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Physical Fitness and Body Shape (Physical Shape)

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Abstract

The purpose of this study was to determine Zulu women's perceptions of their body image relative to weight status attending a noncommunicable disease (NCD) clinic in South Africa. A cross-sectional exploratory study design was used and included 328 (91%) Zulu women who were sampled systematically. The women were subjected to anthropometric measurements and engaged the Stunkard's body image figures to determine perception. The study showed that 61% of the sample was in the 40–59 age strata. The mean body mass index (BMI) was 37kg/m^2 ($\pm 9.41~\text{kg/m}^2$), with over 90% being overweight or obese. A discrepancy between Zulu women's perceived body image and actual BMI existed in all weight status categories with overweight and obesity demonstrating the widest variations (p < 0.000). Women perceived themselves to be thinner than their actual BMI. More than 99% associated an underweight body image to one with disease. Diabetes mellitus (72%) was the most frequent NCD encountered. Only 23% with this condition correctly perceived their body image. It was shown that the negative impact of preferring a larger body image in Zulu women with preexisting NCDs could be refueling their existing comorbidities.

Keywords: Zulu women, body image, non-communicable diseases (NCD's), weight status

1. Introduction

Overweight and obesity are conditions which have had an increase in children, teenagers and adults in recent years. According to the World Health Organisation (WHO), obesity has had a



300% increase since 1975, and in 2016, 39% of adults presented overweight, 13% presented obesity and more than 4 million children presented both conditions. Such conditions are more troubling at a young age, for they can trigger a metabolic memory, which can make adults more prone to obesity and to present more adipose tissue at organic and body levels. This may condition the person to suffer metabolic syndrome consequences or complications.

Overweight and obesity have a multifactorial aetiology, and in order to eradicate such diseases, there have been different unsuccessful attempts. Healthy eating and exercise are frequently encouraged, but there are other factors which determine and influence the optimal results with regard to weight loss, the main purpose of which is losing fat in the organs and, of course, in the body. Physical activity and nutritional advice should be optimal to achieve the expected results; however, maybe due to poor training of health personnel, the population results have not been satisfactory.

It is well known that carbohydrates and fat intake increase carbohydrates and fat at body and organic levels. Fat can be chronically increasing and being stored if it is not metabolised or "wasted" as energy. The obesity and overweight appear to directly impact organs and systems. Different systems like the cardiorespiratory systems, the haematology/circulatory system, the endocrine-metabolic system, the muscle skeletal system and the psycho neural system suffer a decrease in homeostasis, and malfunction in these systems may influence vital organ functions, even at a personal development level.

Fat and lipids metabolism is carried out regularly; however, a percentage of these are stored in the body for future needs, but such storing should not become chronic. Physical activity carried out on a regular basis has impacted physical condition, which can be considered healthy or unhealthy and which is an important morbidity mortality indicator and predictor. Healthy physical fitness protects against metabolic diseases. Physical fitness turns healthy with adequate organ systems and organs, that is, through physical adequacy: discipline and body exercises which improve health.

Physical activity should be carried out by any person able to do it, regardless of the age, and independently from overweight or obesity, for, besides helping reduce fat tissue (reach and keep the ideal weight), it helps create a healthy physical condition. Exercise produces benefits at hormonal level, releasing endorphins and serotonin, known as "happiness hormones". Besides the regulation of systems like satiety and appetite, which help reach the ideal weight.

2. Physical fitness and physical shape

According to the World Health Organisation (WHO), overweight and obesity are on the rise on a global scale, reaching pandemic proportions, and killing 2.8 million people each year [1]. It is well known that overweight and obesity are non-transmittable, chronical, metabolic diseases whose causes are multifactorial and where weight increase is due to fat excess in the fat tissue. These ailments have enormous repercussions in public health and were previously limited to first world countries. However, nowadays even developing countries are suffering from such complications. Such effects used to be seen only in adults, but can now be seen at any stage of life: childhood and adulthood alike. Hearth diseases, intestine cancer, cerebrovascular events, dyslipidaemia, musculoskeletal disorders, type II diabetes mellitus, obstructive sleep apnoea, hypertension, metabolic syndrome and productivity and quality of life decrease stand out among potential complications, affecting significantly children's and adults' physical wellness and physical performance [2, 3].

Despite the ethology in these procedures, there are precedents that support physical activity that can help reach and keep our ideal weight. Regular physical activity seems to be a protective factor in the decrease in accumulation of subcutaneous fat [4, 5], while a sedentary lifestyle is one of the factors that contributes the most to gaining weight and it is associated with lower physical fitness levels [5–7]. In the last years, the latter has gained ground when it comes to health, but it used to be used only as a tool in sports areas.

Specifically, the physical fitness is the ability of the skeletal muscle system to act as a result and in synchrony of the integration of other systems and that will allow movements appropriate to sex, age and maturation of the central nervous system as well as the development of motor skills. These movements can be achieved in favour of or against the severity and the ease with which they are made which can depend on muscle tone, the amount of muscle fibres and the level of muscular strength.

On the other hand, the physical shape of the body can be considered from two points of view. The first is the category according to the body mass index (BMI) established by international standards where a person can be in the category of undernutrition, underweight, overweight or obesity. However, the one considered in this chapter refers to the physical shape of the healthy or unhealthy body, which is established from specific tests of physical fitness and therefore not based on body weight.

In this sense, physical fitness connected to health is defined as the ability someone has to perform everyday activities vigorously, delaying fatigue and avoiding injuries [8]. It is also defined as the ability a person has to do physical activity or exercise and it brings musculo-skeletal, cardiorespiratory, haematology and circulatory, endocrine-metabolic and psychoneurological [9, 10] functions together. Physical fitness is an important predictor of the health of an individual; it is also an important mortality and morbidity predictor [11, 12]. It is true that in the sports field, physical fitness has been categorised as good, regular or bad or low, average or high [13, 14], but physical fitness has not yet been defined. However, in a stricter, more connected to health way, physical fitness could be considered as healthy or unhealthy, taking into account clinical factors and physical evaluation factors.

Up until now, the "healthy weight" paradigm states that a person with an average or ideal weight, according to the standard body mass index (BMI), is an apparently healthy individual who can be related to good health statistics [1, 15], either present or future, with the small possibility of suffering a metabolic disease or even others, such as dyslipidaemia, which may manifest in obesity or overweight but are not caused by them.

