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Sex and physical exercise: one only size does not fit all. Differences between men and women in regulation and adaptations in response to exercise

Elisa Lodi[1,2], Eleonora Rodighiero[1,2], Federica Donati [1,2], Massimiliano Pergreffi[1,2], Lucio D'Antonio[1,2], Claudio Guicciardi[1,2], Jonathan Rosero Morales[1,2], Giulia Lodi[3,4], Maria Grazia Modena[1,2]

[1]University of Modena and Reggio Emilia, School of Sports Medicine and Physical Exercise CHIMOMO, University-Hospital Polyclinic of Modena, Italy; [2]PASCIA Center (Programma Assistenziale Scompenso cardiaco, Cardiopatie dell'Infanzia e A rischio), University-Hospital Polyclinic of Modena, Italy; [3]University of Modena and Reggio Emilia, School of Orthopaedic and Trauma Medicine SMECHIMAI, University-Hospital Polyclinic of Modena, Italy; [4]Orthopedics and Traumatology Unit, Ramazzini Hospital, Carpi (MO)

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Summary. Physical exercise has been traditionally considered with an "androcentric" view, and most of our knowledge on training is derived from studies which mainly included male athletes. Nevertheless, several undeniable physical and physiological differences exist between women and men in terms of athletic performance, response and adaptations to physical exercise.

The increasingly larger participation of women in a broad variety of sports – together with the growing awareness of the existence of significant sex-related differences in response to training – confirm the need to include sex as a biological variable to be considered for an optimal tailored exercise intervention.

Identifying and understanding sex-specific differences is crucial, both from a clinical point of view, as they could impact exercise rehabilitation and prevention strategies, and from a sporting and physiological perspective, in terms of improving performances and reducing injuries.

Keywords. Sex differences, athlete's heart, physical exercise.

Introduction

Men and women differ in characteristics that go far beyond primary and secondary sexual characters. Men are endowed with physical characteristics that make them capable of objectively superior performance in sports. This is certainly due to social reasons, that in the past allowed men greater access to the practice of sports and physical activity than women: at the debut of modern sports, in the 1896 Olympics, women were excluded from any competition, and it took a long time for them to be granted the same opportunities as men. The number of female athletes participating in the Olympic Games has increased significantly, from 34% in Atlanta 1996 to 48% at the last Olympic Games in Tokyo 2020, with a high probability of achieving full gender parity at the Paris 2024 Olympic Games.[1]

Even considering all the above, there is no doubt that the difference between the two genders in terms of athletic performance is mainly due to the constitutional characteristics of the two sexes.

One method that is both objective and straightforward is to analyze the differences between men and women in competitive athletics world records. The performances recorded in athletics (track and field) allow the most accurate assessment, since they are less affected by tactics and by the evolution of materials compared to other sports, and are easily quantifiable in terms of times and measures. Athletics, moreover, includes various specialties, ranging from the pure expression of power and coordination (jumps) to speed and endurance. This type of analysis shows a rather significant difference in the running disciplines, where males achieve about 10% shorter times than females, because of higher average speeds over both short and long distances. For example, excluding the 100 meters for controversies related to the homologation of the female record, the difference is 10.07% in the 200 meters and 9.26% in the marathon.[2] In disciplines requiring explosive force (mainly jumps, since throws are not comparable, due to sex differences in equipment), an even sharper discrepancy emerges, equal to 15-18% in favor of men, in line with what can be observed in weightlifting.[3]

A seemingly small difference of 10% – or one second – actually represents a big difference in high-level sport. Indeed, males who achieve times or measures equal to women's world records – despite certainly belonging to a relatively small elite of athletes – are unlikely to compete at the highest levels (World Champions and Olympics).

To understand such differences between women and men in sports, it is necessary to analyze the constitutional characteristics of the two sexes.

