appearance of metabolic syndrome. The conclusion of this work is that more research is needed to prevent the development of metabolic syndrome. Also, there is a great need to promote healthy life in the community and physical activity.

Keywords: postprandial state; metabolic syndrome; non-communicable disease; obesity

Resum: Els estudis postprandial són essencials per comprendre el funcionament del metabolisme després de la ingesta d'aliments i, la síndrome metabòlica és una combinació de diferents factors de risc cardiovascular que poden posar en perill la salut humana. Així, aquesta revisió pretén descriure la relació entre el metabolisme postprandial de l'organisme i la possible connexió amb la síndrome metabòlica. Es va realitzar una cerca electrònica utilitzant les bases de dades "Cercabib", "PubMed", "Scopus" i "Google Academy" i es van seleccionar els articles publicats després dels anys 2000. Les dades indiquen que la resposta postprandial està vinculada a la capacitat de patir de síndrome metabòlica. Alteracions en el metabolisme postprandial de l'organisme, adherència a dietes occidentals, disminució de l'activitat física, etc., són característiques que formen part de la definició complexa de l'estat postprandial, i afavoriran l'aparició de la síndrome metabòlica. La conclusió d'aquest treball és que cal més investigació per prevenir el desenvolupament de la síndrome metabòlica. A més, hi ha una gran necessitat de promoure la vida saludable a la comunitat i l'activitat física.

Paraules clau: estat postprandial; síndrome metabólica; malaltia no transmissible; obesitat

Sustainable Development Goals (SDG): This review tries to find out the possible relation between the postprandial state of the organism and the metabolic syndrome. This will allow us to understand how the metabolic syndrome develops, what are its causes and consequences and, therefore, the measures that should be taken to prevent it are discovered. This review also acknowledges us to understand the evolution of nutrition worldwide and how that has triggered the appearance of metabolic syndrome increasingly in our society. Thus, the goal for sustainable development discussed in this TFG addresses aspects of human health in order to promote it, being the main objectives health and well-being (SDG 3).

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1. Introduction

The development and conduction of postprandial studies nowadays are crucial, as it is known that humans spend more than 16 hours a day in a postprandial state [1]. Thus, the postprandial studies aim to understand the metabolic processes that occur in the body after food intake, and it also embodies the digestion and absorption of nutrients [1].

1.1. Metabolic syndrome

Metabolic syndrome refers to the combination of different cardiovascular risk factors, including insulin resistance, obesity, atherogenic dyslipidemia and hypertension. All of these conditions are intertwined and share underlying mediators, mechanisms, and pathways [10]. To all of these factors is interesting to include the family history of premature coronary disease, hypertension, hyperlipidemia, diabetes, and smoking [10].

The metabolic syndrome ties together insulin resistance, visceral adiposity, dyslipidemia, and hypertension, which are known to be interrelated. When considering pathophysiology, it is important to recognize that people with isolated components, but who do not fit the definition of metabolic syndrome, do not have such a high risk of T2D or CVD [10]. For example, people with isolated high blood pressure or isolated hyperlipidemia are at risk for CVD, but less than people who meet multiple criteria. People with isolated obesity are at risk for T2D, but less than people with metabolic syndrome [10]. There are patients who are obese but who do not manifest any of the other components of metabolic syndrome, so both metabolic predisposition to insulin resistance and obesity appears to be necessary for expression of the metabolic syndrome phenotype [10].

Therefore, the four central characteristics mentioned (insulin resistance, obesity, atherogenic dyslipidemia and hypertension) will constitute the simplest complete definition for metabolic syndrome. Although to this feature other mechanisms are associated such as systemic inflammation, hypercoagulability, or microalbuminuria, they will not be necessary as part of the definition as they develop independently [10].

For a better understanding of all mentioned above it is interesting to see figure 1 where the definitions of metabolic syndrome are explained.

	NCEP ATP III (2005 revision)	WHO (1998)	EGIR (1999)	IDF (2005)
Absolutely required	None	Insulin resistance* (IGT, IFG, T2D or other evidence of IR)	Hyperinsulinemia‡ (plasma insulin >75th percentile)	Central obesity (waist circumference[6]): ≥94 cm (M), ≥80 cm (F)
Criteria	Any three of the five criteria below	Insulin resistance or diabetes, plus two of the five criteria below	Hyperinsulinemia, plus two of the four criteria below	Obesity, plus two of the four criteria below
Obesity	Waist circumference: >40 inches (M), >35 inches (F)	Waist/hip ratio: >0.90 (M), >0.85 (F); or BMI >30 kg/m^2	Waist circumference: ≥94 cm (M), ≥80cm (F)	Central obesity already required
Hyperglycemia	Fasting glucose ≥100 mg/dl or Rx	Insulin resistance already required	Insulin resistance already required	Fasting glucose ≥100 mg/dl
Dyslipidemia	TG ≥150 mg/dl or Rx	TG ≥150 mg/dl or HDL-C: <35 mg/dl (M), <39 mg/dl (F)	TG ≥177 mg/dl or HDL-C <39 mg/dl	TG ≥150 mg/dl or Rx
Dyslipidemia (second, separate criteria)	HDL cholesterol: <40 mg/dl (M), <50 mg/dl (F); or Rx			HDL cholesterol: <40 mg/dl (M), <50 mg/dl (F); or Rx
Hypertension	>130 mmHg systolic or >85 mmHg diastolic or Rx	≥140/90 mmHg	≥140/90 mmHg or Rx	>130 mmHg systolic or >85 mmHg diastolic or Rx
Other criteria		Microalbuminuria†		

*IGT, impaired glucose tolerance; IFG, impaired fasting glucose; T2D, type 2 diabetes; IR, insulin resistance; other evidence includes euglycemic clamp studies.
†Urinary albumin excretion of ≥20 μg/min or albumin-to-creatinine ratio of ≥30 mg/g.
‡Reliable only in patients without T2D.