Recent studies warn that a normal weight does not precisely protect against metabolic diseases [16, 17], for such "healthy weight" indicates the adequate mass of the individual according to their sex and age. However, it is to be considered a not-so-close relation to health, nor present or future. In consideration, independent of the BMI, the combination with regular physical activity would help improve physical fitness, turning it from not healthy to healthy, and that would have a direct impact on the individual's health. This information could be presented in a practical way in **Figure 1**.

The predisposition to a metabolic disease could be inferred through physical fitness and not through body physical shape, the latter depending on the BMI. An appropriate physical fitness could help the individual have a healthy physical shape (ideal weight) and an appropriate physical fitness; it would favour an unhealthy physical shape greatly: overweight and obesity; malnutrition and low weight. On the contrary, a healthy or unhealthy physical shape does not suggest an appropriate or inappropriate physical fitness (Figure 2).

Similarly, there might be people with an apparent appropriate physical fitness and an unhealthy physical shape, thus there might also be people with a healthy physical shape who have an inappropriate physical fitness [16, 17]. This could be exemplified with a Zumba instructor who is over 90 kilos (198 lb) with an apparent appropriate physical fitness when performing flexibility movements, an apparent muscle resistance and an adequate cardiorespiratory resistance, without considering his body complexion. On the contrary, there are people with an adequate body complexion whose flexibility, muscle resistance and cardiorespiratory capability, when trying to dance, are not in optimal conditions. This may suggest that there are overweight or obese people who have an appropriate physical fitness and that there are people in shape but unhealthy (Figure 3).

Physical fitness is evaluated through specific components within batteries (set of physical tests) for children, teenagers and adults, respectively [18–20]. Such evaluations determine the physical aptitudes connected to the health of the individual, which is the main approach of this section. They are also related to the motor skills and to sport performance, respectively [18-22]. There are five physical aptitudes to do with health, a medical approach can be observed in those five aptitudes, and this can be used as a health predictor of the individual (Table 1). An adequate physical fitness is reached through physical activity. Exercise is

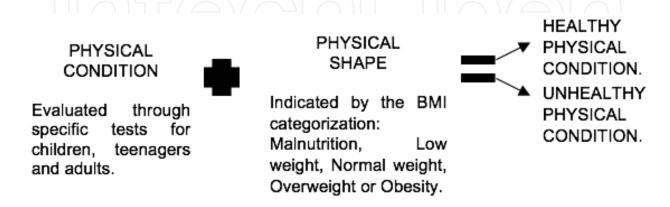


Figure 1. Physical fitness and physical shape graphic analysis with which it may be determined if there is a healthy or unhealthy physical fitness.

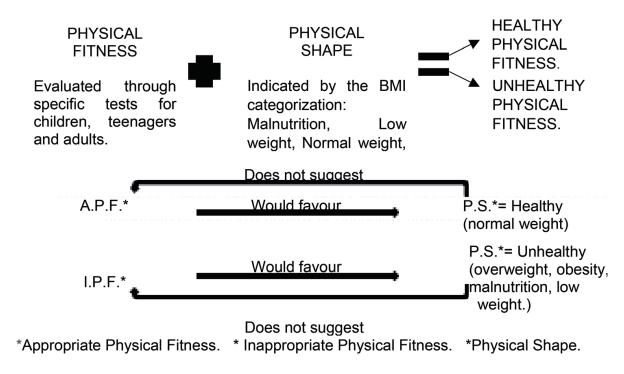
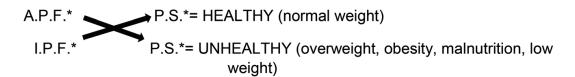


Figure 2. Graphic inference of the appropriate and inappropriate physical fitness that would favour a healthy and unhealthy physical shape.



*Appropriate Physical Fitness. * Inappropriate Physical Fitness. *Physical Shape.

Figure 3. Graphic proposition of an appropriate physical fitness in an unhealthy physical shape and vice versa, inappropriate physical fitness in a healthy.

essential in order to make neuromuscular and metabolic training contribute and favour the adequate organic and systemic operation and adequate physical fitness that may be a protective factor for health.

It is well known that the main objective for public health of the governments in all countries has been the promotion of healthy eating habits and, above all, a balanced diet, as well as doing exercise. However, this objective has not been reached, for not a single country has seen a decrease in obesity rates in the last 30 years [23] which has led to thinking twice about the benefits of physical activity in weight loss and about the inefficiency of exercise and exclusive diets.

Shook et al. studied the relation between the intake of energy, physical activity, appetite and weight increase, and it was discovered that people with less physical activity showed higher levels of appetite in comparison with people who had high levels of physical activity. The authors noticed that an energy balance could be reached with an activity corresponding to 7116 steps a

1. Cardiorespiratory resistance	Resistance to an aerobic effort. It requires the adaptation of different systems: cardiorespiratory, haematology and circulatory, endocrine-metabolic, musculoskeletal, etc. The energy obtained is through the aerobic metabolism where carbohydrates (aerobic glycolysis) and fats (Krebs cycle) oxidise in oxygen presence, that is, there is an equilibrium between the intake of oxygen and its consumption			
2. Muscle strength	Manifestation of the muscle contraction, isometric and isotopic in favour or against gravity. The effort is proportional to the strength it has: more strength, less required effort			
3. Muscle resistance	Repeated below maximum tension capability in a period of time. It allows us to perform everyday activities avoiding tiredness and delaying muscle fatigue			
4. Physical composition	Evaluations and measurements in the individual based on four basic components: mass, fat, lean mass, water, and minerals. It helps in the detection of the nutritional state, growth, physical activity and as a tool for timely diagnosis and detection of overweight and obesity and its possible complications for health			
5. Flexibility	Muscle capability to perform the maximum joint effort without injuries. Flexibility does not generate movement, but allows it			

Table 1. Aptitude connected to health and their clinical approach.

day [24]. This might suggest that a sedentary person, despite following a diet for losing weight, may be less successful if no physical activity is carried out, for exercise is the most important factor in everyday energy consumption and it could directly affect the energy balance [25].

Physical fitness is closely related to physical activity, which includes muscle activity during exercise [26-28]. The approach of the physical activity must be prescribed by experts in a multidisciplinary group, according to BMI, age and sex, for there are neuroendocrine and metabolic indicators that refer to the cardiac cycle and hormonal regulation, as well as the equilibrium of dietary intake to lose weight and to keep the ideal weight. For prevention, modification and control, some studies state that physical activity may have an important contribution for weight control [29].