Sex and gender are separate terms with distinct meanings, although they are often used as synonyms. Sex, genetically defined through sex-specific hormones and molecules, is a binary feature, with rare exceptions, responsible for the development of reproductive organs and secondary sex characteristics. Gender is a multifactorial concept that includes psychosocial self-perceptions, social constructs, and cultural attitudes and expectations that people have about men and women.[4]

Since our aim is to discuss the biological differences between men and women in relation to physical exercise,

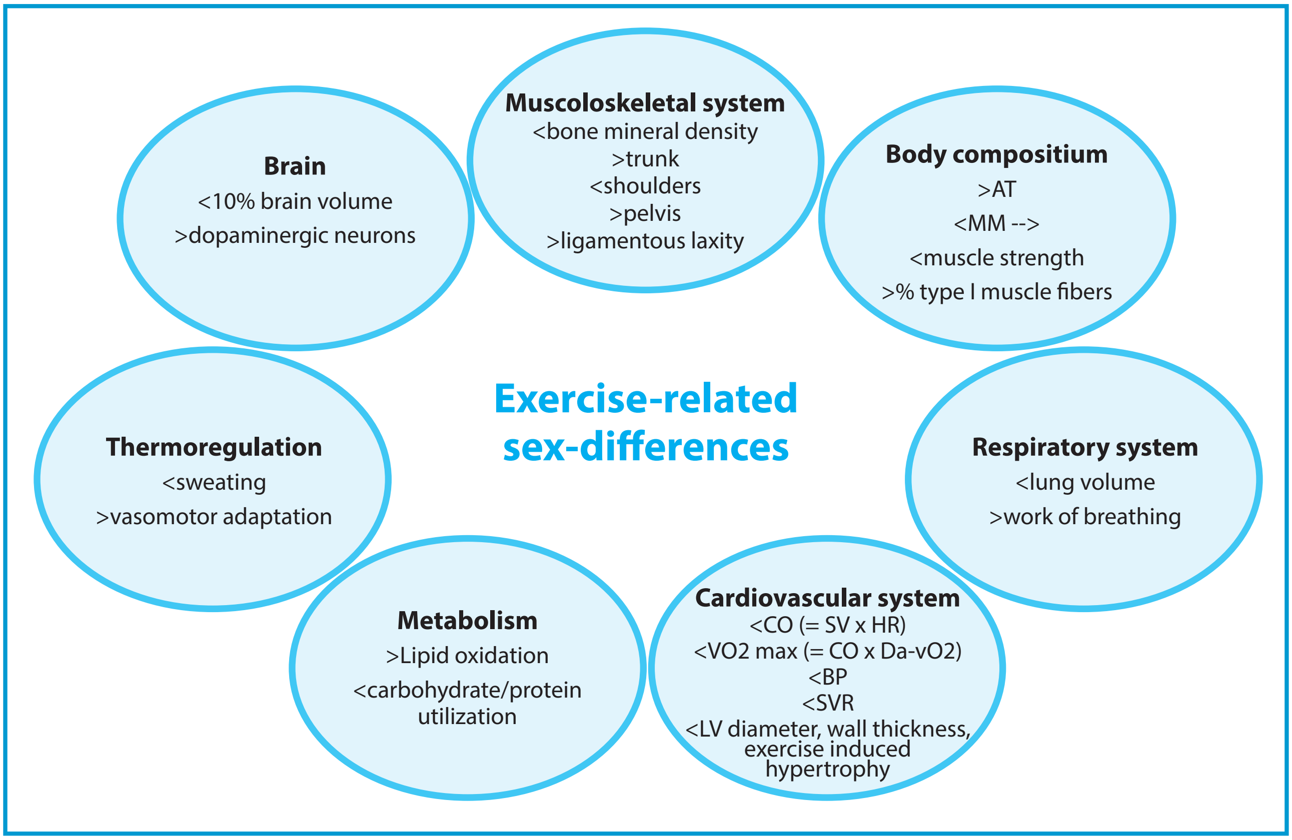

Figure 1. Exercise-related sex-differences in females compared to males.

<: lower, >: higher, AT: adipose tissue, MM: muscle mass, CO: cardiac output, SV: stroke volume, HR: heart rate, VO2 max: maximal oxygen uptake, Da-vO2: arterio-venous O2 difference, BP: blood pressure, SVR: systemic vascular resistance, LV: left ventricle.

the following text will concern sex – rather than gender – differences.

Identifying and understanding sex-specific differences in exercise-induced regulation and adaptations is important for the optimization of exercise interventions, both from a clinical point of view, as they could impact exercise rehabilitation and prevention strategies, and from a sport and physiological one, in terms of improving performances and reducing injuries (figure 1).