Figure 1. Definitions of metabolic syndrome. (Adapted from L. Huang. P, 2009[10])

1.2. Postprandial state

The postprandial state is defined as the period following meal intake. This period is characterized by net input of energy substrates and other nutrients from the gastrointestinal track into the circulation [13]. Therefore, it is under normal circumstances, an anabolic state also characterized by complex neurohormonal responses and dynamic changes in blood substrate appearance and disappearance rates [13]. Its duration is variable depending on the digestive rate of the substrate, for example: from 3 to 4h for glucose to >6 h for dietary fatty acid metabolism [13].

It is known that humans are spending most of the time in the postprandial state because most individuals eat three or more meals per day [13]. So, to understand the relationship between the metabolic syndrome and the postprandial state, it is interesting to know that metabolic disorders often become evident only after a metabolic challenge, for example, after a meal [13].

Disordered postprandial metabolism of energy substrates is one of the main defining features of prediabetes and contributes to the development of several chronic diseases associated with obesity, such as type 2 diabetes and cardiovascular diseases [13] and, as mentioned earlier, these diseases are the four central characteristics that contribute to the definition of metabolic syndrome [10].

1.3. Overview of postprandial studies

Postprandial studies are gaining importance today as it is essential to understand the relationship between diet, lifestyle, and the processes that occur in the body. Such studies are necessary to understand metabolism functioning after food intake as food intake results in a complex and multifactorial metabolic and neuroendocrine response that influences postprandial inflammation and cardiovascular risk [1]. This type of postprandial inflammation is usually caused by dietary patterns high in calories, fat, and refined sugars, usually called Western-style diets [1]. Increased eating frequency of dietary patterns rich in fat and sugar along with a sedentary lifestyle, results in an exaggerated postprandial increase in plasma glucose, very-low-density lipoproteins (VLDLs), and remaining chylomicrons, well as increased postprandial inflammation, directly affecting cardiovascular risk [1].

Non-communicable diseases are increasing the risk of mortality worldwide and Western-style diets seem to trigger it [1]. That is why it is especially important to understand the functioning of metabolism since the postprandial state is a complex interaction between nutrients, hormones, and metabolites derived from the diet that also depends on other characteristics, such as body weight (and the body mass index - BMI), age, etc [1]. Thus, the postprandial period will show a reflection of the ability of the metabolism to efficiently process the content of the food/meal. Hence, the nutritional composition of the food can be variable and the interindividual differences can affect the absorption process, altering the future postprandial metabolic response [5].

Metabolic health is defined as an integral condition of well-being, rather than the absence of metabolic diseases [5]. Thus, the metabolic flexibility is essential for metabolic health since it is the key to maintaining energy homeostasis and physiologic responsiveness of the body [5]. Furthermore, when the metabolic health condition is altered it increases the risk of non-communicable diseases which are one of the causes of global mortality [5]. For example, alterations in macronutrient oxidation such as fasting and feeding states are associated with metabolic diseases as obesity, type 2 diabetes mellitus, and insulin resistance [5] and all of them are considered non-communicable diseases.

1.4. Obesity: the concept of obesity and how it affects worldwide morbidity and mortality

Obesity is a global epidemic that affects both women and men and, to control it, it is important to understand the mechanisms of appetite control, particularly those that control the energy needs and energy intake of individuals [7].

The human body is in a state of energy balance when the nutrient intake continually equals energy expenditure and energy waste, thus allowing for the maintenance of body weight mass [12].

Alterations in energy balance can occur due to a deregulation between the energy intake and energy expenditure. This can lead to both positive and negative changes in energy balance state and, it must result in changes in body energy stores such as adipose tissue and, therefore, changes in body weight over time [12].

It has been observed that relatively high energy expenditure measured during energy balance coincides with a greater susceptibility to weight gain over time, perhaps because an over-compensatory increase in energy intake because of greater energy requirements [12]. Therefore, it is suggested that energy expenditure may drive energy intake and this link may only manifest over longer periods of time and at specific levels of physical activity and daily energy expenditure [12].

According to the World Health Organization (WHO), a body mass index (BMI) of 25 kg /m2 is considered overweight and a BMI of 30 kg /m2 is obesity [2]. Thus, the WHO describes obesity as the state of excess fat accumulation that entails a wide range of health disadvantages. In fact, in Europe, 54.8% of the population is overweight/obese according to the World Health Organization [2].

To raise awareness of the intensity of this epidemic, it is interesting to compare the percentages of overweight/obesity worldwide and, for example, in two countries such as Spain and Norway. In Spain, 62% of the adult population (>20 years) were overweight and 26.6% were obese in 2008. The prevalence of overweight was higher in men (67.7%) than in women (56.6%). Adult obesity prevalence is expected to increase by 2030 when 36% of men and 21% of women will be obese in Spain [25]. In Norway, 57.6% of the adult population (>20 years) were overweight and 21.5% were obese in 2008. The prevalence of overweight was higher among men (64.4%) than among women (51.1%). Adult obesity prevalence projections indicate that, by 2030, 30% of men and 17% of women will be obese

in Norway [24]. So, as shown before, the prevalence of overweight will increase progressively in the future.

1.5. Relation between satiety and obesity

Nevertheless, the current obesity epidemic shows that many mechanisms can alter appetite control when a powerful annulment of inhibitory mechanisms occurs [7].

There are two types of mechanisms involved in the process of inhibiting food intake: satiation and satiety. Satiation can be defined as a set of complex processes that progressively inhibit the motivation of eating during the feeding action, therefore, satiation will determine the size of the food [7]. In contrast, satiety is an inhibitory mechanism that occurs after finishing eating and prevents us from feeling hungry again for a certain period [7].