Children and adults are affected differently by obesity and overweight. It has been proved that less physical activity is associated with obesity and that regular activity in children and adults improves physical fitness, which helps treating obesity and overweight. According to the component of physical fitness related to health, cardiorespiratory aptitude has been more frequently studied and it has been associated to obesity, impacting cardiovascular risks [30]. For this reason, and in order to plan and promote physical activity that favours physical fitness more accurately, it is necessary to understand the parameters that affect the energy consumption in the physical composition and that may help prevent overweight and obesity or that may help improve weight to achieve the ideal weight.

3. Fat tissue and muscle mass modification for physical activity

In order to be aware of the process that modifies fat tissue (FT), it is important to know that the total energy consumption (TEC) represents a 100% and it is the result of three primary components: basal metabolic rate (BMR) = 60% + thermic effect of food (TEF) or dietary-induced thermogenesis (DIT) = 5–10% and thermic effect of exercise (TEE) = 15–20% of the TEC.

The studies of physical activity and TEC during adolescence and adulthood show evident changes in habits, factors that may be associated with a risk increase to suffer from overweight or obesity and from comorbidities [31]. In sedentary people, more that 75% of the TEC is consumed by basal metabolism and only 15–20% is consumed in physical activity, increasing the possibility of accumulating fat tissue and thus being obese or overweight. Such fat tissue will not only affect the body image, but it will, at molecular and organic level, take visceral space and other anatomic places that compromise biological homeostasis.

From a biological point of view, lipids play a very important role due to their diverse and irreplaceable functions: they make up cell membranes, they help transport fat-soluble vitamins and other substances like hormones. Due to their high caloric content (9 kcal/g), they are the most important energy reserve. However, they are metabolised more slowly, they are stored almost in an anhydrous way and they need the presence of oxygen, in comparison to carbohydrates, which are metabolised faster, may or may not use oxygen and are stored in the presence of water.

The primary cell of the fat tissue (FT), the adipocyte, works as a real endocrine organ. Individuals with a high storage of central or deep visceral fat would be more sensible to the B-adrenergic stimulation of the adipocytes, which would increase the production of fat acids (FA) which are digested in the liver and generate dyslipidaemia, insulin resistance, and hepatic steatosis, among other effects [32]. Such problems, when combined with obesity or overweight, create complications in the health of the individual, thus making the oxidation of such fat acids essential.

The oxidation of fat acids takes place in three steps, one depending on the other: (1) the transportation of fat acids from fat tissue, (2) the transportation of fat acids to the muscle and (3) the muscle cell consuming the fat acids, which through physical activity allows energy expenditure.

Such energy expenditure will depend on the time and the intensity of the activity and on the prescribed physical activity. Only a few observational studies have included details on the kind of physical activity that should be carried out, or the duration or the frequency. The total amount of the activity is generally determined by the coaches or by the individual itself without taking into account health factors or the medical history, which are important matters always to be considered in a programme designed to lose body fat.

During physical activities and our everyday movements, the FA are perennially moving in the adipocyte, while triglycerides are transported to the cytoplasm. This process may be triggered by catecholamines, where some receptors known as B-adrenergic (B-AR), situated in the plasma membrane, allow its entrance. The stimulation of the B-AR generates cyclic adenosine monophosphate (cAMP) through the activation of adenylate cyclase. A rise in the intracellular cAMP activates the kinase A (PKA), which stimulates the hormone-sensitive enzyme (LHs). Once activated, it is translocated to the lipid vacuole and hydrolyses the FT, resulting in two fat acids and a monoacylglycerol, which can be spread into the circulation. The latter will be hydrolysed into glycerol and another fat acid [33].

Unlike glycerol, once FA are in the cytoplasm of the muscle cell they can be stored in intracellular FT or re-esterified to form new FT through the triacylglyceride. For this to happen, glycerol-3-phosphate (G3P) must be present; however, by reducing the glycerol kinase enzyme, the G3P results in glucose [33]. Once the FT molecule has been hydrolysed inside the adipocyte, fat acids can passively go through the cell membrane, or associated to the FA transporting protein, located in the membrane of the adipocyte. FA are transported by passive diffusion and facilitated through the plasmatic membrane linked to FA linking proteins (FALP) through the sarcolemma of the muscle cell. Albumin will join in the interstitial space, which is responsible for transporting 99.9% of the FA in the plasma. FA transport conditions seem to be the saturation of the complex fat albumin acid and the proper perfusion of the tissue. Cardiac muscle and skeletal muscle depend the most on fat acids as source of energy. However, the content of FT can vary due to internal and external factors, among which are diet and physical exercise. A lack in the consumption of energy of this fat acids may lead fat tissue to increase. There are two ways this may happen: (1) an already existing increase in the size of the adipocyte (hypertrophy) or (2) a rise in the number of adipocytes (hyperplasia).

The use of fat as the main source of energy will be conditioned to the intensity of exercise. During low-intensity exercise (25% VO2 max), fat acids and plasma glucose seem to be the most important substrates. For the muscle triglycerides (MTG) contribution to energy provision is minimal. On the other hand, with moderate exercise (65% VO2 max), substrates in the muscle (triglycerides and glycogen) are essential, for they were oxidised at high rates, while fat acids were used at lower rates. Finally, with high-intensity exercise (85% VO2 max) the predominant substrate was muscle glycogen, with a decrease in the MTG and plasmatic FA (Table 2) [33].

Several studies have shown that the loss of fat induced by exercise seems to be higher in the abdominal region or the arms than in the femoral region [34, 35]. This suggests that the changes in fat tissue triggered by training vary in different regions of the body, and that exercise may reduce the adipose tissue reservoir and modify fat distribution. However, this is not yet settled. Such knowledge of the lipid cell brings the possibility of correctly programming exercise to people who suffer from obesity or overweight and with the primary objective of reducing adipose tissue.

