Physiological Adaptation

16

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Abstract

The guidelines and research show that exercise and physical activity are the primary treatment methods for maintaining and improving health. The application of appropriate exercise approaches with maximum benefit and at minimum risk is the basis of exercise training. Physiotherapists have important duties in increasing physical activity and exercise capacity. Educational and behavioral physical activity and exercise programs are planned and developed by physiotherapists. Safe and effective results are achieved with correct and well-prescribed exercise training. To achieve these results, knowing the effects of exercise on the body is the first rule. Therefore, in the third part of *Exercise Anatomy and Physiology for Physiotherapists*, the physiological adaptation of all body systems to exercise is explained in detail. In this first chapter, the physiological adaptation of the body to exercise is examined from a general point of view, while in the other chapters, the adaptation mechanisms of body systems to exercise are revealed.

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16.1 Adaptation

In English, "to adapt" means to make (something) suitable for a new use or purpose; it is derived from the Latin term "apere," which means "to bind." The word "adaptation" in English is derived from the Latin term "adaptatio." Adaptation is a central concept in many major social disciplines, such as psychology, anthropology, and geography, and in many areas of biology. Adaptation refers to both the process and the result of the process. The term adaptation can be defined as hereditary changes or adjustments in the structure or habits of a species or individual that improve its condition in relation to its environment. In its broadest sense, adaptation is the adaptation of all systems and states of a living organism to survive. The concept of adaptation, which has emerged mainly in studies related to living things, continues to be the focus of biology. Adaptation in biology encompasses all behavioral, physiological, and structural changes that make an organism more suitable for an environment (Fig. 16.1). Behavioral adaptations describe the actions that enable an organism to survive in its environment. In contrast, structural adaptations refer to the physical properties that enable an organism to survive in its environment. Biological adaptation refers to a process that originates from the genetic organization at the cellular level, which can be transferred to the

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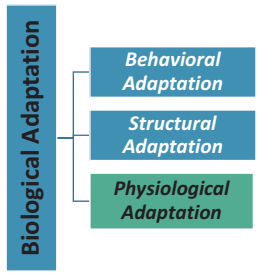

Fig. 16.1 Types of biological adaptation

individual level. Thus, the systems in our body have the ability to perceive and acquire at the physiological level. One of the most important concepts of biological adaptation is the physiological adaptation.

16.2 Physiological Adaptation

Physiological adaptation refers to the metabolic or physiological adjustment within the cells and tissues of the organism in response to an environmental stimulus, which ensures the survival of an organism. It indicates the cellular- or systemic-level response of the individual's ability to cope with a particular external stimulus and its changing environment to maintain the homeostasis of the body. In short, physiological adaptation is the process that regulates and maintains the body's homeostasis for an organism to survive in its environment.

Examples of physiological adaptations can be diversified as skin tanning when exposed to the sun for a long time and regulation of body temperature at different ambient temperatures. Apart from these, physiological adaptation occurs in every changing environment. From pregnancy to birth, and from birth to the end of life, the body shows physiological adaptation to this developmental process, all changing environmental conditions, diseases, nutritional status, and any activity or inactivity.

16.2.1 Exercise and Physiological Adaptation

When the human body encounters any physical activity, physiological systems respond through a series of integrated functional changes. For many years, exercise has been used by physiologists as a research tool to understand the functioning of various body systems, particularly skeletal muscle, metabolism, heart, and peripheral circulatory system. More recently, physiologists have focused on understanding exercise itself because regular physical activity is thought to be important for the prevention of diseases and the protection of health. Chronic diseases associated with physical inactivity have become increasingly common in modern society. Exercise has been proven to have a number of adaptive responses in the body that contribute to numerous positive health benefits. Studies have shown that exercise is effective in the primary prevention of many chronic diseases, including type 2 diabetes, non-alcoholic fatty liver disease, cardiovascular diseases, and some types of cancer. For this reason, great attention has been paid by researchers to the effects of exercise on body systems similar to those of pharmacological agents. Knowledge of the biology of regular exercise is used to improve therapeutic approaches to combat chronic disease. Incorporating even some of the adaptive responses to exercise into therapeutic approaches can provide significant health benefits. When the body receives regular exercise training on certain days of the week, each of these physiological systems is subjected to specific physiological adaptations that increase the body's efficiency and capacity. Although most of the physiological adaptations to exercise are observed primarily in skeletal muscle, exercise also has positive effects on other tissues at the cellular level, including the neural system, cardiovascular and respiratory systems, endocrine and metabolism, renal system, and immune system.