In view of all the above and considering the need to establish guidelines to improve people's health, this bibliographic search has been proposed to understand the functioning of the organism after ingestion. Therefore, the objective of this thesis is to understand what the postprandial metabolism of the organism is and demonstrate its possible relationship with metabolic syndrome.

2. Materials and Methods

For this study, a qualitative research strategy has been applied. The literature used for this study was available in English, so the searched keywords were “postprandial metabolism”. For a more thorough search, terms such as obesity, lipid metabolism, glucose metabolism, protein metabolism, satiety and satiation were also included and literature concerning the human metabolism and obesity was selected based on its relevance to the study objectives.

The databases used to conduct this thesis were “Cercabib”, “PubMed”, “Scopus” and “Google Academy”. For the introductory part, the documents were searched in the following way: “western diets”, "obesity” AND "satiety”, “postprandial studies” AND “metabolism” “satiety” OR “satiation”, “obesity” AND “physical activity”, ”postprandial studies” AND “lipid metabolism”, ”postprandial studies” AND “glucose metabolism” and ”postprandial studies” AND “protein metabolism”.

Finally, the exclusion criteria were articles published before the 2000’s and articles that did not talk about postprandial metabolism since they talked only about metabolism in general. On the other hand, the inclusion criteria were the following: all those articles that talked about obesity, physical activity, hedonic and homeostatic hunger and postprandial metabolism of micro and macronutrients.

3. Results

Metabolic syndrome has become increasingly relevant in recent times due to the exponential increase in obesity worldwide. Early diagnosis is important in order to effectively employ lifestyle and risk factor modification [14].

Thus, the metabolic syndrome is a set of all these diseases mentioned above: hyperglycemia/insulin resistance, obesity, and dyslipidemia. So, to find out if a subject suffering from metabolic syndrome is interesting to identify first those patients with high risk of developing atherosclerotic cardiovascular disease and type 2 diabetes. Secondly, when considering the relationships between the different diseases that make up the metabolic syndrome, it may be easier to better understand the pathophysiology that binds them together. Thirdly, this will facilitate clinical, lifestyle and preventive studies [10]. Furthermore, the lifestyle modifications of dietary change and increased physical activity can significantly affect several risk factors simultaneously and, in so doing, reduce the risk of CVD [10].

Therefore, it is also of special interest to emphasize the importance of environmental and lifestyle factors such as excess calorie consumption and lack of physical activity. Visceral adiposity has been shown to be a primary trigger for most pathways involved in the metabolic syndrome along with high caloric intake as the main causal factor. Of all the proposed mechanisms, insulin resistance, neurohormonal activation, and chronic inflammation appear to be the main players in the initiation, progression, and transition of metabolic syndrome to CVD [14].

To better understand all of the above, see figure 2 where the triggers of metabolic syndrome are found.

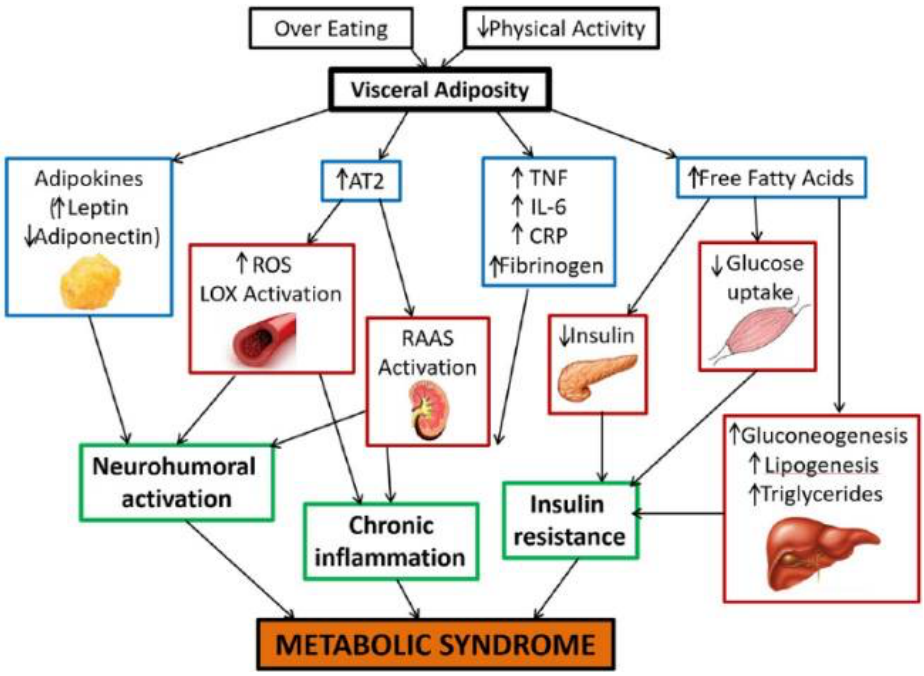

Figure 2. Pathophysiological mechanisms in metabolic syndrome. AT2, angiotensin II type 2 receptor; CRP, C-reactive protein; IL-6, interleukin 6; LOX, lectin-like oxidized low-density lipoprotein; RAAS, renin-angiotensin-aldosterone system; ROS, reactive oxygen. (Adapted from Rochlani, 2017 [14])

3.1 Postprandial lipid metabolism

A high lipid response in the postprandial state is demonstrated to be a characteristic of metabolic alteration of a series of lifestyle-related factors and conditions that are associated at the same time with increased morbidity and mortality: type II diabetes, hypertriglyceridemia, metabolic syndrome, and obesity [6]. The study of postprandial lipid metabolism has been gaining importance in recent studies since the number of lipids and lipoproteins in fasting are parameters that reflect body homeostasis only to some extent. The accumulation of lipids and lipoproteins in the blood after a meal high in fatty acids can be more precise in reflecting the individual's ability to use fat efficiently [6].