As previously stated, body weight is determined by a percentage of water, minerals, fat and muscle. It is important to remember that the human body has more than 650 muscles, which make up half the body weight of a person (50%), however, when dealing with obesity or

Intensity exercise	VO2 max (%)	Substrate use			
		Plasma glucose	Plasma fat acids	Muscle triglycerides	Muscle glycogen
Low-intensity exercise	25	•	•		
Moderate intensity exercise	65			•	•
High-intensity exercise	85				•

Table 2. Substrate use at different intensity of exercise.

overweight, this percentage is lower, with more fat tissue. It is important to prepare the neuromuscular system to be adapted and used to regular physical activity through regular exercise. The objective of training when obese or overweight is to lose fat tissue or to maintain the ideal weight while increasing and improving physical fitness. This will depend on the efficiency with which chemical energy can be transformed into mechanical energy, energy consumption and the modification of fat tissue and its adaptation in the neuromuscular system (physical fitness).

When performing physical activity, fat tissue transforms, and the same happens to skeletal muscle. The modifications that take place in the muscle cells due to training are known as chronic or acute, and will depend on the evolution of the activity. Such modifications occur through an increase in the blood flow and through the liberation of autocrine and paracrine muscle factors, which stimulate receptors on the cell surface and activate torrents of signals and muscle contraction per se. One of the main signals in the metabolic adaptation of the skeletal muscle is the activation of the protein sensing the cell energy state represented by the adenosine monophosphate-kinase (AMPK), whose activation depends on the energy state induced by exercise and favours the density of mitochondrion and capillary, as well as the increase in the enzymatic, activity.

Added to this biochemical aspect is the importance of the characteristics of the physical activity, as well as the intensity in the training session. It is believed that an increase in the intensity could trigger a change in the muscle recruitment pattern, which would go from a predominance of slow-twitch oxidative fibres (type I) to the predominance of fast-twitch glycolytic fibres (type II). Recent studies have shown that athletes who trained for speed have more type II fibres in their muscles, while athletes who trained for endurance have a higher percentage of type I fibres. Endurance training brings a higher glycolytic flow in the skeletal muscle, thus provoking a decrease in the maxim activity of the glycolytic enzymes. This adaptation favours fat oxidation over carbohydrates during exercise [36]; in this way, training for resistance with moderate-high-intensity decreases the production, consumption and oxidation of plasma glucose.

Low-moderate density exercise (50–60% VO2 max) has been suggested to treat obesity and overweight; however, the reduction of the fat mass has been insufficient for health purposes, thus intermittent high density exercise (HIIT) is considered an alternative, for it has bigger effects on the subcutaneous and abdominal fat due to the throbbing release of lipolytic factors through the secretion of catecholamine and peptide natriuretic which produces the segregation of fat acids from body fat reserves [37]. The main characteristic of this form of exercise is the short periods of exercise (seconds or minutes) carried out at high density (equal or less to 100% VO2 max), followed by rest (more dark mass and less fat tissue quantity), which is proportional to the intensity of the exercise.

Adequate prescription of exercise may produce changes at organic and physical levels in people who suffer from overweight or obesity, in which the continuous state of tissue inflammation (lipoinflammation) also generates a hormonal imbalance, in which the adipocyte alters its segregation, producing less leptin and more adiponectin, and a decrease in insulin sensibility which, in the end, has an impact on the mitochondrial functioning accompanied by a more

stressed endoplasmic reticulum in the presence of fat tissue. For this reason, it is important to acknowledge the importance of the endocrine system when exercising and its relation to overweight and obesity.

4. Overweight and obesity: neuroendocrinology of exercise

The hypothalamus is made up of nuclei specialised in the elaboration and segregation of hormones to stimulate the hypophysis. The hypophysis, or pituitary gland, is located in the Sella, and it is divided into the anterior lobe, or adenohypophysis. In normal situations, the hypothalamus-pituitary system, which is made up of minuscule blood vessels, is in charge of transporting such factors.

The term hormone derives from the Greek root 'Hormón', which means 'to move'. Hormones are protean chemical substances, produced by organs with secretory functions, which are transported by the bloodstream to different parts of the body and produce inhibitors and activators. Hormones are classified in three groups: (1) steroid hormones. Synthesised from cholesterol and are not stored. They are fat-soluble (2) non-steroid hormones. They are hydrosoluble; thus, they cannot go through membranes with the permeability mechanism, using the activation of the receptors of the membrane and (3) hormones originating in the thyroxine.

The secretion of a hormone may be fast (Ad and NAd) or gradual (GH), and for this reason, there might be different hormone levels during the day, derived from the circadian system, for each hormone secretion is regulated by a negative feedback through the hypothalamushypophysis, interconnecting with peripheral sensors that indicate how an activity is being carried out. Thanks to this information, the system decides which hormone group is to be secreted into the bloodstream. It is important to mention that hormones are eliminated from the bloodstream in different ways: (1) by the metabolic destruction of tissue, (2) by the bonding of tissue (3) by the excretion of bile or hepatic transformation and (4) urine.

In normal conditions, the neuroendocrine system tends to be balanced, that is, there is a catabolism process after an anabolism process or vice versa. However, in certain pathologies the endocrine system is disturbed and it is not strange that in cases where there is an excess of fat tissue, the subcutaneous adipose tissue is not capable of storing the energy excess, while the adipose tissue visceral becomes the main triglyceride storage. Such conditions require an energy balance, along with appetite and anxiety, where the neuroendocrine system becomes important in order to regulate, but it is disturbed by the toxic conditions of overweight and obesity.

The adipose tissue secretes specific hormones, and the adipocyte is the main effector of the lipogenesis and lipolysis. While the mature white adipocyte produces leptin, the brown adipocyte produces adiponectin which raises sensibility to insulin in the muscles, liver and other organs and favours the oxidation of fat acids. Adiponectin is an important hormone for exercise, for its production increases during physical activity, improving fat tissue reserves metabolism [38].

People with higher concentrations of this hormone seem to have less risks of suffering from cardiovascular and metabolic diseases [39], and people who do more physical activity often have higher levels of adiponectin, in comparison with sedentary people, improving resistance to insulin, glycaemia, and lipidema.

Exercise brings immediate hormone responses and adaptation in the long term. These endocrine responses are linked to external factors such as the time in which the physical activity is carried out, in which the circadian cycle plays an important role, because the knowledge that the biological clock in the hypothalamus times the functions in the body was established by studying this cycle [39]. In this sense, exercising during hours when a person should be resting disturbs the metabolic circadian rate coordination with regard to the biological clock.

