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Synergistic Regulation of Human Metabolic System and Disease Mechanism Research

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Abstract. The metabolic system is a complex, interconnected network that ensures efficient nutrient processing, energy production, and homeostasis. This review explores the coordinated interplay between digestion, absorption, energy transformation, and hormonal regulation, using analogies such as a “food processing factory” and “orchestra” to illustrate systemic integration. The study synthesizes established literature on enzymatic breakdown, transport protein mechanisms, and hormonal signaling (e.g., insulin, glucagon, CCK) to map key metabolic pathways. Case analyses of type 2 diabetes and obesity highlight how disruptions in one component—such as insulin resistance or adipose tissue dysfunction—trigger cascading failures, emphasizing the system’s interdependence. The review concludes that metabolic health hinges on precise coordination across all phases, with imbalances leading to systemic pathologies. While focusing on well-documented mechanisms, the study acknowledges limitations in addressing gut microbiota’s role and epigenetic influences. Future research should prioritize personalized metabolic responses and novel interventions, advancing targeted therapies for metabolic disorders.

Keywords: Metabolic regulation, Nutrient absorption, Energy transformation, Hormonal signaling, Systemic diseases

1. Introduction

If our body is compared to a city, then the metabolic system is the city's energy management authority. It is responsible for converting the food we consume into the energy our bodies require to function, just as refining crude oil produces petrol.

This transformation process requires the collaboration of three key systems: the digestive system, which utilizes enzymes to break down large pieces of food into absorbable small molecules [1]. Next, the absorption system acts as the 'transport sector,’ where mature enterocytes, which express nutrient transporters, facilitate the uptake of nutrients like sugar into the bloodstream [2]. Finally, there is the "energy conversion sector" (cellular metabolism), which uses the cytoplasm and mitochondria to produce energy [3].

This report aims to elucidate:

1. How food is broken down step by step.
2. How nutrients are absorbed
3. How cells use these nutrients to produce energy

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4. How the body regulates this process

Understanding these processes highlights the importance of a balanced diet and illustrates the systemic problems that can arise from metabolic disorders. Just as urban power outages affect everything, metabolic disorders can impact overall health.

2. Collaboration in the digestion phase

Our bodies are akin to a sophisticated food processing factory, and from the moment food enters the mouth, all departments of the digestive system commence working together. This processing can be divided into three main stages:

2.1. Oral cavity: food crushing station

Initially, the teeth function like grinder blades, chewing and grinding large pieces of food [4]. Then amylase in saliva begins to break down carbohydrates [5]. Finally, the tongue thoroughly mixes food with saliva to form a bolus.

2.2. Stomach: protein breakdown workshop

After the food enters the stomach, the stomach wall muscles continue to contract, mixing the food into a paste similar to that produced by a blender. Gastric acid (hydrochloric acid) activates pepsin, which initiates the breakdown of proteins [6]. The stomach functions as a sophisticated container, creating an environment in which ingested food can be safely subjected to proteolytic enzymes and acidic solutions [7].

2.3. Small intestine: core processing plant

The liver and pancreas are important foreign aids.

The liver secretes bile to assist in the breakdown of fats [8]. The pancreas provides a variety of digestive enzymes.

The villi on the lining of the small intestine significantly increase the absorption area [9].

Different enzymes specialise in processing different nutrients.

Amylase continues to break down carbohydrates in the digestive system.

Proteases break down proteins into smaller peptides and amino acids.

Lipase breaks down fats into fatty acids and glycerol.

2.4. Intestinal microflora: specialised assistants

The intestinal microflora functions primarily in the large intestine. The large intestine plays an important role by absorbing water, vitamins, and electrolytes from waste products [10].

This collaborative process resembles an efficient production line, with each component precisely coordinated. Should there be an issue in a particular link, such as insufficient stomach acid or reduced enzyme secretion, it can impact the entire digestive process and result in nutrient malabsorption. Comprehending this collaborative mechanism can aid in understanding why chewing slowly and consuming a balanced diet is of utmost importance for digestive health.