A pronounced elevation of triglycerides in the blood is observed approximately one hour after eating the meal and may remain elevated for the next 5-8h after eating. In healthy subjects who are provided with a meal with more than 60g of fat, plasma triglyceride values increase by 2-3h and reach their peak at 3-4h and return to their baseline values at 6h [6]. After a meal with a high fat/energy content, it is advisable to measure the concentrations at baseline levels and 4h of intake [6]. The individual's ability to regulate triglyceride levels in the blood and eliminate lipoproteins rich in triglycerides is a process that reflects one's metabolic efficiency of the individual. It has been shown, for example, that a diet high in fat, sugar, and a sedentary lifestyle predisposes the body to have high concentrations of triglycerides circulating in the blood, even in healthy [6]. Therefore, the popularity of cheap, calorie-rich foods associated with sedentary living has also contributed substantially to the global rise in obesity [26]. The excess weight combined with hyperglycemia can affect insulin signaling and promote the development of comorbidities, such as type 2 diabetes mellitus (DM2), hypertension, and other factors that induce cardiovascular complications [26].

Western diets, which usually contain a high quantity of saturated fatty acids, refined sugar, and calories [1] and a high percentage of n-6 polyunsaturated fatty acids (n-6 PUFA), can increase postprandial inflammation. An elevated intake of n-6 PUFA compared to n- 3 PUFA leads to an increase in inflammation in the body since n-6 PUFA would be used as precursor of pro-inflammatory leukotrienes [1]. The ratio between these two types of fatty acids, n-3, and n-6, is important because it will affect the metabolic health of the individual and it would be interesting to maintain the ratio between both, n-6, and n-3, of 1. Although, in many types of diets, as is the case of western diets, this ratio is altered being 15/1 respectively [1]. Thus, as we mentioned earlier, a diet high in carbohydrates and fatty acids produces an inflammatory response in the postprandial state characterized by the high presence of lipopolysaccharides in plasma, IL-6, TNF-α and the production of reactive oxygen species (ROS) [1].

On the contrary, diets rich in monounsaturated fatty acids (MUFAs) or PUFA n-3 tend to decrease the postprandial lipid response compared to saturated fatty acids. Diets rich in n-3 PUFAs decrease triglycerides in the postprandial response if there is enough adherence to this type of diet [6]. In addition, a high intake of n-3 fatty acids has given favorable results in terms of inflammation. High n-3 PUFA consumption appears to reduce inflammation and the risk of cardiovascular disease [1]. In contrast, healthy

individuals who eat a meal rich in saturated fatty acids have increased inflammatory parameters which could be decreased after a meal abundant in n-3 PUFA, but not after a meal rich in n-6 PUFA [1].

Furthermore, chylomicrons are shown to play an important role in the development of non- communicable diseases as they are potent activators of the complement system's C3 protein. This complement system is part of the innate immune system and causes antibodies to increase in blood. C3 levels increase after a meal rich in fatty acids and this can also trigger metabolic diseases such as insulin resistance, hypertension, obesity, and coronary artery disease [1].

With all the above mentioned, it is known that the postprandial state is generally associated with a high concentration of triglycerides and glucose, as well as an increase in oxidative reactions [6]. The oxidative reactions are reactions in which there is electron transfer involving reduction (electron gain) and oxidation (electron loss) of the participating molecules and are denominated oxidation-reduction (reduction) reactions [27]. This mechanism induces the production of free radicals and creates oxidative stress in the body. In the situation of oxidative stress, the damage occurs in cellular structures and proteins, carbohydrates, nucleic acids, and lipids. Consequently, high postprandial oxidation contributes to an increased risk of atherosclerosis and endothelial dysfunction [16]. In situations of oxidative stress, alterations in the oxidation of macronutrients can occur when there is an imbalance between caloric restriction (fasting) and caloric excess (intake) [7]. This imbalance can lead to non-communicable diseases such as type II diabetes mellitus, obesity, metabolic alterations, or insulin resistance [7].

3.2 Postprandial glucose metabolism

It is not only important to understand lipid metabolism during the postprandial state but also glucose metabolism since it has an essential role in the postprandial response. Including the use of multiple macronutrients in this type of studies is important because it allows a representative view of the physiological changes that occur after a meal [6].

Postprandial glycemic response is an important health determinant. Glycemic control is just one part of a more complex equation involving triglyceride and insulin [4]. Therefore, insulin plays an important role in triglyceride metabolism, so it is especially important to include carbohydrates in the test meals to ensure effective postprandial processing of insulin- dependent dietary triglycerides [6]. For that reason, the amount and/or nature of carbohydrates in an individual meal may alter the postprandial metabolism of lipids [6]. That is why, if test meals with different macronutrients are provided, the glucose units provided by digestible carbohydrates will temporarily increase blood sugar and postprandial insulinemia [6]. Both, glycemia and insulinemia, can alter postprandial lipemia.

Insulin resistance is a key component to indicate metabolic inflexibility [11]. In an insulin resistance state, a reduction in the amount of glucose entering the muscle cells and adipocytes from the bloodstream, along with a reduced suppression of hepatic glucose

production, will elevate glucose in the blood in the absence of a corresponding increase in insulin release from the pancreatic beta cells [11]. Therefore, diabetes will develop if pancreatic betta-cells fail to appropriately compensate for this insulin resistance with higher insulin secretion [11]. Thus, insulin resistance often precedes hyperinsulinemia and hyperglycemia [11].

Interestingly, in subjects with insulin resistance, the intake of different foods with different glycemic indices can modulate the postprandial accumulation of apoB100, a marker of the VLDL, and apoB48 that contains lipoproteins rich in triglycerides [6]. Thus, apoB48 will reflect the number of TRL (triglyceride rich lipoprotein) particles present in the organism because an apoB moiety is associated with a TRL particle [6]. Therefore, the measurement of apoB-100 (VLDL marker) and apoB-48 (chylomicron marker) can help in quantifying the relative proportion of endogenous and exogenous TRL [6].