It is vital that certain hormones are present and active when doing physical activity. The growth hormone (GH), a small protean molecule which contains 191 amino acids, is essential for hormonal growth in kids and also plays an important role in the increase of fat acids transportation in the adipose tissue; it increases the quantity of free fat acids in blood as well, favouring its use as a source of energy.

In exercise, GH modulates the adaptations to the training of strength. Most studies seem to indicate that GH may perform directly on the tissue. It mainly enhances other hormones known as somatomedins or insulin growth factor (IGF), whose main actions are to increase and decrease protein synthesis, stimulate cartilage growth and the retention of nitrogen, sodium, potassium and phosphorus [40]. The importance of some particular mineral salts when exercising becomes more important, like potassium ion responsible for the nervous excitability along with sodium, calcium and magnesium, which contribute to keeping neuromuscular health and can improve the physical capability, or at least keep its level, which would favour muscle resistance.

It is important to mention that the quantity of GH during a workout depends on the intensity, amount and resting time in between series. A higher secretion of GH is through a higher hypertrophy stimulus (maximum of muscle twitching). GH response decreases as we age. However, after 21 weeks of strength training there has been an increase in GH response, which may continue high up to 30 min after exercising [40].

On the other hand, testosterone is a steroid hormone with anabolic effect on the tissue and whose production depends on the luteinizing hormone (LH). It has been observed that patients with higher cardiovascular risk, metabolic syndrome, hypertension, diabetes mellitus type II and obesity have lower levels of testosterone [41]. Such deficiency in overweight and obesity may have it grounding in low sex hormone binding globulin (HGB) due to the hyperinsulinemia state, creating a lipid profile.

Testosterone in the blood enters muscle cells in its free form, biologically active, through a diffusion mechanism. It is believed that this connection with the genetic code may be the main factor for the increase in size of the muscle cell observed after strength training. Testosterone stimulates, on the one hand, nervous elements (a rise in transmitters and receptors) and, on the other hand, type II muscle fibres (turning them into type IIx, stronger, less resistant and with

more glycolytic) [40], improving dark mass increase and reducing fat mass through physical activity.

There is not always an increase in the basal blood concentration of testosterone and/or an increase in the proportion of testosterone/cortisol when a strength-training programme is carried out. Some authors suggest that such an increase is observed after training for 8 weeks or more, but it is not observed when the training is short. When sportsmen have been training intensively for years, the increase of basal blood concentration of testosterone is no longer evident, and it is probably close to the hormonal adaptation limit.

The known stimuli capable of acting at hypothalamus level, reducing appetite and increasing energy expense, comes from the gastrointestinal system (glucagon, bombesin, cholecystokinin, and glucose); from the endocrine system (insulin, adrenaline through its b-adrenergic effects and oestrogen); from fat tissue (leptin); from the peripheral nervous system (noradrenalin b-adrenergic effects) and from the central nervous system (dopamine, serotonin and gamma amino butyric acid).

The hypothalamus produces most integration and interpretation of the humoral and neural afferent signals for the coordination of the ingestion (hunger and satiety) and the energy expenditure (increases or decreases basal metabolism and thermogenic efficiency of the brown adipose tissue, as well as changing the secretion patterns of different hypophysis hormones) in response to conditions that modify the energy balance in the organism.

The arcuate nucleus, where all these mediators arrive, is situated in the base of the hypothalamus and has two main types of cell systems: (1) those which reduce appetite or neurons containing proopiomelanocortin (POMC) and (2) those which stimulate appetite and have neuropeptide Y neurons (NPY) and the peptide related to the agouti protein (AgRP), which acts as antagonist endogenous of the MC3 and MC4 receptors.

This integration unleashes mediators, which, through the stimulation of the sympathetic and parasympathetic nervous systems, and through the secretion of thyroid hormones, regulate the sense of hunger, the ingestion of nutrients, the type of selected nutrients, the basal metabolism and the necessary energy expenditure for growth and physical activity [41].

Like the previously mentioned hormones, leptin, made up of 167 amino acids and belonging to the cytokines family, is primarily synthesised by white fat tissue and in less quantity by muscle tissue, placenta, adenohypophysis, central nervous system, mammary gland, stomach and tumour tissue. Synthetisation occurs after a flow of nutrients into the adipocyte which guarantees the generation of triglycerides, but also by hormones such as insulin, glucocorticoids, oestrogens, melatonin and transition factors which positively regulate the expression of the adipocyte "ob" gene, while inhibited by androgens, tumour necrosis factor alpha and by thyroid hormones [41]. Plasma leptin concentrations are directly proportional to total fat mass. The biggest receptor is located mainly in the hypothalamus, hippocampus and cerebellum, while small molecule receptors are located mainly in the choroid plexus and its function seem to be to facilitate leptin circulation into the brain.

Leptin biological actions can be classified into two groups: (1) central nervous system tissue (hypothalamus) regulates corporal weight, reduces food intake, increases basal energy expenditure and modifies some endocrine functions and (2) peripheral tissue: has effects on tissue metabolism proliferation, differentiation and peripheral tissues.

There is another hormone that is related to overweight and obesity: adiponectin, which is a hormone secreted specifically in the adipocytes, involved in the regulation of the metabolism of glucose and fat acids and in the protection of artery walls against atherosclerosis. Low adiponectin levels are associated with insulin resistance and breast cancer, for this hormone may directly control the growth of the cancer cells, and it also has anti-inflammatory properties. Individuals with higher concentration of adiponectin have a lower risk of suffering metabolic or cardiovascular diseases. On the other hand, lower serum levels are associated with obesity and metabolic syndrome [42, 43]. Among the activities that produce changes in adiponectin concentration are aerobic exercise and endurance exercise.

Exercise is beneficial, for it increases the serum level of different hormones, and the expression of their receptors. Thus, exercise benefits must be considered on insulin resistance, glycaemia and lipidemia, for besides regulating important endocrine systems, it favours the secretion of other hormones such as serotonin and endorphin, which produce benefits for our health.

In the same way exercise is important for losing fat tissue, gaining lean mass, and improving physical condition, proper diet is also necessary in order to reach these objectives, thus the importance of studying food and diet when overweight or obese.