Musculoskeletal system

Between men and women, there are some typical constitutional sex differences. While human height and weight vary globally, all human populations exhibit the same pattern, where on average adult males are 10-15 cm taller than adult females and have 10-20 kg more body weight.[5,6] Usually males are taller due to sexual selection and females are broader due to natural selection for childbirth.[7] This is mainly due to the more rapid skeletal maturation and, therefore, to the earlier closure of the growth plates in females. From birth, females seem to have an advantage of at least two weeks compared to men in terms of bone development, despite a lower body weight, and this advantage gradually reaches two years at the time of puberty, which occurs earlier in women. This disparity may depend on the greater development and hormone secretion of the ovaries compared to the testes. Both skeletal growth and menarche depend on estrogen levels. Prepubertal females have 8 times the estradiol levels of age-matched males, which helps to explain their earlier skeletal maturation and growth arrest as well as their earlier onset of puberty compared to males.[7] Thus, while males continue to grow in height, females slow to a stop as they start their monthly cycle,[7,8] and females who reach menarche relatively late continue to grow at a faster prepubertal rate until the onset of menses, and end up being relatively taller adults.[9]

After peak bone mass is reached, skeletal aging begins. In women, bone loss is markedly accelerated in the peri-menopausal period, and then continues at a lower rate, whereas in men a persistently lower rate of bone loss occurs with aging. Using high-resolution peripheral quantitative computed tomography (HR-pQCT), it was possible to precisely asses *in vivo* bone microarchitecture and volumetric bone mass density (BMD): young men had a higher osteoclastic resorbing activity in cortical bone than young women, but trabecular number and thickness were higher in young men than in young women and, getting older, total bone area resulted being larger in men than in women.[10,11] By applying an engineering technique called finite element analysis (FEA) to HR-pQCT readings, it was possible to calculate the mechanical strength of the bone and to determine that bone strength was 34-47% greater in young men than in young women; consequently, the prevalence of osteoporosis and osteoporotic fractures is greater among the latter.[10,12]

Since different sports include a complexity of multiarticular movements and stimuli which put bones under various types of loads, the role of physical activity in preventing osteopenia and osteoporosis should be further analyzed. A Finnish study comparing dancers, squash players and speed skaters to non-athlete active and non-athlete sedentary referents demonstrated that all three groups of athletes had significantly higher BMD values at the lumbar spine, proximal tibia, femoral neck and calcaneus than the sedentary reference group.[13]

From an anatomical point of view, women typically have wider pelvis, shorter legs, more oblique femurs, larger ratio of leg weight to body weight and greater carrying angle of the arm.[14,15,7]

Specifically compared to men, women usually have shorter extremities and a relatively longer trunk. These different structural proportions may affect technique and ability in specific sport disciplines, as the mean height of the center of gravity of a woman is lower than that of a man. In particular, females seem to have an advantage in balance sports, while activities such as high jump and long jump, in which a higher center of gravity at take-off will enhance performance, may slightly favor male athletes.

The major differences between a male and female skeleton concern the bones of the pelvis. In women, the width of the pelvis is larger relatively to the length of the trunk; the iliac wings are wider and more inclined compared to men; and the upper opening of the pelvis is transversely elliptical. The branches of the pubic bone in women form an angle of 90-100 °, in men one of 70-75 °. Due to the greater width of the pelvis, women have a physiological compensatory valgus of the lower limbs, which contributes to the lowering of the center of gravity mentioned above.

Women also have narrower shoulders. Furthermore, women seem to have a hyperextensibility and an "X" conformation of the angle between the arm and forearm (elbow carrying angle), which is greater in females than in males.[16] The resulting greater joint mobility represents an advantage in sports with artistic expression (such as artistic gymnastics and free body exercise), while the "X" angle worsens performance in throwing disciplines, and has a negative action in support exercises. This is one of the reasons why in artistic gymnastics women perform exercises at the uneven (asymmetric) parallel bars (as opposed to the symmetric ones): it's because the greater distance between the bars – made necessary by the greater width of the pelvis compared to the shoulders' – would make support even more difficult.