3.3 Postprandial protein metabolism

Postprandial protein metabolism in obesity has not been studied in much detail, however the postprandial changes correspond to a physiologic response to food intake, representing stimulated insulin release and a reversal of negative protein balance resulting from a decline in protein catabolism and enhancement of anabolism [17].

The presence of amino acids in the gastrointestinal tract promotes the release of certain substances that affect the postprandial state of the individual. Amino acid absorption kinetics in the diet is an important determinant of protein quality. This is because the postprandial period involves modifications in the breakdown and synthesis of proteins and the acidification of amino acids [18]. Slower digestion of dietary proteins has been shown to produce better postprandial utilization than faster digestion [18]. In this regard, it is especially important to evaluate the effects of non-protein energy sources since they can affect both, the digestion rate, and the metabolism of proteins in the postprandial state [18].

However, digestion and absorption kinetics of the dietary protein should not be considered static properties of the protein, as they are highly dependent on individual conditions, such as the amount of protein ingested, the duration of the postprandial evaluation period, age, and the presence or absence of disease [19].

The proteins present in biological tissues are constantly in a balance between synthesis and decomposition. The ingestion of dietary protein, therefore, provides amino acids that stimulate the synthesis of muscle proteins functioning as both substrate and signaling molecules in anabolic pathways [19]. Therefore, in addition to the number of proteins and the composition of amino acids, the protein digestion rate is an independent factor that produces the deposition of proteins in the postprandial state [18].

Additionally, alterations of branched-chain amino acid plasma concentrations may affect protein metabolism [17]. For example, branched-chain amino acid, specifically leucine, stimulate protein synthesis and inhibit protein degradation but may also induce

insulin resistance, since elevated plasma branched-chain amino acids concentrations in obesity correlate with insulin resistance [17].

Dietary protein in a mixed meal does not independently stimulate insulin release, insulin-dependent protein anabolism may be stimulated as a collateral effect of plasma insulin concentrations reacting to carbohydrate content in a mixed meal [17].

Insulin has anti-proteolytic effects on the whole-body level and on skeletal muscle protein breakdown, as well as protein synthesis stimulating properties [17]. Insulin-mediated vascular effects are necessary for the protein anabolic effect of insulin and these mechanisms could fail in the skeletal muscle of obese subjects, which might affect their protein metabolism [17].

3.4 Satiation, satiety, and obesity

Sensory factors like taste, smell, and texture of food can stimulate intake, but also signals such as gastric distention or the release of specific hormones and peptides or the increased blood sugar exert the same effect. the gastrointestinal tract and the increased blood sugar exert the same effect [7]. Among these signals highlighted leptin, insulin, glucagon, ghrelin and numerous peptides and hormones released into the gastrointestinal tract after food intake such as cholecystokinin (CCK), glucagon-like peptide -1(GLP-1), gastric inhibitor peptide (GIP), and peptide YY (PYY) [7]. The brain integrates signals that reflect energy load and expenditure and acts as a homeostatic regulator adjusting the intake to maintain the energy balance of the body [7]. Homeostatic adjustment of energy intake and expenditure is more difficult to control when energy expenditure is significantly reduced through interventions such as diets to reduce body weight. There is a positive relationship between post-obesity adaptation and increased hunger, suggesting that the relationship between hunger and satiety is altered and will be more difficult to regulate after a period of weight loss [7]. This can lead to a subsequent recovery of the weight lost during the slimming period.

On the other hand, to understand the effects of satiety on obesity, it is important to recognize the role of the hypothalamus in regulating hunger and satiety. Therefore, obesity and satiety are states that are closely related. When ventromedial and paraventricular hypothalamic nuclei are damaged, hyperphagia and obesity arise [3]. Moreover, the damage to the lateral hypothalamus produces severe anorexia and body weight loss. Thus, the ventromedial hypothalamic nucleus is the center of satiety, and the lateral hypothalamus is considered the center of hunger [3] so, to achieve greater regulation of body homeostasis, it is essential to keep both, lateral and ventromedial hypothalamus in perfect balance.

Moreover, the adipose tissue is known to secrete the hormone leptin and send signals to the brain, informing the current state of body adiposity. A loss of body fat will favor the reduction of leptinemia, and the sympathetic nervous system (SNS) activity associated with increased hunger [7]. Therefore, fat loss modifies appetite control through biological effects.

Thus, the hormone leptin derives from adipocytes and this hormone contributes, as has been said, to the homeostatic regulation of energy balance and metabolism through the humoral and neural pathways [20]. If there is a pathological increase of leptin in the blood, this acts as a biomarker of leptin resistance, which is a common feature in obese individuals [20]. Leptin resistance could be defined by reduced sensitivity or a failure in the brain's response to leptin, this produces a decrease in the ability of this hormone to suppress appetite or increase energy expenditure, which will cause an increase in food intake and will conclude, with cardiovascular diseases, overweight, obesity and other metabolic disorders [20].

Long-term maintenance of satiety effects is a clear condition for satiety-related weight effects. However, the maintenance of satiety effects should be interpreted with caution after weight loss in obese individuals. Substantial weight loss favors numerous metabolic changes: a decrease in leptinemia and SNS activity, an increase in hunger, and a greater reduction in the projected energy expenditure [21].

Thus, there is evidence that following a diet to improve the feeling of satiety cannot produce a significant weight loss, but there is evidence that satiety can be increased by selecting the appropriate food [7]. This would be the case with foods rich in fiber, proteins, or functional ingredients that promote satiety as they could help maintain long-term body weight loss. On the other hand, it seems that the weak satiety efficiency of fatty acids could be explained by their high energy density and/or their palatal effects on many foods: taste, aroma, and texture improve with fat, which stimulates excessive consumption with relatively low-intake satiety [7].