Healthy eating is based on the nutritional pyramid, who consider demographic characteristics, not taking into account the characteristics of the individual [44] (genetic and metabolic profile), which affect the absorption process, distribution, metabolisation, and elimination of each nutrient. For instance: triglycerides, sterols and tocopherols guarantee a variety of effects, with different metabolic and cell procedures [45, 46]. In overweight and obesity conditions, this metabolic situacion is counterproductive by the concentration of fat acids, which during low-energy expenditure, are stored in big quantities and impact directly body image.

The existence of metabolic memory may explain why kids may suffer from overweight or obesity in their adolescence or adulthood and that kids with normal weight reach their adolescence or adulthood with the ideal weight. It is advisable to work such metabolic memory through healthy eating and physical activity so as to keep the ideal weight, and to carry out such recommendation for population groups susceptible to overweight or obesity of any age in order to improve their health and reduce the risk of illnesses, consequences or complications.

5. Physical activity and endocrine effects

Like metabolic memory, endocrine memory plays an important role in the appropriate hormonal functioning and its efficiency on molecular, neuromolecular and on specific systems level. The effects of exercise for the brain to function properly have been reported in a variety of studies. Psychology studies have reported the beginning of disorders in emotional states, depression and anxiety in people who suffer from obesity or overweight [47, 48] and which affect performance with family, work and at a personal level, which may compromise their health even more.

There are reports of exercise influences at a genetic level, and that more than 500 genes are located in the muscle, skeletal, vascular and neuronal tissue, among others [49]. In the same way, exercise may decrease sodium/potassium ATPasas, increasing the resistance to oxidative stress through the expression of proteins such as superoxide dismutase 1 (SOD1), catalase and Bcl-2, which suppress oxidative stress, regulating the ATP levels in the neurons, prompting enzymes into the Krebs cycle [50–52].

The exercise increases the level of substances such as lactate and glucose, constituting an indirect measure in cell activity through physical activity at glial and neuronal level; and oxygen, metabolism and blood flow are modified by physical activity.

Muscular training through physical exercise produces hormone changes, regulating growth, metabolism and reproduction; responding to circadian cycles and, presenting immediate responses in short or long terms. The endocrine system is controlled by a negative feedback.

All changes produced during exercise are beneficial, for they control blood sugar and ensure that energy is transported all through the nervous system and muscles. Exercise also improves the cardiorespiratory parameters; it increases the size and quantity of mitochondria. It also produces muscle hypertrophy and the electrolytic regulation impedes dehydration. Thus, exercise and exercise intensity are decisive in hormone secretion. The active participation of the neuroendocrine system helps eliminate fat tissue, improving physical fitness and physical composition.

It is known that the regions of the brain involved in the release of hormones during exercise are the motor-sensor systems: cerebellum, primary cortical areas and the basal ganglia; as well as the hypothalamus, hypophysis, the hippocampus, among others. With the knowledge of neuroendocrine effects, the characteristics of physical exercise could be determined in terms of frequency, intensity and duration, achieving a weight loss.

6. Conclusions

Muscle and adipose tissue are benefited from the presence of regular, acute and chronic physical activity, in kids, teenagers and adults. Physical activity is essential to improve body composition in obesity and overweight conditions, and also to keep the ideal weight, which will serve as protection against metabolic disease. It will also improve the emotional state and physical fitness of any person who practices it. Thus, being sedentary, even with the ideal weight, will reduce organic functions, favouring weight increase. It is important to continue this research, analysing the level of exercise of people with normal weight, overweight and obesity, in order to determine neurotransmitter levels, clinical health state and physical fitness in general.

The main consequence of fat tissue excess in the organs and in the body is that, at anatomical and physiological levels, such fat occupies space, which limits or disables organs and keeps them from performing adequately. Take, for instance, the "fatty liver", known as hepatic steatosis. Fat surrounding the heath predicts cardiovascular diseases and diabetes mellitus type II. This is a risk factor which can be associated to an excess of fat around the myocardium and the limitation of coronary blood vessels. Our pancreas is also affected by high levels of triglycerides in the blood and by the excess of fat, among others.

Sleep apnoea and pulmonary embolism and pulmonary fibrosis are among the complications of sleep apnoea. The skeletal muscle suffers from the excess of body weight, mainly in the joints in the knees with chronic gonarthrosis, lower limb bursitis, herniated discs, mainly lumbar, thus posing a difficulty or impeding carrying out every day personal work, family and social activities. Organ and physical affectation may impact the emotional state, where at a psychological level, depression, anger or anxiety may be triggered by a lack of health.

However, considering the previous information, there are complications derived from an excess of organic fat and body fat and that arise independently from the weight category: malnutrition, low weight, normal weight, overweight or obesity. Thus, aside from the weight category, regular physical activity is necessary for the following reasons: (1) regular physical exercise helps reach a balance between the O₂ intake and the CO₂ disposal, (2) it favours blood circulation, in which proteins such as haemoglobin have higher participation in the cells, (3) the arcs of movement are generally within joint ranges in normal conditions, allowing more flexibility, strength and endurance, among others, (4) mitochondrion production is higher and of more quality, improving lean tissue which substitute fat tissue, (5) organs and systems keep a homeostasis, mainly in the cardiorespiratory and neuroendocrine-metabolic systems, (6) carbohydrates and fat acids intake as main sources of energy, (7) improving of physical performance, (8) physical fitness turns healthy, being an indicator and predictor of morbidity mortality in all ages, (9) protection against metabolic diseases and (10) releases endorphin and serotonin, known as "happiness hormones", which allows a better self-perception, better performance and better quality of life.

To sum up, carrying out regular, physical activity may help achieve the ideal weight and, at the same time, stay in it, for it works as a protective factor by doing the following: it prevents the storage of fat in the organs and in the body, it helps keep a healthy physical fitness, it improves body weight, increasing lean mass and decreasing fat mass, it keeps the ideal weight, it improves the immune system, it improves the neuroendocrine system, it improves the cardiorespiratory system, it improves the haematology/circulatory system, it improves self-perception and it helps to become a productive, active person who carries out everyday regular activities with more ease and enthusiasm.

With this data it will be possible to determine the characteristics of physical exercise with regard to frequency, intensity and duration, which may also be appealing and beneficial for sedentary people with normal weight, and for sedentary people with overweight and obesity, offering efficient methods for them to adopt a healthy, more active lifestyle.

Conflict of interest

The authors inform no conflict of interest.