Female athletes seem to be more prone to ligamentous laxity than males, as well as to have an increased predisposition (2 to 8 times) for anterior cruciate ligament (ACL) rupture and injury, but the relationship of ligamentous laxity with ACL injury is uncertain.[17] A study assessed that female ski racers were 3.1 times more likely to sustain an ACL disruption than their male counterparts.[18] Most trauma generally occurs without opposition from an opponent. Compared with males, females have smaller recess width and anterior cruciate ligament cross-sectional area, but there is no evidence that these may increase the risk of injury.[19,20] In football, there also appear to be gender-specific stress differences in running movements (side steps, cross steps, forward accelerations) that produce a different load on the feet (less load on the metatarsal and phalanges) than in men. Some authors also suggested a link between hormonal fluctuations in women within the menstrual cycle and changes in neuromuscular control and, therefore, ACL injury risk, although results in literature are discordant.[21-23]

Body composition

Sex differences exist in term of body composition (BC), with women having relatively more adipose tissue (AT) and less muscle mass (MM) than men.[24,25] Sex differences also exist in terms of AT distribution, with women having a greater amount of subcutaneous AT (SAT) and men having a greater predisposition to accumulate visceral AT (VAT) at abdominal level.[26] VAT correlates with an increased cardiovascular and metabolic risk, while SAT is associated with a lower risk.[27,28]

In sport, BC assessment is an extremely important practice, given its many implications on the health and performance status of the athletes.[29] For example, a higher body fat percentage negatively correlates with the quality of movement and physical performance of sports that involve sprinting or jumping.[30] Furthermore, MM contributes to the production of strength and power[31] and total body water influences cognitive neuromuscular functions.[32]

Analyzing bio-impedance data, male athletes have a lower percentage of AT than women. High-level athletes have on average a percentage of AT between 15 and 18%, but with values that can fluctuate, in endurance athletes, between 6 and 8%, and in volleyball and basketball players between 18 and 24%.

Regardless of gender, endurance athletes, who mostly exploit aerobic metabolism, have a lower fat free mass (FFM) than speed/power or team sports athletes, in whom glycolytic energy production mechanisms are privileged.[33]

Bio-impedance data of a very large population of athletes, male and female, was analyzed in many studies in the past, and the optimal values of BC and differentiated phase angle have been defined for male and female athletes practicing different sports, underlining the usefulness of the phase angle as an indicator of optimal BC and improved athletic performance specific to sport and gender.[34,15]

Women have lower absolute and relative MM compared to men and a different muscle-fiber composition. In women, type I muscle fibers dominate, characterized by slow contractions, low force generation and high fatigue resistance, predestining them for endurance performance. On the other hand, men seem to have a greater amount of type IIa muscle fibers, leading to improved rapid strength endurance performance.[35]

Understanding the sex differences in fatigability could allow to design more effective exercise regimens in athletes, and should be considered when prescribing practical exercise regimens for patients with muscle atrophy. For example, the vastus medialis obliquus (VMO) and vastus medialis longus (VML) are less fatigable in women than in men, in consideration of their relatively high percentage of type I fibers.[36,37]

Males possess a greater quantity of MM than females, which contributes to greater maximal strength, since muscle strength is closely related to the section of the muscle.[38] Muscle sex different composition can be mainly attributed to the higher testosterone level – together with its anabolic action – in men. In fact, until puberty MM and sports performances are similar in males and females; then, after the hormonal boost and the sudden increase in testosterone in males during adolescence there is a clear differentiation between men and women in terms of MM, strength and sports performances.[39] From this point of view, however, it is interesting to note that the endogenous levels of testosterone can vary with training, with the highest levels of testosterone in most trained and best-performing athletes of both sexes.[40]

The lower amount of MM, together with its peculiar anatomical structure and the hormonal influences, are possible causes why female athletes seem to have an increased predisposition (2 to 8 times) to ACL injury,[17] as mentioned above.