It is also necessary to take physical activity into account when it comes to obesity and satiety since physical exercise is considered an important component of weight control in addition to energy restriction. After the industrial revolution, modern technology and the development of motor transport systems have drastically decreased physical activity in daily life, among them the old activities that demanded a lot of energy [22]. The consequence of this is a sedentary lifestyle that can lead to overweight or obesity, and/or progressive atrophy or physical weakness throughout the organism, and even increased morbidity [22].

In fact, in the management of obesity, the objectives of physical activity should be to reduce sedentary behaviors and increase daily activities. An increase in physical activity reduces intraabdominal fat and increases lean mass. It also reduces blood pressure and improves glucose tolerance, insulin sensitivity, lipid profile, and physical fitness [22]. All these are conditions of special interest to improve since, obesity produces non-communicable diseases such as hypertension, coronary disease, and type II diabetes among others. Thus, ideally, to prevent overweight or obesity, the time of physical activity and a reduction of sedentary time should be promoted [14].

4. Discussion

The interaction of genetics and environment, nature, and nurture is the foundation for all health and disease and, nutrition is the environmental factor of major importance [8].

Nowadays, industrialized societies are characterized by an increase in energy intake and decrease in energy expenditure. Today, one of the most consumed diets is the Western diet that is mainly characterized by high amounts of saturated fatty acids, omega-6 PUFA and trans-fatty acids, and low intake of omega-3 PUFA, a decrease in complex carbohydrates and fiber, together with an increase in the intake of cereal grains and a decreased consumption of fruits and vegetables, and a decrease in protein, antioxidants, and calcium intake [8].

As mentioned earlier, evolution has replaced aspects of prehistorical diets making modern diets more unsafe to human health and with postprandial response that are different to the ones we were used to.

One of these aspects is, as has been observed, the ratio omega-6/omega-3 which would be about 1-2/1 [8]. It has been widely demonstrated that this kind of dietary patterns promote the pathogenesis of many diseases, including cardiovascular disease, cancer, and inflammatory and autoimmune diseases, whereas increased levels of omega-3 PUFA an low omega-6/omega-3 ratio exert suppressive effects [8].

Cereal grains as staple foods are relatively recent in the human diet and human's beings have become entirely dependent to this food [8]. The nutritional consequences for human health of such high cereal consumption are huge [8]. Cereal grains are high in carbohydrates and omega-6 fatty acids, but low in omega-3 fatty acids and in antioxidants. Thus, adherence to diets where this type of ingredients is the basis, are characterized by a low presence of fatty acids/high in carbohydrates [8]. This diet increases insulin resistance and hyperinsulinemia, conditions that increase the risk factor for coronary heart disease, hypertension, diabetes, and obesity [8].

Additionally, there may be possible differences in the way some individuals are (un)able to sense the extent to which they must compensate for their own energy expenditure by eating [12]. In other words, some individuals may "sense" to offset their energy expenditure to a degree greater (or lesser) than is truly needed by consuming more (or less) food than required [12]. Although almost all subjects use to overeat in context of ad libitum food intake implying that these individuals could not adequately "sense" or perhaps, they "over-sense" their metabolic demands [12]. Thus, reactions to energy expenditure vary across individuals in terms of the mount of food consumed, such that some individuals over-sense while others under-sense their metabolic requirements [12]. Specifically, for those who over-sense and therefore positively misinterpret their energy needs by consuming food as if they had greater energy expenditure, the propensity to gain weight is greater [12]. In sum, the degree to which some individuals over-sense their metabolic demands may be another indicator of the susceptibility to weight gain in humans [12].

On the other hand, today in our society the food supply is constant and that is why it is much easier to access food at any time. Humans, despite the easy access to food, are not always eating because of the periodic signs that control food intake [7]. These types of signals are the result of psychological, sensory, cognitive, environmental, and social processes [7].

To understand these processes mentioned above, it is interesting to place oneself in the context of human history and prehistory, where the main objective of the food search was survival through the maintenance of energy homeostasis and the avoidance of the feeling of hunger [9]. Therefore, the world has seen a notable change in dietary behaviors, which is related to the nutritional transition associated with changes in foods and beverages consumed [23]. Consequently, throughout human existence, diet and nutritional status have gone through different patterns of food and beverage consumption, which has led to subsequent changes in body composition and nutrition-related diseases [23]. The nutritional transition emphasized the understanding of the magnitude of these changes, and the results of dietary change over the centuries and millennia [23]. Hence, in these modern times, among the nourished populations, food consumption occurs for different reasons, not only hunger itself. As suggested by the growing prevalence of global obesity mentioned above, there seems to be a greater urge to consume food only for pleasure and not just for the need for calories [9].

Everything mentioned above is of special interest today given that one of the most difficult problems in the obesity epidemic is to try to maintain the weight loss achieved after an energy- restricted diet. Maintaining previous weight loss and preventing weight regain are the objectives of any study focused on obesity [7]. It is evident that the composition of nutrients is one of many factors affecting satiety, and satiety is one of the many influences that determine energy intake and body weight [7].

Some people may experience frequent thoughts, feelings, and urges about food in the absence of any short- or long-term energy deficits [9]. These experiences do not occur in response to prolonged food deprivation, i.e., homeostatic hunger. Therefore, is essential to refer to this trend as hedonic hunger and this term refers to a subjective state, to the physiological mechanisms that can mediate in it, and not to the actual food intake [9].

The hedonic and homeostatic mechanisms that control eating behavior are schematically captured in figure 3.

As has been seen, obesity is a consequence of evolution since there are changes in our routines that promote the appearance of this disease. On the other hand, visceral adiposity has been shown to be a primary trigger for most pathways involved in the metabolic syndrome along with high caloric intake as the main causal factor. As mentioned earlier, obesity occurs because an alteration in energy balance between the energy intake and energy expenditure and because some individuals over-sense while others under-sense their metabolic requirements. This can lead to the development of metabolic syndrome.