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References

- [1] World Health Organization. Preventing and managing the global epidemic. Geneve: WHO; 2012. Report of a WHO Consulation (Technical Report Series): 894
- [2] Delgado FP, Caamaño NF, Jerez MD, Cofré LA, Osorio PA, Campos JC, et al. Obesity, selfesteem and fitness in students. Revista De La Facultad De Medicina. 2017;65(1):43-48. DOI: 10.15446/revfacmed-v65n1.57063
- [3] Roldán GE, Paz OA. Relation of overweight and obesity with level of physical activity, fitness, psychomotor profile and school performance in children population (8 to 12 years) of Popayán. Movimiento Científico (Scientific Moviment). 2013;7(1):71-84
- [4] Muñóz AA, Mata E, Pedrero CR, Espino L, Gusi N, Villa G, et al. Sarcopenic obesity and physical fitness in octogenarians; the multicenter EXERNET project. Nutrición Hospitalaria. 2013;28(6):1877-1883. DOI: 10.3305/nh.2013.28.6.6951
- [5] Ara I, Moreno LA, Leiva MT, Gutin B, Casajús JA. Adiposity, physical activity and physical fitness among children from Aragon, Spain. Obesity. 2007;15(8):1918-1924. DOI: 10.1038/ oby.2007.228
- [6] American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, Fiatarone MA, Minson CT, Nigg CR, et al. American College of Sports Medicine Position Stand. Exercise and physical activity for older adults. Medicine & Science in Sports & Exercise. 2009;41(7): 1510-30. DOI: 10.1249/IMSS.0b013e3181a0c95c
- [7] Morales S, Gómez-Cabello A, González-Aguero A, Casajús JA, Ara I, et al. Sedentarism and physical fitness in post-menopausal women. Nutrición Hospitalaria. 2013;28(4):1053-1059. DOI: 10.3305/nh.2013.28.4.6459
- [8] Lavielle-Sotomayor P, Pineda-Aquino V, Jáuregui-Jiménez O, Martha C-T. Physical activity and sedentary lifestyle: Family and socio-demographic determinants and their impacto n adolescent's health. Revista De Salud Publica. 2014;16(2):161-172 Spanish

- [9] Escalante FY, Jacinto RA. Actividad física, ejercicio físico y condición física en el ámbito de la salud pública. Revista Española de Salud Pública. 2011;85(4):325-328. http://www.redalyc.org/articulo.oa?id=17019926001
- [10] Becerra CA, Reigal RE, Hernández-Mendo A, Matín-Tamayo I. Relationship of physical fitness and body composition with self-rated health. RICYDE. 2013;**IX**(34):305-318. DOI: 10.5232/ricyde2013.03401
- [11] Greco BC, Rull SJ. Physical activity, fitness and health: The model and key concepts. International Proceedings and Consensus Statement: Human Kinetics. 2012;23(11):77-88
- [12] López AA, Ramírez VR, Sánchez GE, Constanza ML. Anthropometric and functional characteristics of phisically active individuals. Iatreia. 2008;21(12):121-128
- [13] Arruza GJ. La actividad física y el deporte. Revista psicodidáctica. 2010;21(10):32-41
- [14] Rodríguez FA, Nan GA, Valenzuela NJ, Nogués MM. Valoración de la condición física saludable en adultos (I): Antecedentes y protocolos de la batería AFISAL-INEFC. Apuntes Educación Física y Deportes. 1998;**52**:54-75
- [15] Centers for Disease Control and Prevention. Physical Activity and Health. CDC; National Center for Chronic Disease Prevention an Health Promotion: 2012. p. 134
- [16] Cruz EF, Tlatempa SP, Valdés-Ramos R, Hernández-Murúa JA, Manjarrez-Montes de Oca R. Overweigth or obesity, gender, and age influence on high school students of the city of Toluca's physical fitness. BioMed Research International. 2017;2017:11. DOI: 10.1155/2017/ 9546738
- [17] Mirzaei B, Abdi H, Serhati S, Barzin M, Niroomand M, Azizi F, et al. Cardiovascular risk in different obesity phenotypes over a decade follow-up: Tehran lipid and glucose study. Atherosclerosis. 2017;**258**:65-71. DOI: 10.1016/j.atherosclerosis.2017.02.002
- [18] Asmussen E. Testing Physical Fitness; Eurofit, Experimental Battery, Provisional Handbook; 2011. Republished on the Internet by http://www.bitworks-engineering.co.uk
- [19] Secchi JD, García GC, España-Romero V, Castro-Piñero J. Physical fitness and future cardiovascular risk in argentine children and adolescents: An introduction to the ALPHA test battery. Archivos Argentinos de Pediatría. 2014;112(2):132-140. DOI: 10.1590/S0325-00752014000200005
- [20] Ferran AR, Valenzuela A, Gusi N, Nacher S, Gallardo I. Valoración de la condición física saludable en adultos (y ll): Fiabilidad, aplicabilidad y valores normativos de la batería AFISAL-INEFC. Educación física y deportes. 1998;54:54-65
- [21] Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. Public Health Reports. 1985; 100(2):126-131
- [22] Adam C, Klissouras, Ravazzolo M, Renson R, Tuxwort W. A comparison of children's fitness in the Northwet and Southwest on England 1989: Public Health Reports. 1985;**100**: 126-31