The most important factor in revealing the positive effects on systems and tissues is the type and frequency of exercise. The physiological responses of various systems to aerobic and resistance exercise training vary. These responses have been studied in controlled laboratory settings, where exercise stress can be precisely regulated and physiological responses can be carefully observed. These physiological responses should also be classified as adaptations to chronic (long-term) and acute exercise training.

Chronic exercise training, which results in continuous exposure of the body to the changing hemodynamics and hormonal environment caused by acute exercise, also has physiological effects on many organs. Regular chronic exercise training with individually planned intensity, frequency, and duration produces many adaptations in the human body that are beneficial for health.

These adaptations that occur in response to chronic aerobic exercise compared with acute exercise are given in Table 16.1. The revelation of

Table 16.1 Physiological adaptation to acute and chronic exercise

	Physiological adaptation to acute exercise	Physiological adaptation to chronic exercise
Brain	↓↑Neural activity or ↔Perfusion ↑Blood flow distribution ↓Metabolism ↑ or	Neural activity ↑ or**?** Perfusion**?** Metabolism**?** Changes at the receptor level**?**
Lungs	Ventilation and gas exchange ↑ Perfusion ↑ Blood flow distribution ↑	Ventilation and gas exchange ↑ or**?** Lung volume ↑ or ↔ Capillary surface area ↔
Heart	Cardiac output ↑ Coronary blood flow ↑ Oxygen consumption ↑ Blood flow distribution ↑	Wall thickness↑ Perfusion and oxygen consumption ↑ or ↔ Blood flow distribution**?** Size of chambers ↑ Oxygen extraction ↔
Blood	Hemoconcentration ↑ Oxygen content ↑ Energy substrate levels ↑	Blood volume ↔ Red blood cells ↑ Energy substrate levels ↑ or ↓ Hemoglobin ↓ or ↔
Vessels	Arterial dilation ↑ Capillary pressure and energy substrate exchange ↑ Blood flow distribution ↑ Venous constriction ↑	Arterial diameter ↑ Dilatation capacity ↑ Capillary density ↑
Muscles	Metabolism blood flow ↑ Oxygen extraction ↑ Mechanical strain ↑	Blood flow at rest and exercise ↓ Maximal blood flow ↑ Oxygen extraction ↑ Amount of mitochondria ↑
Bones	Blood flow ↑ Mechanical strain ↑ Stem cell release ↑	Blood flow**?** Metabolism**?**
Pancreas intestines kidney	Blood flow ↑ Metabolism ↑	Blood flow**?** Metabolism**?**
Skin	Blood flow ↑ Metabolism ↑	Blood flow**?** Thermoregulation ↑ Sweating capacity ↑
Adipose tissue	Blood flow ↑ Metabolism ↑	Blood flow**?** Metabolism**?** Browning of white adipose tissue**?**

↑: increase. ↔: no change. ↓: decrease.**?**: effect is unknown

the physiological adaptations at the organ level to acute exercise and chronic exercise training is the result of exercise training and positron emission tomography, a molecular imaging method based on radioactive isotopes, which is mostly performed in healthy people.