Therefore, to conclude this review, it is important to understand the relationship between the postprandial state and metabolic syndrome. The postprandial response in our body is linked to the ability to suffer from metabolic syndrome. Disordered postprandial metabolism of energy substrates is one of the main defining features of prediabetes and contributes to the development of several chronic diseases associated with obesity, such as type 2 diabetes and cardiovascular diseases [13]. All of these conditions are the simplest definition of metabolic syndrome. So, as defined earlier, the metabolic processes that occur in the postprandial state of the organism will be a factor that will act as an intermediary bridge for the development of the metabolic syndrome in humans.

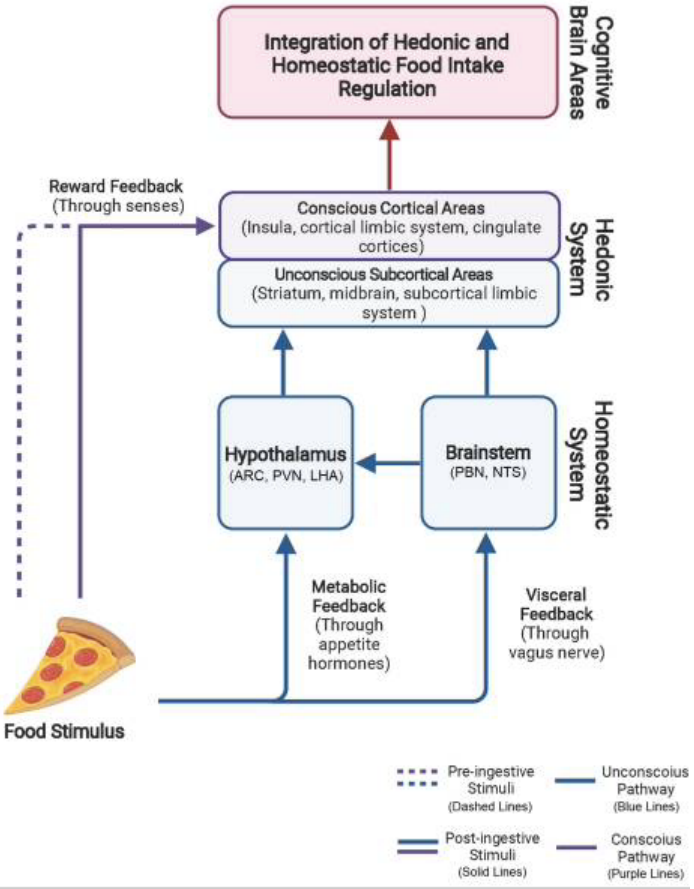

Figure 3. The hedonic and homeostatic mechanisms that control eating behavior. The unconscious metabolic and visceral feedback (bottom blue lines and boxes) and the conscious reward feedback (left dashed and solid purple lines) are integrated within brain areas associated with aversion, cognition, reward, motivation, memory, and decision making (middle blue and purple boxes). From these areas, information projects to higher cognitive brain centers to ultimately regulate eating behavior (top red lines and boxes). (Adapted from Campos, 2022 [15]).

Thus, it can be concluded that obesity is a disease that occurs by alterations in the postprandial state and, this is highly linked to suffer metabolic syndrome. With which, it can be affirmed that the postprandial state and the metabolic syndrome are linked and fed back. A postprandial alteration can compromise the organism and trigger metabolic syndrome and a subject suffering from metabolic syndrome will have an altered postprandial response.

However, a better understanding of the metabolic differences among individuals may lead to individualized therapies for preventing or treating metabolic syndrome. On the other hand, further investigation is highly recommended concerning the postprandial studies to be able to improve research in this field and prevent the development of metabolic syndrome. There is a need to promote nutritional education in the community to encourage healthy diets and also support physical activity in our day to day.