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3. Regulation of absorption process

After food is digested into small molecules, it does not automatically enter the body, and most substances enter the intestinal cells from the intestinal lumen, and then from the intestinal cells into the interstitial fluid. Absorption is a precisely regulated process, just like an airport's smart security system, which identifies, screens, and regulates flow to ensure that the right substances enter the right channel in the right amount.

3.1. The absorption of 'VIP channels' and 'ordinary channels': the role of transport proteins

The lining of the small intestine has millions of finger-like projections (villi), each with smaller microvilli, which greatly increases the absorption area [9]. These surfaces are covered with various transporters that are the "gatekeepers" and "channels" that control the entry of substances into the body.

Specific channel (VIP service): For important nutrients such as glucose and amino acids, the body employs active transport. This process is akin to a VIP channel that requires ticket swiping, consuming energy to “pump” nutrients into the body against the concentration gradient [11]. For example, glucose needs to partner with sodium ions to enter cells through a dedicated channel known as SGLT1.

Selective channel (ordinary channel): For fructose, water, and some minerals, facilitated diffusion occurs. This is like a regular security checkpoint that follows a concentration gradient and does not require energy [11], but still requires specific protein channels (e.g., GLUT5 transporting fructose).

Free passage (green channel): Fat-soluble substances (such as fatty acids, vitamins A/D/E/K) and a small amount of water can pass directly through the cell membrane, functioning as the green channel.

In summary: different nutrients utilize distinct entry methods, with transporters determining both which substances can enter and their specific mechanisms.

3.2. "Remote control" of the body

The rate and intensity of absorption are not static, but are regulated in real time by hormones, a "remote control", mainly in response to whether we eat or not [12].

3.2.1. Absorption begins signal (when eating)

When we consume food, particularly those containing fat and protein, the small intestine releases a hormone known as cholecystokinin (CCK).

It functions by:

Notify the gallbladder: "Release the bile quickly!" [13]

Notify the pancreas: "Secrete digestive enzymes quickly!" [14]

Indirectly prepares for fat absorption.

3.2.2. "Energy storage" signal (after a meal)

Blood sugar rises after a meal, stimulating the pancreas to secrete insulin [15]. Insulin is not only a regulator of blood sugar, but also a "promoter" of absorption. It can:

Control energy conservation and utilisation during eating and fasting [16].

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In summary: hormones direct absorption organs to “speed up” or “slow down” based on the body’s needs, ensuring efficient and orderly nutrient processing.

4. Energy transformation interaction

The absorbed nutrients undergo a series of reactions in the cell, with the goal of becoming fuel for the mitochondria, the "power plant", and finally producing the energy currency ATP.

4.1. Aerobic respiration and counterattack of fatty acids (β-oxidation)

This is the core energy supply pathway, which is divided into three stages:

Glycolysis: In the cytoplasm, one molecule of glucose is initially broken down, yielding a net gain of 2 ATP [17].

Tricarboxylic acid cycle: The decomposition products enter the mitochondria and are completely "incinerated", producing a large amount of energy vouchers (NADH, $FADH_2$) [18].

Oxidative phosphorylation: Energy carriers are “converted” into substantial amounts of ATP in the inner mitochondrial membrane, representing the primary energy-producing process [19].

When glucose is in short supply, fat is mobilised. Fatty acids enter the mitochondria, are cut into pieces through the β-oxidation cycle, sent directly into the tricarboxylic acid cycle, and produce more energy tokens, ultimately producing more ATP than glucose [20].

4.2. Key interactions and competition

Competition (Randle cycle): When fatty acids are broken down in large quantities, the metabolites produced by them inhibit the breakdown and utilisation of glucose [21]. This means that a high-fat diet reduces the efficiency of cells in consuming sugar, an important mechanism of insulin resistance [22].

Collaborative relationship: During moderate exercise, glucose and fat work synergistically to supply energy. Glucose provides quick bursts, while fat delivers enduring stamina.

In summary, cells function as astute energy managers, dynamically adjusting the utilization ratios of glucose and fat based on blood glucose levels, hormonal signals, and energy demands to maintain optimal energy efficiency.