16.2.2 Brain

Studies in humans and animals have shown that cerebral blood flow is not greatly altered in response to acute exercise. During exercise, blood flow is directed to areas that control locomotor, vestibular, cardiorespiratory, and visual functions by stimulating neurons and vascular cells. The redistribution of blood flow follows the changes in metabolic activity. Regarding the use of energy substrates, the brain is an organ that can use glucose, fatty acids, and lactate. In general, while increased fatty acid oxidation is a characteristic of the fasting state, glucose uptake is the predominantly preferred substrate, especially during light and moderate exercises. However, as exercise intensity increases, brain glucose uptake decreases. The regional differences in brain glucose uptake are also affected by the physical fitness level. Thus, the reduction in glucose uptake in the dorsal portion of the anterior cingulate cortex during exercise is significantly more pronounced in individuals with higher exercise capacity. Recent advances in imaging techniques have made it possible to investigate opioid receptors in the human brain, but studies examining the effect of acute exercise on opioid receptor expression and function are needed.

Compared with acute exercise, physiological adaptations to chronic exercise training in the human brain have been less studied. A physically active lifestyle has been shown to lead to higher cognitive performance and delayed or averted neurological conditions in humans. Also, evidence shows that brain size, which is one of the determinants of cognitive performance, is greater in people with higher exercise capacity. Exercise training provides synaptic and receptor reorganization in various parts of the brain, including areas that control satiety and anxiety.

The production of brain-derived neurotrophic factor (BDNF), a key protein that regulates the maintenance and growth of neurons, which may contribute to learning and memory, is known to be stimulated by acute exercise. A study in mice showed BDNF formation in the hippocampus and cortex. Studies in humans reported that aerobic training increased the release of BDNF from the brain, which improved not only brain health but also overall whole-body metabolism.

16.2.3 Heart and Skeletal Muscle

Skeletal and cardiac muscles have been the most intensively investigated organs in exercise physiology. Cardiac and skeletal muscles play a central role in determining the level of whole-body metabolism, not only at rest but especially during exercise. This can be explained by the fact that the myocardium and skeletal muscle receive 85–95% of cardiac output and oxygen during maximum exercise.

The sympathetic nervous system plays an important role in the distribution of blood flow between active and inactive skeletal muscles. The distribution of blood flow among active skeletal muscles is important in oxygen transmission and consumption and formation of energy substrates according to metabolic needs in skeletal muscles. Thus, regional uptake is not associated with local muscle perfusion, although glucose uptake increases in response to exercise, and even more so with hypoxia. This is especially true for low-intensity exercise, where free fatty acids are tightly associated with local muscle perfusion. The glucose uptake is controlled by nitric oxide during low-intensity exercise. Although glucose uptake in skeletal muscle increases in direct proportion to exercise intensity, the glucose uptake in the myocardium increases only during moderate-intensity exercise. Strikingly, the myocardial glucose uptake returns to resting levels when the circulating lactate level increases with higher exercise intensities. However, compared with glucose uptake, the cardiac blood flow increases with increasing exercise intensity. This highlights the role of lactate and demonstrates

that glucose uptake is inversely proportional to the levels of circulating free fatty acids at low exercise intensities.

Studies using the needle biopsy muscle sampling technique have shown that aerobic exercise training significantly increases the aerobic respiratory capacity of the skeletal muscle. This physiological adaptation is due to an increase in mitochondrial mass, mitochondrial enzyme concentrations, and activities. In addition, aerobic exercise training stimulates angiogenesis, which leads to higher muscle capillary densities that facilitate oxygen transport to the mitochondria. A high level of capillary density increases the mean blood transit time, facilitating increased oxygen extraction and thus allowing lower blood flow at rest and at the submaximal exercise level. The enlarged capillary surface area and longer blood transit time facilitate the uptake of substrates with the contribution of glucose, free fatty acids, and lactate at different exercise intensities.