The differences explained result in a different response to exertion from men and women. From a practical point of view, this implies the need to optimize the training programs of each discipline according to the athlete's sex. It is known that for the same duration and intensity of exercise, women show greater endurance and better recovery from exertion. This, combined with the fact that women tend to lose muscle strength faster, implies that they are at the same time more capable – and more in need – of more continuous and consistent strength training sessions. In a discipline with mixed components (requiring both anaerobic and aerobic efforts), such as the 400 and 800 meters, for example, strength workouts are more frequent throughout the competitive season in women than men.[41,42]

Sex-related differences may be considered also in the rehabilitation setting, in order to personalize exercise interventions. As an example, women's greater ligamentous laxity must be compensated by greater skeletal muscle tone. While it is true that skeletal muscle in women is more efficient than in men in long duration efforts (at the same intensity and duration), women's lower maximal strength implies that women must work at higher intensity and more frequently (with the help of their better muscle recovery). This is especially true in sports characterized by abrupt changes of direction or explosive efforts, such as soccer and high jump, where ACL injury and patellofemoral instability, respectively, are typical issues for the female athletes that are prevented and treated with intense thigh muscle strengthening.[43,17]

Respiratory system

Sex-based differences in the anatomy and function of the human respiratory system also exist, and may affect airway responsiveness, ventilation, and gas exchange, especially during conditions of high ventilation rates, such as exercise.[44]

Females typically have smaller lung volume (even when adjusted for height and body size), narrow airway diameters and different lung geometry relative to males.[45]

These morphological sex differences impact the development of flow, the regulation of lung volume, the pressure swings and the consequent work of breathing, and they become critically important during dynamic exercise.

Smaller lung volumes and lower maximal expiratory flows result in women having a relatively reduced ventilatory capacity and a lower respiratory efficiency than men.[45]

This may predispose women to be more susceptible to respiratory system limitations during exercise than their male counterparts. Specifically, women are more likely to experience expiratory flow limitation, and have a higher mechanical work of breathing and oxygen cost of breathing than man, that becomes even twice that of men when ventilation is above 90 $L \cdot min^{-1}$.[46] The greater oxygen cost of breathing in women means that a greater fraction of total oxygen uptake (VO2) and, thus, cardiac output (CO), is directed to the respiratory muscles. The greater demand for blood supply at respiratory level is likely to have detrimental effects on locomotor muscle blood flow, thus affecting exercise performance.

Furthermore, reproductive hormones – estrogen and progesterone – can influence ventilation, metabolism, thermoregulation, lung inflammatory processes and pulmonary function during exercise.[40,47] Respiratory function and symptoms are known to be affected by the different phases of the menstrual cycle, and tend to get worse during the mid-luteal to mid-follicular phases. Fluctuations in asthmatic symptoms are also reported during the menstrual period, possibly due to hormonal influence on airways.[48] Estrogens potentially influence the outcomes of developmental, inflammatory and disease processes by influencing cytokines and inflammatory mediators in the lung through both up-regulation (interleukin (IL)-1β, IL-6, type I interferon (IFN), tumor necrosis factor (TNF)-α, NF-κB and toll-like receptor 8) and down-regulation/inhibition (transforming growth factor (TGF)-β1 and IL-10).[49]

Progesterone makes the contractility and the relaxation of bronchial smooth muscle decrease and increase, respectively; it is positively associated with peak expiratory flow rate during the luteal phase of the menstrual cycle. Testosterone is generally proposed to have protective roles, because it seems to cause bronchial tissue relaxation, to reduce the response to histamine and to attenuate airway inflammation.

Cardiovascular system

Numerous cardiovascular adjustments occur during exercise, so that CO rises linearly as a function of VO2 to meet the increased demands of muscular work. There are several genetic, anatomical and hormone sex-related differences that impact the hemodynamic and structural cardiovascular response to exercise.[50-52]

From a hemodynamic point of view, women have lower CO.[53] CO is the product of heart rate (HR) and stroke volume (SV). Females have lower SV and smaller increase in SV in response to exercise, mainly due to their smaller cardiac size/mass, so the main mechanism to enhance CO in women is the increase in HR. Although increasing HR does enhance CO, maximum HR during exercise has been shown to be similar between females and males,[54,55] regardless of fitness levels, and to depend mainly on age rather than on gender, with advancing age being associated with a decrease in peak HR in both sexes.[56,57]