5. Whole body regulation network

The metabolic system is akin to an orchestra that requires precise direction. Three key hormones constitute the core command system. Insulin, secreted after a meal, acts as a "storage hormone". It signals cells throughout the body, particularly muscle and fat cells, to open channels to absorb glucose from the blood. Additionally, it promotes the synthesis of glycogen and fat, storing energy for future requirements [23]. Conversely, glucagon serves as the “energy-releasing hormone”. During fasting, its levels rise, instructing the liver to break down its stored glycogen into glucose and release it into the bloodstream. It also triggers gluconeogenesis, creating new glucose from non-carbohydrate sources [23]. Adrenaline is an emergency responder and is released under the pressure of "fight or flight" [24]. It rapidly mobilizes all available energy sources, allowing blood glucose levels to rise [25].

This hormonal trio is managed by a complex gut-brain axis. The brain, particularly the hypothalamus, continuously monitors energy status through hormonal signals such as leptin, which is produced by fat cells and signals satiety, and ghrelin, which is produced by the stomach and

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signals hunger [26]. In response, it sends out neural and hormonal commands to regulate appetite and metabolism. Moreover, the digestive tract itself functions as a significant endocrine organ. Hormones such as cholecystokinin and glucagon-like peptide-1 provide critical local feedback, directly linking digestive status to systemic energy regulation.

6. Common problem cases

The metabolic system is analogous to a delicate symphony orchestra, and any imbalance in any link can lead to chaos in the entire movement. Diabetes and obesity are two typical "symphonies of dysregulation".

6.1. Type 2 diabetes

At the heart of type 2 diabetes lies the inability of cells to properly receive insulin signals, a condition known as “insulin resistance” [27]. Imagine that insulin holds the key (signal), but the cell has a broken lock and cannot open the door to let glucose in.

Interaction breakdown points:

1. Digestion and absorption as usual: Food is broken down normally, and glucose is absorbed into the bloodstream in large quantities.

2. Energy conversion is blocked: Because the cells reject glucose, the cells "starve" (fatigue) and the blood is flooded with "sugar disaster" (hyperglycemia).

3. Regulatory feedback fails: The body mistakenly thinks that there is not enough energy, so glucagon desperately instructs the liver to "produce more sugar", further exacerbating high blood sugar. This perfectly illustrates the complete disintegration of the interaction of absorption, utilisation and regulation.

6.2. Obesity

Obesity is not only excess fat, but also a pathological change in the energy distribution and storage pattern of the entire metabolic system.

Interaction breakdown points:

1. Digestion and absorption are overly efficient: Long-term intake of high-energy foods places a significant strain on the digestive system.

2. Energy storage overwhelms consumption: The excess energy ingested is converted into fat and stored.

3. The regulation system becomes 'hijacked’: Adipose tissue contributes to insulin resistance [28], creating a vicious cycle of “obesity → insulin resistance → increased fat accumulation”. This suggests that adipose tissue is no longer a passive storage tank, but an active organ actively involved in disrupting metabolic interactions.

These two cases profoundly illustrate that metabolic health depends on the precise coordination of all components, with any imbalance triggering a chain reaction that leads to disease.

7. Conclusion

The metabolic system operates as a highly coordinated network, where digestion, absorption, energy transformation, and hormonal regulation interact seamlessly to maintain homeostasis. Each phase—from oral processing to cellular energy production—relies on precise mechanisms, such as transport proteins, enzymatic breakdown, and hormonal signaling, ensuring efficient nutrient utilization.

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Disruptions in any component, as seen in type 2 diabetes and obesity, trigger cascading failures, highlighting the system's interdependence. Insulin resistance and adipose tissue dysfunction exemplify how localized imbalances can lead to systemic pathologies, underscoring the importance of balanced diet and metabolic health. This review primarily focuses on well-established pathways, with limited exploration of emerging research on gut microbiota's role in metabolism. Future studies should investigate personalized metabolic responses and the impact of epigenetic factors, potentially leading to targeted interventions for metabolic disorders.

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