Structural cardiac adaptations begin to emerge with high-intensity exercise training. A difference in physical activity level has been shown to have no effect on the heart structure of genetically identical twins. Significant changes in cardiac function due to exercise training are not apparent because most comparative studies are conducted at rest. The results regarding the cellular mechanisms of exercise-induced adaptations in the human heart are scarce due to the ethical considerations regarding cardiac biopsies in healthy humans. However, evidence from animal studies shows that exercise training increases myocardial contractility; at the same time, a well-trained individual's heart relaxes rapidly. Therefore, increased cardiac output in an educated, healthy person is mainly due to increased cardiac mass, cardiac volume, and diastolic performance.

Positive skeletal muscle adaptations occur with exercise training without a notable increase in skeletal muscle mass (e.g., in marathon runners). The exercise-trained skeletal muscle has the capacity to do more work and consumes more oxygen per unit mass than the sedentary muscle. These adaptations are combined with increased skeletal muscle vasodilation capacity, while coronary adaptations occur in proportion to the degree of hypertrophy induced by exercise training.

The aerobic-trained heart shows reduced cardiac oxygen consumption per unit mass as a result of exercise-induced bradycardia, as the main determinants of oxygen consumption are not changed. Considering the high circulating levels of free fatty acids and low insulin levels, the resulting increase in free fatty acid utilization leads to higher oxygen consumption per phosphate, reducing oxygen consumption in trained individuals. In addition, studies on the structural adaptations of the right ventricle have shown the adaptations of right ventricular blood flow and oxygen use to acute exercise. For this reason, more research is needed to examine the effect of chronic exercise training.

Although it is well known that a high physical fitness level is associated with higher insulin sensitivity and insulin resistance improved by physical activity, the physical fitness level affects insulin sensitivity differently in skeletal and cardiac muscles. At rest, insulin-stimulated whole-body and skeletal muscle glucose uptake was significantly higher in subjects with aerobic training but no resistance training compared to sedentary controls. However, the glucose uptake was significantly reduced in both aerobic and resistance exercise training groups due to decreased myocardial wall stress and energy.

Exercise is known to enhance glucose uptake in the skeletal muscle. Low serum insulin levels and decreased fasting glucose levels are detected with regular physical activity. The stimulation of muscle glucose uptake independent of the effects of insulin and long-term adaptations in skeletal muscle activity with high insulin action independent of insulin signaling pathways demonstrates the beneficial effects of exercise. It is reported that exercise is important for dynamic muscle glycogen metabolism, regulation of blood glucose levels, and prevention of insulin resistance.

16.2.4 Bones

Exercise has numerous benefits for strengthening bone tissue, which provides the basic framework

for human movement. The changes in bone mineral content and structure are possible with increased blood flow due to acute exercise, which nourishes the bone in the recovery phase and in accordance with its metabolic needs. A study investigating the responses of the femoral bone to exercise and other physiological disturbances showed that blood flow and glucose uptake increased in response to acute exercise, and the human bone was surprisingly an active tissue.

However, blood flow is diverted to active muscles rather than bone and other less active tissues with increasing exercise loads. This mechanism is similar to the metabolism in human tendons. Human bone also has a significant capacity for vasodilation (higher than exercise-induced), but the blood flow is not altered by acute systemic hypoxic gas respiration. This is due to arterial chemoreceptors stimulated by local hypoxic vasodilation in the bone. It is known that exercise-induced enhanced bone perfusion is responsible for increasing the outflow of stem cells from the bone marrow.

Moreover, although the inhibition of nitric oxide synthase reduces bone blood flow at rest, it does not affect bone blood flow during exercise when combined with the inhibition of prostanoids. However, inhibition of adenosine receptors has been shown to significantly reduce bone blood flow during exercise. Adenosine receptors are known to be expressed in bone and adenosine, which acts as the primary signaling molecule. Studies examining the changes in bone blood flow caused by exercise and mechanistic studies should be performed in humans in the future.