References

1. Meessen, E. C. E., Warmbrunn, M. V., Nieuwdorp, M., & Soeters, M. R. Human Postprandial Nutrient Metabolism and Low-Grade Inflammation: A Narrative Review. *Nutrients* **2019** *11*(12), 3000. https://doi.org/10.3390/nu11123000
2. Yatsuya, H., Li, Y., Hilawe, E. H., Ota, A., Wang, C., Chiang, C., Zhang, Y., Uemura, M., Osako, A., Ozaki, Y. & Aoyama, A. Global Trend in Overweight and Obesity and Its Association With Cardiovascular Disease Incidence. *Circulation Journal* **2014** *78*(12), 2807-2818. https://doi.org/10.1253/circj.cj-14-0850
3. González, M.E., Ambrosio, K.G. & Sánchez, S. Regulación neuroendocrina del hambre, la saciedad y mantenimiento del balance energético. *Artemisa* **2006** *6*, 191-200. https://www.medigraphic.com/pdfs/invsal/isg-2006/isg063i.pdf
4. Berry, S. E., Valdes, A. M., Drew, D. A., Asnicar, F., Mazidi, M., Wolf, J., Capdevila, J., Hadjigeorgiou, G., Davies, R., Al Khatib, H., Bonnett, C., Ganesh, S., Bakker, E., Hart, D., Mangino, M., Merino, J., Linenberg, I., Wyatt, P., Ordovas, J. M., Gardner, C. D., … Spector, T. D. Human postprandial responses to food and potential for precision nutrition. *Nature medicine* **2020** *26*(6), 964–973. https://doi.org/10.1038/s41591-020-0934-0
5. Yu, E. A., Le, N. A., & Stein, A. D. Measuring Postprandial Metabolic Flexibility to Assess Metabolic Health and Disease. *The Journal of nutrition* **2021** *151*(11), 3284–3291. https://doi.org/10.1093/jn/nxab263
6. Lairon, D., Lopez-Miranda, J., & Williams, C. Methodology for studying postprandial lipid metabolism. *European journal of clinical nutrition* **2007** *61*(10), 1145–1161. https://doi.org/10.1038/sj.ejcn.1602749
7. Tremblay, A., & Bellisle, F. Nutrients, satiety, and control of energy intake. *Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme* **2015** *40*(10), 971–979. https://doi.org/10.1139/apnm-2014-0549
8. Simopoulos A. P. The importance of the ratio of omega-6/omega-3 essential fatty acids. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie* **2002** *56*(8), 365–379. https://doi.org/10.1016/s0753-3322(02)00253-6
9. Lowe, M. R., & Butryn, M. L. Hedonic hunger: a new dimension of appetite? *Physiology & behavior* **2007** *91*(4), 432–439. https://doi.org/10.1016/j.physbeh.2007.04.006
10. Huang P. L. A comprehensive definition for metabolic syndrome. *Disease models & mechanisms* **2009** *2*(5-6), 231–237. https://doi.org/10.1242/dmm.001180
11. Goodpaster, B. H., & Sparks, L. M. Metabolic Flexibility in Health and Disease. *Cell metabolism* **2017** *25*(5), 1027–1036. https://doi.org/10.1016/j.cmet.2017.04.015
12. Piaggi P. Metabolic Determinants of Weight Gain in Humans. *Obesity (Silver Spring, Md.)* **2019** *27*(5), 691–699. https://doi.org/10.1002/oby.22456
13. Schrauwen-Hinderling, V. B., & Carpentier, A. C. Molecular imaging of postprandial metabolism. *Journal of applied physiology (Bethesda, Md. : 1985)* **2018** *124*(2), 504–511. https://doi.org/10.1152/japplphysiol.00212.2017
14. Rochlani, Y., Pothineni, N. V., Kovelamudi, S., & Mehta, J. L. Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. *Therapeutic advances in cardiovascular disease* **2017** 11(8), 215–225. https://doi.org/10.1177/1753944717711379
15. Campos, A., Port, J. D., & Acosta, A. Integrative Hedonic and Homeostatic Food Intake Regulation by the Central Nervous System: Insights from Neuroimaging. *Brain sciences* **2022** *12*(4), 431. https://doi.org/10.3390/brainsci12040431
16. Bae, JH., Bassenge, E., Kim, KB., Kim, YN., Kim, KS., Lee, HJ., Moon, KC., Lee, MS., Park, KY., Schwemmer, M. Postprandial hypertriglyceridemia impairs endothelial function by enhanced oxidant stress. *Atherosclerosis*. **2001** *155*(2), 517. https://doi.org/10.1016/S0021-9150(00)00601-8
17. Liebau, F., Jensen, MD., Nair, KS., Rooyackers, O. Upper-body obese women are resistant to postprandial stimulation of protein synthesis. *Clinical Nutrition*. **2014** *33*(5), 802. https://doi.org/10.1016/j.clnu.2013.11.001
18. Dangin, M., Boirie, Y., Garcia-Rodenas, C., Gachon, P., Fauquant, J., Callier, P., Ballèvre, O., & Beaufrère, B. The digestion rate of protein is an independent regulating factor of postprandial protein retention. *American journal of physiology. Endocrinology and metabolism* **2001** *280*(2). https://doi.org/10.1152/ajpendo.2001.280.2.E340
19. Trommelen, J., Tomé, D., & van Loon, L. J. Gut amino acid absorption in humans: Concepts and relevance for postprandial metabolism. *Clinical Nutrition Open Science* **2021** *36* https://doi.org/10.1016/j.nutos.2020.12.006
20. Liu, J., Yang, X., Yu, S., & Zheng, R. The Leptin Resistance. *Advances in experimental medicine and biology* **2018** *1090*, 145–163. https://doi.org/10.1007/978-981-13-1286-1_8
21. Doucet, E., St Pierre, S., Alméras, N., Mauriège, P., Richard, D., & Tremblay, A. Changes in energy expenditure and substrate oxidation resulting from weight loss in obese men and women: is there an important contribution of leptin? *The Journal of clinical endocrinology and metabolism* **2000** *85*(4), 1550–1556. https://doi.org/10.1210/jcem.85.4.6500
22. Galanakis, C. M. *Galanakis, Ch. M., Tendencias en Nutrición Personalizada* (1.ª ed.). **2021** Elsevier España, S.L.U.
23. Popkin, BM. Nutrition Transition and the Global Diabetes Epidemic. *Current Diabetes Reports* **2015** *15*(9):64. https://doi.org/10.1007/s11892-015-0631-4
24. Health Organization, W., & Office for Europe, R. (1 C.E.). Nutrition, Physical Activity and Obesity Norway Demographic Data Monitoring and surveillance Prevalence of Overweight and Obesity (%) Among Norwegian Adults based on WHO 2008 estimates. http://www.euro.who.int/en/nutrition-country-profiles.

25. Health Organization, W., & Office for Europe, R. (2013). Nutrition, Physical Activity and Obesity Spain Demographic Data Prevalence of Overweight and Obesity (%) Among Spaish Adults based on WHO 2008 estimates. http://www.euro.who.int/en/nutrition-country-.
26. de Oliveira Dos Santos, A. R., de Oliveira Zanuso, B., Miola, V. F. B., Barbalho, S. M., Santos Bueno, P. C., Flato, U. A. P., Detregiachi, C. R. P., Buchaim, D. V., Buchaim, R. L., Tofano, R. J., Mendes, C. G., Tofano, V. A. C., & Dos Santos Haber, J. F. Adipokines, Myokines, and Hepatokines: Crosstalk and Metabolic Repercussions. *International journal of molecular sciences* **2021** *22*(5), 2639. https://doi.org/10.3390/ijms22052639
27. Corrales MSc, L. C., & Muñoz Ariza, M. M. Estrés oxidativo: origen, evolución y consecuencias de la toxicidad del oxígeno. *Nova* **2012** *10*(18), 213. https://doi.org/10.22490/24629448.1010