Women have lower maximal oxygen uptake (VO2max) values, approximately 80% of age- and training status-matched males.[55] VO2max is the best objective measure of aerobic fitness. VO2max is a function of CO and total system arteriovenous O2 difference (Da-vO2), thus the ability to increase one or both these variables determines aerobic capacity and VO2 max is a valid index of the integrity of cardiovascular function.[58] Women's lower CO is the main reason for their lower VO2max, together with differences in peak Da-vO2, with men having higher Da-vO2.[59] Blood volume, hemoglobin, and hematocrit values are 15-20% lower in women, including elite athletes, and sex-based differences exist in pulmonary structure and respiratory function, resulting in a lower oxygen supply for the same quantity of blood flow than men.[44]

Females have lower systolic and diastolic peak blood pressures (BP) than males.[53] BP is the result of CO and systemic vascular resistance (SVR). During physical activity, peripheral vasodilation in the capillary beds of muscle tissue leads to a decrease in SVR. In healthy subjects, CO rises, avoiding BP drops that would otherwise impair the perfusion of organs, such as the brain. Female athletes experience a greater drop in SVR because of a lower sympathetic activity, a higher parasympathetic activity, and their circulating sex hormones, which all contribute to a more vasodilatory state. As reported above, women have lower CO.[60] This could be the reason why BP is often lower in women than in men of similar age at rest, during exercise and in recovery after exercise, especially when recovery is performed inactively,[61] explaining the higher occurrence of post-exercise hypotension in women.[62]

From a structural point of view, regular physical training induces cardiac remodeling and structural adaptations to improve SV reserve. Trained women exhibited smaller left ventricular wall thickness, cavity size and mass compared to age- and fitness-matched men.[63-65] Moreover, women have been reported to maintain a normal left ventricular geometry, with a relatively larger increase of cavity dimensions than men, evidently depending on the type of sport practiced.[66] These sex-related differences in cardiac adaptations may be partially explained by the higher concentrations of endogenous anabolic hormones in males and the higher hypertrophic potential of male cardiac tissue compared to women. Heart hypertrophy is a rare finding in female athletes, therefore a left ventricular wall thickness greater than 12 mm should be carefully evaluated, to exclude other possible etiologies.

Heart size accounts for many of the sex-based differences in cardiac functional and structural responses, however, it may not entirely account for sex-related cardiovascular differences, as they tend to shrink when parameters are normalized for body surface area and lean body mass, suggesting that other factors, such as different BC, may play a role, and that indexed parameters should be analyzed, rather than absolute values.

Metabolism

Sex differences affect both basal and functional metabolism. At rest, women have a 10% lower basal metabolism.[67] This is due to the women's more efficient thermal insulation, determined by the higher quantity of SAT and, therefore, by the lower heat transfer, and to the different percentage of AT and MM. Since muscles have a higher O_2 consumption than AT, both at rest and during physical exercise, the lower percentage of MM in women determines a lower energy expenditure. Furthermore, it seems that androgenic steroids perform a specific impulse action on the basal metabolic rate, which could help explain its increase.[68]

During endurance exercise, women have been shown to oxidize proportionally more lipids and fewer carbohydrates than males, whereas higher carbohydrate oxidation was observed in both sedentary and athletic men. Thus, men rely more on carbohydrates, whereas women rely more on lipids to sustain moderate aerobic exercise.[69] These metabolic sex differences are partially mediated by higher estrogen concentrations in females, that affect body composition – with female having a greater percentage of AT – and are also responsible for their higher fat metabolism.[70]

Beneficial effects of physical activity – including a more efficient utilization of fat stores during exercise, a more efficient adjustment of energy expenditure during recovery, and an improved insulin sensitivity – were shown to be most pronounced in females. This may due to the fact that females are likely to utilize more fat and less protein as an energy source during exercise.[71]

Thermoregulation

Human thermoregulatory responses to heat stress include two main mechanisms of heat dissipation: increased skin blood flow and sweating. Sex differences seem to exist in thermal responses to exogenous and endogenous heat load and heat loss during exercise.[72] Many factors seem to contribute to these sex differences, including anthropometric, hormonal and functional factors, with women having a larger ratio of body surface to body mass and greater SAT.

It appears that women's sweating response to heat load is smaller than that of men, but they can maintain their core body temperature on a similar level to that of men because of greater vasomotor adaptations. In addition, in women, thermoregulatory responses vary over the menstrual cycle, due to the influence of the reproductive hormones.[73] In the luteal phase of the menstrual cycle, the thermoregulatory control of both sweating and cutaneous vasodilation is shifted by ~0.5 °C towards higher core body temperatures.

