The Metabolomics

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Metabolomics is a combined set of strategies to identify and quantify cellular metabolites using advanced analytical tools. This is typically achieved through the use of liquid or gas chromatography, which allows for the detection of individual metabolites through their specific mass-to-charge ratio (*m*/*z*) and their fragmentation in a mass spectrometer. By matching detected metabolites against databases of known metabolites, it is possible to identify the specific metabolites altered by exercise in a biological sample.

Keywords: exercise ; metabolomics ; metabolites

1. Introduction

Exercise benefits every part of the human body and plays an important role in preventing chronic diseases. The effects of exercise are mediated by a complex process involving the activation of integrated body systems at the molecular and cellular levels. The growing use of metabolomics technologies in this field has made it possible to comprehensively study the exercise metabolome and understand the many benefits of exercise on the mental and physical wellbeing of humans. Tissues such as skeletal muscle, bone, and the liver were found to release metabolites into our blood [1][2] and are involved in pathways for respiration, lipolysis, and metabolic stress, helping to improve cardiovascular fitness and maintain muscle mass. In addition, metabolomics approaches helped identify the underlying mechanisms, pathways, and biomarkers involved in diseases and aging processes. For example, many exercise-induced metabolites were found to play key roles in the pathways involved in oxidative stress regulation, neurotrophic signaling, and autophagy, which were documented to positively influence a range of ailments including muscular aging, neurodegeneration, and heart disease [3][4][5][6]. Metabolomics is also a promising tool for the early diagnosis of diseases that cannot be treated, such as Alzheimer’s, helping to identify biomarkers and aiding in assessing therapeutic efficacy [7].

Moreover, many of these exercise-induced changes can lead to long-term metabolic adaptations, as documented in studies on elite and professional athletes [1][8][9][10] as well as chronic exercise interventions [11][12][13]. In athletes, for example, years of training coupled with a unique genetic makeup result in significant metabolic adaptation specific to their type of sport: endurance training tends to increase mitochondrial content and the activity of oxidative enzymes [14], and resistance training is associated with increases in muscle fiber and increased glycolytic enzymes in skeletal muscle [15]. As this is an emerging field, there are potentially many underlying metabolic mechanisms that have yet to be uncovered; further elucidation of these processes could help to identify potential therapeutic targets for athletes and the general population as well as provide the crucial information needed for the optimal balance between exercise training and recovery, allowing exercise programs to be finely tailored to individuals and athletes.

Exercise has numerous benefits for both physical and mental health, which are studied through metabolomics and the analysis of the metabolites released by tissues such as skeletal muscle, bone, and the liver. These metabolites play crucial roles in the energy production and respiration pathways, leading to metabolic adaptations and improved cardiovascular fitness, reduced inflammation, and increased muscle mass. Endurance training increases mitochondrial content and oxidative enzymes, while resistance training increases muscle fiber and glycolytic enzymes. Acute endurance exercise leads to changes in amino acid metabolism, fat metabolism, and cellular energy metabolism as well as cofactor metabolism and vitamin metabolism. Subacute and chronic endurance exercise result in alterations in amino acid metabolism, lipid metabolism, and nucleotide metabolism and improved lipid metabolism. Acute resistance exercise increases succinate metabolism, lactate metabolism, pyruvate metabolism, malate metabolism, and amino acid metabolism, leading to increased anaerobic processes and muscular strength. Chronic resistance exercise affects amino acid metabolism, energy metabolism, lipid metabolism, and bone metabolism, resulting in improved cardiovascular risk factors and skeletal muscle adaptations. Combined endurance–resistance exercise leads to changes in lipid metabolism, carbohydrate metabolism, and amino acid metabolism, improved anaerobic metabolic capacity and fatigue resistance, and the involvement of purine metabolism. The study of exercise-induced metabolites is a growing field, with the potential for uncovering more metabolic mechanisms and tailoring exercise programs for optimal health and performance.

2. Metabolomics

Metabolomics is a combined set of strategies to identify and quantify cellular metabolites using advanced analytical tools. This is typically achieved through the use of liquid or gas chromatography, which allows for the detection of individual metabolites through their specific mass-to-charge ratio (*m*/*z*) and their fragmentation in a mass spectrometer [16]. By matching detected metabolites against databases of known metabolites, it is possible to identify the specific metabolites altered by exercise in a biological sample [17]. This allows researchers to characterize metabolic differences between groups and individuals, helping them to understand the biological mechanisms underlying key differences. The metabolome can indicate past and present exposure to exercise [8][18][19][20], reflecting the physiological adaptations of an individual and even predicting their future responses. The increasing body of literature involving metabolomics indicates its growing role in the field of sports medicine.

2.1. Diagnostic and Therapeutic Use

Metabolomics is widely regarded as a promising tool for diagnostics, which is used to determine the significant biological pathways playing a role in disease development. Blood-based metabolomics, for example, is ideal for the early detection of a wide variety of diseases, such as breast cancer, leukemia, Alzheimer's, and heart failure [21]. In addition, metabolomics can be used to determine potential targets for therapeutic intervention by identifying pathological metabolic changes. For example, the examination of the metabolites up-regulated by the progression of prostate cancer points to the role of sarcosine in promoting cancer cell invasiveness, helping to identify the enzyme responsible for sarcosine production as a potential therapeutic target [22]. Metabolomics identifies biomarkers for the diagnosis, therapy, and monitoring of disease—making further classification of disease possible and enabling treatment options to be more specifically tailored to patients.

2.2. How Does Exercise Affect Metabolism?

The metabolome, which comprises all metabolites within an organism, is highly susceptible to external influences such as exercise. The literature to date overwhelmingly concludes that different degrees of physical exercise are responsible for quantifiable changes in the human metabolome, as measured in biological samples. These metabolic alterations are most commonly characterized by changes in lipid metabolism, amino acid metabolism, energy metabolism, carbohydrate metabolism, and nucleotide metabolism, among others [2][8][10][18]. Across the literature, findings widely reflect the known positive impacts and beneficial physiological adaptations linked to physical exercise. All reported metabolic pathways are inextricably linked: they play interconnected roles in aerobic and anaerobic respiration, fatty acid oxidation, branched-chain amino acid catabolism, and oxidative stress. While there is some debate in the literature about which components of exercise lead to the most pronounced changes, the research overwhelmingly supports a multifactorial dose relationship between exercise and the human metabolome, with factors such as the duration, intensity, and type of activity causing significant changes in the metabolic response.

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