Although repeated exposure to exercise-induced mechanical stress improves the physical properties of bone, studies investigating the effects of exercise training on blood flow or metabolism of human bone are needed. Such studies will be important because the role of bone in influencing whole-body metabolism is increasingly recognized. Similarly, the effects of exercise training on vascularity and bone marrow integrity have not been extensively studied in humans. Exercise training can potentially ameliorate vascular disorders and attenuate the endothelial progenitor cell release observed in the bone marrow in disease states such as diabetes. Exercise-induced physiological adaptations in bone have been less studied in humans to date, and hence many of these issues should be the subject of future studies.

16.2.5 Liver, Pancreas, and Intestines

Despite no studies in humans that detected tissue perfusion in the liver, pancreas, and intestine in response to acute exercise, studies that have described reduced arterial inflow in the arteries supplying these organs are available. It was observed that splanchnic organs were not affected by exercise. Until moderate-intensity exercise, the blood flow dropped to 20% of the resting value. This was more pronounced in splanchnic organs outside the gut, thus helping prevent intestinal hypoperfusion. Further increase in exercise intensity leads to intestinal hypoperfusion and gastrointestinal compromise. This physiological adaptation can have a negative impact on exercise performance and recovery. Epithelial integrity and gut wall barrier function may be compromised by repeated exposure to strenuous physical stress, which may explain why some patient populations may have to avoid vigorous exercise.

In response to acute exercise, the pancreas and liver perform important functions. Although insulin production from pancreatic cells is decreased mainly by sympathetic stimulation, glucagon production is increased in pancreatic cells. It allows the maintenance of blood glucose levels and the effective mobilization and utilization of free fatty acids, especially during prolonged exercise. The gluconeogenesis capacity of the liver during exercise is also well known. Increased insulin resistance due to a physically inactive lifestyle is seen not only in skeletal muscles but also in the liver, where insulin cannot suppress glucose production. Although exercise training effectively improves insulin sensitivity in the muscles, whether exercise similarly improves insulin resistance in the liver is not fully known. Hepatic insulin sensitivity plays an important role in the control of whole-body

metabolism. In the gut, insulin resistance develops before systemic glucose tolerance is impaired. Physical activity is essential for the early absorption of food, processing of pathogens, and immunity to maintain a normal metabolic state.

In active twins with lower liver and pancreatic fat percentages, the liver free fatty acid intake was associated with body fat percentage, while the pancreatic fat percentage was associated with the physical fitness level, insulin resistance, and hepatic fat content. These findings clearly supported the concept that ectopic fat accumulation in internal organs is harmful, but excess fat in these organs can be prevented by regular physical activity.

A previous study examined the effect of different exercise types on liver enzymes in a rat type 2 diabetes model. No statistical difference was observed in liver enzyme levels in all exercise trainings. When the studies on this subject were examined, it was shown that the liver enzyme levels increased in studies showing the acute response to exercise and decreased with long-term regular exercise. It was stated that liver functions might differ depending on the intensity and duration of exercise. Human studies on different exercise types and intensities are needed in the future.

The renal blood flow has been shown to decrease in response to acute exercise. In addition, chronic aerobic exercise training has also been shown to reduce renal sympathetic nerve activity in sedentary normotensive men, which has been associated with reduced renal vascular resistance. Extremely high blood flow is repeated during high-intensity exercise, and hence endurance-trained individuals have a higher epinephrine-secreting capacity compared with sedentary individuals.

16.2.6 Adipose Tissue

Adipose tissue is of two types in humans: white and brown adipose tissue. White adipose tissue is mainly distributed subcutaneously throughout the body and expands when the energy levels are high. When the subcutaneous fat storage capacity is exceeded, white adipose tissue begins to accumulate around and inside the internal organs, which is associated with impaired health and metabolic diseases. Conversely, brown adipose tissue is localized only in special small deposits, mostly in the neck region, and is activated by exposure to cold. Unlike white adipose tissue, which stores fat, brown adipose tissue burns the energy released as heat. It is well known that lipolysis in white fat is activated by exercise. Free fatty acids are released into the circulation to be consumed by other tissues, and this becomes more evident as exercise duration increases.