Cutaneous vasodilation and sweating during heat stress lead to a marked redistribution of blood flow to the periphery. If heat stress is combined with exercise, the resulting "competition" between muscle and skin for a relatively limited CO is considered to be a major contributor to increased fatigue and decreased exercise tolerance relative to a cooler environment.[74] The increase in blood flow directed to the skin results in a lower venous return, that is somehow mitigated by the muscle pump during exercise. If an individual stops suddenly and stands still, the lack of muscle pump, together with the lower SVR, can result in a transient decrease in cerebral perfusion pressure that can contribute to symptoms of orthostatic intolerance. During exercise in the heat, both fatigue and orthostatic intolerance are more likely to occur in women.[75] Women tend to have smaller blood volume, lower CO, greater drop in SVR (because of a lower sympathetic activity), higher parasympathetic activity, and circulating sex hormones, which all contribute to a more vasodilatory state[76,77] compared with men of similar age:[78] all mechanisms that contribute to both lower resting BP and lower orthostatic tolerance.[75]

Brain and nervous system

In mammals, sex differences are evident in many aspects of brain development, brain function and behavior. Although the male brain is 10% larger than the female one, it does not impact intelligence,[79] as the number of neurons is similar in men and women. Intelligence, in fact, is not determined by brain mass, but by the number of neurons and the quality of neuronal connections.[80] Since birth, females have a smaller cortical surface, lighter cortex and smaller volumes of white mass, without differences in the cerebral convolutions.

Gender-specific differences in brain anatomy and function begin as early as the embryonic stage, when male sex hormones affect brain development.[81] However, male sex hormone is not the only reason of sex differences in brain development. Genes on the Y chromosome stimulate the multiplication of dopaminergic neurons in the brain, which are therefore more numerous in men than in women. These neurons appear to contribute to the development of special motor skills and behaviors (eg., throwing). From a sports point of view, this could be one of the reasons why men are more willing to take risks, to tend more towards physical aggression, to have a more pronounced ability to orient themselves, as well as better throwing skills than women.

Exercise participation remains low, despite clear benefits. A study conducted on rats documented that the acquisition and maintenance of voluntary wheel running involve unique neural substrates in the dorsal striatum that vary by sex, suggesting the need for sex-specific strategies to promote exercise.[82]

Furthermore, a gender difference has been shown in learning basketball tactical actions from video modeling and static pictures, with females benefiting particularly from video modeling than from static pictures compared to men, suggesting that a consideration of a learner's gender is crucial to further boost learning of basketball tactical actions from dynamic and static visualizations.[83]

Conclusion

Most of the current knowledge about responses and adaptations to exercise are derived from studies conducted predominantly in the male athletes, and then translated to women without evidence, ignoring the undeniable sex and gender differences. The increasingly larger participation of women in a broad variety of sport, together with the growing awareness of the existence of significant sex-related differences in response to training, seem to be promising factors to satisfy the urgent need to make a more complete interpretation of the specific physiological characteristics of female and male athletes.

Inclusion of sex as a biological variable to be considered for an optimally tailored exercise prescription seems to be mandatory, since biological sex affects properties of the physiological systems involved in exercise and in the adaptations to chronic exercise, with crucial implications for both athletic performance and clinical outcomes.

Key messages

- Several physical and physiological differences exist between women and men in terms of athletic performance, response and adaptations to physical exercise.
- Sex must be considered as a biological variable for optimally tailored exercise prescription.
- Most of the current knowledge about responses and adaptations to exercise derived from studies conducted predominantly in the male athletes, then translated to women without evidence.
- Identifying and understanding sex-specific differences is crucial for athletic performance and clinical outcomes.
- The increasing participation of women in a broad variety of sports, together with the growing awareness of the existence of sex-related differences, seem to be promising factors to make a more complete interpretation of the specific characteristics of female and men athletes.

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Correspondence to:
Elisa Lodi
Centro PASCIA
AOU Policlinico di Modena
Via del Pozzo 71
41124 Modena, Italy
email elisalodi@unimore.it