- [23] Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, Mullany EC, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;30(384):766-781. DOI: 10.1016/S0140-6736(14)60460-8
- [24] Robin PS, Gregory AH, Clemens D, James RH, Amanda EP, Jhon EB, et al. Low levels of physical activity are associated with dysregulation of energy intake and fat mass gain over 1 year. The American Journal of Clinical Nutrition. 2015;102:1332-1338. DOI: 10.3945/ ajcn.115.115360
- [25] Petri W. The role of physical activity and exercise in obesity and weight management: Time for critical appraisal. Journal of Sport and Health Science. 2016;5:151-154. DOI: 10.1016/j.jshs.2016.04.001
- [26] Sjogaard G, Reffstrup CJ, Bendix JJ, Murray M, Dalager T, Hansen FG, et al. Exercise is more than medicine: The working age population's well-being and productivity. Journal of Sport and Health Science. 2016;5:159-165. DOI: 10.1016/j.jshs.2016.04.004
- [27] Must A, Tybor DJ. Physical activity and sedentary behavior: A review of longitudinal studies of weight and adiposity in youth. International Journal of Obesity. 2005;29(2):S84-S96. DOI: 10.1038/sj.ijo.0803064
- [28] Ortega FB, Ruiz JR, Castillo MJ, Sjostrom M. Physical fitness in childhood and adolescence: A powerful marker of health. International Journal of Obesity (London). 2008;32(1): 1-11. DOI: 10.1038/sj.ijo.0803774
- [29] Wanner M, Martin WB, Autenrieth SC, Schaffner E, Meier F, Brombach C, et al. Associations between domains of physical activity, sitting time, and different measures of overweight and obesity. Preventive Medicine Reports. 2016;3:177-184. DOI: 10.1016/j.pmedr.2016.01.007
- [30] Christian CE, Kathy JL, Jeff WK, Stancukas MC, Laskowski S, et al. Exercise prevents weight gain and alters the gut microbiota in a mouse model of high fat diet-induced obesity. PLoS ONE. 2014;9(3):e92193. DOI: 10.1371/journal.pone.0092193
- [31] Vargas ZM, Lancheros PL, Barrera PM. Energy expenditure in repose related to body composition in adults. Revista de la Facultad de Medicina. 2011;59(1):43-58. DOI: 10.15446/ revfacmed
- [32] Lopez CJ, Lopez ML. Fisiología Clínica del Ejercicio. 2nd ed. Ed. Panamerica 2008. 501 p. EAN: 9788498351675
- [33] Jeukendrup A, Saris WH, Wagenmakers AJ. Metabolismo de Las Grasas Durante el Ejercicio Una Revisión. Parte I: Regulación del Metabolismo y los Efectos del Entrenamiento. PubliCE Standard. 1999:142-158
- [34] Hawley JA. Adaptations of skeletal muscle to prolonged, intense endurance training. Clinical Experimental Pharmacology and Physiology. PubliCE. 2002;29(3):218-222. DOI: 10.1046/j.1440-1681.2002.03623.x

- [35] Idoate F, Ibañez J, Gorostiaga EM, García-Unciti M, Martínez-Labari C, Izquierdo M. Weight-loss diet alone or combined with resistance training induces different regional visceral fat changes in obese women. International Journal of Obesity. 2011;35(5):700-713. DOI: 10.1038/ijo.2010.190
- [36] Gómez FJ, Hernández LS, Quintana RA, Vera MH, Pérez MJ. La musculación: Una alternativa de actividad física. EFDeportes. Buenos Aires: Digital Magazine; January 2012;**164**(16)
- [37] Molina C, Citafuentes G, Martínez C, Mancilla R, Díaz E. Effects of 12 sessions of high intensity intermittent training and nutrition counseling on body fat in obese and overweight participants. Revista médica de Chile. 2016;144(10):1254-1259. DOI: 10.4067/S0034-98872016001000003
- [38] Sánchez JC, Romero CR, Muñóz LV, Rivera RA. Adipose organ, a metabolic and endocrine regulating rainbow. Revista Cubana de Endocrinología. 2016;**27**(1):105-119
- [39] Rosa G, Mello DB, Fortes MS, Dantas EH. Adipose tissue, metabolic hormones and physical exercise. Revista Andaluza de Medicina del Deporte. 2013;6(2):78-84
- [40] Lopez CF, Fernández VA. Fisiología del ejercicio. 3rd ed. Madrid: Ed. Panamericana; 2006. 1005 p. EAN: 9788498354829
- [41] Calzada-León R, Altamirano-Bustamante N, Rulz-Reyes ML. Neuroendocrine and gastrointestinal modulators of appetite and saciety. Boletín Médico del Hospital Infantil de México. 2008;65(6):468-487
- [42] Bee KT, Raghu A, Farhatullah S, Lewandowski KC, O'Hare P, Lehnert H, et al. Omentin-1, a novel adipokine, is decreased in overweight insulin-resistant women with polycystic ovary syndrome. Diabetes. 2008;57(4):801-808. DOI: 10.2337/db07-0990
- [43] Perello M, Spinedi E. Neuroendocrine aspects of obesity. Medicina (B Aires). 2004;64(3): 257-264
- [44] Joshua MA, Michael AE, Mark JR, Christopher SC, Mark DS, Deborah AN, et al. Population history and natural selection shape patterns of genetic variation in 132 genes. PLoS Biology. 2004;2(10):e286. DOI: 10.1371/journal.pbio.0020286
- [45] García-Vallejo F. La genómica nutricional: Un nuevo paradigma de la investigación de la nutrición humana. Colombia Médica. 2004;35(3):150-160
- [46] Pérez Bravo F. Genómica nutricional. La era molecular de la nutrición. Nutrición. 2006; **21**(15):14-15
- [47] Martínez HF, Tovilla ZC, López NL, Juárez RI, Jiménez SM, González GC, et al. Prevalence and gravity of depression and anxiety in patients with obesity and type 2 diabetes: A study in the population of Tabasco, México. Gaceta Médica de México. 2014;**150**(1):101-106
- [48] Ratcliffe D, Ellison N. Obesity and internalized weight stigma: A formulation model for an emerging psycological problem. Behavioural and Cognitive Psychotherapy. 2015;43(2): 239-252. DOI: 10.1017/S1352465813000763

- [49] Timmons JA, Jansson E, Fischer H, Gustafsson T, Greenhaff PL, Ridden J, et al. Modulation of extracellular matrix genes reflects the magnitude of physiological adaptation to aerobic exercise training in humans. BMC Biology. 2005;3:19. DOI: 10.1186/1741-7007-3-19
- [50] Seo TB, Kim BK, Ko IG, Kim DH, Shin MS, Kim CJ, et al. Effect of treadmill exercise on purkinje cell loss and astrocytic reaction in the cerebellum after traumatic brain injury. Neuroscience Letters. 2010;481(3):178-182. DOI: 10.1016/j.neulet.2010.06.087
- [51] Tsakiris S, Parthimos T, Parthimos N, Tsakiris T, Schulpis KH. The beneficial effect of Lcysteine supplementation on DNA oxidation induced by forced training. Pharmacological Research. 2006;53(4):386-390. DOI: 10.1016/j.phrs.2006.01.008
- [52] Berchtold N, Castello N, Cotman CW. Exercise and time-dependent benefits to learning and memory. Nueroscience, 2010;167(3):588-597. DOI: 10.1016/j.neuroscience.2010.02.050