During prolonged exercise, lipolysis and the associated changes in adipose tissue blood flow are governed by the reductions in plasma insulin and circulating catecholamine levels, particularly epinephrine. However, although adipose tissue blood flow increased from rest to light-to-moderate exercise, the decrease in adipose tissue blood flow during high-intensity exercise was explained by decreased free fatty acid release. Norepinephrine acutely reduces fat blood flow, both at rest and during exercise. This may be through vasoconstriction activated by the sympathetic nervous system in the white adipose tissue. The fat blood flow is regulated by nitric oxide at rest and by adenosine during exercise. Other factors, such as natriuretic peptides released from the heart, also contribute to the regulation of adipose tissue blood flow.

The decrease in fat mass and the increase in capillary density due to the reduction in fat cell size after exercise training have been frequently examined in the literature. However, studies are needed to elucidate the physiological adaptations to long-term physical activity in the adipose tissue. However, as an endocrine organ, the adipose tissue secretes a variety of adipokines that can trigger important physiological functions in various other tissues in the body and can be modulated by endurance training. Recent animal studies suggest that exercise training can regulate various aspects of metabolism in the adipose tissue.

In humans, both glucose and free fatty acid uptake have been shown to be higher in visceral

fat than in subcutaneous fat. Subcutaneous adipose tissue contributes more to the level of free fatty acids due to its larger total mass. Interestingly, the aerobic exercise–induced improvement in insulin-stimulated glucose uptake is limited to the skeletal muscle, with no detectable change in glucose uptake in the adipose tissue. This may be due to the decrease in fat mass in subcutaneous and visceral stores.

Although adipose tissue is not the main tissue mediating the improvement in systemic insulin resistance as a result of exercise training, it may participate in overall energy metabolism leading to the maintenance and prolongation of post-exercise oxygen consumption and weight loss. In this respect, it may be important to investigate whether aerobic exercise training can change the white fat phenotype to a brown phenotype. Recent animal studies support this view. Some studies in humans have shown no or minimal transition to the brown phenotype. The browning of white fat is significantly necessary to demonstrate the physiological effects on whole-body metabolism. Some studies have shown that the level of the irisin hormone, which transforms white fat cells into brown fat cells, increases with exercise; however, a few studies did not detect any change. Many of these studies were performed on animals. In a study examining the effect of different exercise programs on irisin secretion in a rat type 2 diabetes model, irisin levels were found to be higher in all animals that received exercise training compared with those in the control group. However, when the effects of exercise training were compared with each other, it was observed that aerobic exercise training provided a greater increase in the irisin level than resistance exercise training. The literature highlights the need for studies on the physiological adaptation of brown adipose tissue in healthy and sick populations.

These results are important to highlight the potential of physical activity to prevent and treat metabolic diseases. The necessity of exercise as a lifestyle in the primary prevention of cardiovascular diseases is the result of these physiological adaptations.

16.3 Conclusion

Based on the available evidence, physiological adaptation outcomes, particularly of cardiac and skeletal muscles, are better characterized in response to acute and chronic exercise training. Many important issues regarding the perfusion and metabolism in the brain, bone, adipose tissue, and splanchnic organs have been less explored and therefore remain to be clarified.

Although the state of general metabolism does not change significantly in nonmuscular tissues during acute exercise, the changes in central and local hemodynamics and the hormonal changes in the energy substrate provide adaptation in these tissues. The physiological adaptations of chronic exercise training at the organ level have been explored mostly in animal studies. Studies examining the changes in different exercise types, intensities, and duration are needed. Therefore, the physiological adaptations to chronic exercise training in humans should be the focus of future research.

Physiotherapists who plan personalized exercise prescriptions should emphasize the major role of exercise in maintaining health and curing diseases. Also, studies showing the physiological and organ-level adaptations besides the clinical effects of exercise should be performed, and their results should be translated into clinical practice.

Further Reading

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