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Sex Differences in Endurance Running

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Abstract

In recent years, there has been a significant expansion in female participation in endurance (road and trail) running. The often reported sex differences in maximal oxygen uptake (VO_{2max}) are not the only differences between sexes during prolonged running. The aim of this narrative review was thus to discuss sex differences in running biomechanics, economy (both in fatigue and non-fatigue conditions), substrate utilization, muscle tissue characteristics (including ultrastructural muscle damage), neuromuscular fatigue, thermoregulation and pacing strategies. Although males and females do not differ in terms of running economy or endurance (i.e. percentage VO_{2max} sustained), sex-specificities exist in running biomechanics (e.g. females have greater non-sagittal hip and knee joint motion compared to males) that can be partly explained by anatomical (e.g. wider pelvis, larger femur-tibia angle, shorter lower limb length relative to total height in females) differences. Compared to males, females also show greater proportional area of type I fibres, are more able to use fatty acids and preserve carbo-hydrates during prolonged exercise, demonstrate a more even pacing strategy and less fatigue following endurance running exercise. These differences confer an advantage to females in ultra-endurance performance, but other factors (e.g. lower O_2 carrying capacity, greater body fat percentage) counterbalance these potential advantages, making females outperforming males a rare exception. The present literature review also highlights the lack of sex comparison in studies investigating run-ning biomechanics in fatigue conditions and during the recovery process.

Key Points

Female participation in endurance running has increased considerably over the last 20 years. Some physiological factors are known to explain sex differences in 'classic' endurance running performance (e.g. $\dot{V}O_{2max}$); this narrative review discusses via a multidisciplinary approach—physiological, biomechanical and neuromuscular factors that differentiate sexes in prolonged running exercise.

Although males and females demonstrate differences in running biomechanics, they do not differ in terms of running economy. A greater proportion of type I fibres and greater ability to use fatty acids in females could explain the lower neuromuscular fatigue of the quadriceps and triceps surae reported after prolonged running races compared to males, and could confer an advantage to females over ultra-endurance competitions.

More direct comparisons between males versus females in response to fatiguing running exercise are needed.

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1 Introduction

Running, one of the most popular recreational sports, is associated with many health benefits [1–3]. Supported by major sports companies, running as a leisure activity has grown rapidly since the 1970s in North America and in Europe since the beginning of the 1980s [3]. During the last decade, female participation in running events has increased considerably. According to a recent survey (https://runrepeat.com/state-of-running), covering more than 70,000 road races from 5 km to marathons all over the world, female participation had reached 50% in 2018. The International Trail Running Association recently reported an increase in female participation in trail running from 18% in 2013 to 26% in 2019 (https://itra.run/). In ultra-trail races, the participation rate of females is much lower, yet a sixfold increase has also been reported since the 1980s [4]. Despite the increasing female participation, the vast majority of scientific studies are still conducted on males. Indeed, based on data collected from three major sport and exercise medicine journals, the average ratio of male to female participants per article is ~ 65:35 [5]. Part of this difference has been attributed to sex differences in willingness to participate in certain types of research. In other words, a volunteer bias in female participation in running research may exist [6].

With the growth of the number of females engaged in running events, their performance rapidly improved through the 1980s [7] and, from then, researchers started to compare male and female running performance from sprint to marathon distances [8, 9]. In the 1990s, it was believed that there would be a reduction [10–12] or even disappearance [8] of sex differences in running performance. For instance, using a regression analysis between running velocities over several distances and historical time in males and females, Whipp and Ward [8] reported in 1992 that females could outrun males in marathon distance in 1998. However, the difference in performance between sexes remains around 10–12% for running events from sprint to marathon [13–15]. The issue of sex differences in performance as a function of distance is complex. When using the world best times from 100 m to 200 km, Coast et al. [14] reported that the difference in performance increases with distance, particularly in events longer than the marathon. It has also been reported that the difference between sexes when comparing the best male and the best female runners was ~ 17% for the 100-km Lauf Biel in Switzerland [16] and ~ 20% for the 161 km of various north American ultra-marathons [7]. Additionally, da Fonseca-Engelhardt et al. [17] observed the same tendency on two of the hardest ultramarathons worldwide, i.e. the 'Badwater' in the USA and the 'Spartathlon' in Greece, with performances being ~ 20% slower for females than for males (based on the top five finishers). On the contrary, Peter et al. [18] reported a ~ 10–13% gap when comparing the fastest male and female runners ever of the 24-h ultra-marathon. How do we explain the variability in sex differences in running performance between studies regarding events longer than the marathon? First, reported sex differences depend on how the question is framed, for example, comparing the top female and male runners or considering all participants. In the latter case, sex differences seem to even decrease with increasing race distance and no differences were reported in races longer than 315 km (e.g. https://runrepeat.com/state-of-ultra-running), whereas, based on unpublished data, the sex difference in performance appears constant with increasing distance when considering the first males and the first females. Second, the percentage of female participation in these events is much lower than reported for males, being as low as 10% in some events, which may confound the performance differences in the very long-distance races [19]. Third, many of the races above the marathon distance are trail running events. These races are not as standardized as road races, and consist of regular changes in terrain, technical difficulty, elevation gain and exact distance, and it is not known if this has a greater impact on males than females, or vice versa. Despite the substantially lower participation rate of females, ultra-distance in running is one of the rare disciplines where females are able to outperform men. To cite only a few, Corinne Favre, Pamela Reed, Hiroko Okiyama and Jasmin Paris finished at first place overall at the 'CCC' in 2006 (86 km), 'Badwater' 2002 and 2003 (217 km), the 'Deutschland-lauf' in 2007 (1,204 km), and the 268-mile Montane Spine race, respectively. Jasmin Paris not only won the race, but also shattered the previous male record by 12 h. It is, however, likely that these exceptional performances are not only due to the great mental and physical capacities of these runners but also to the fact that the best men were not running in these particular events. In summary, although the question of the evolution of performance across race distance according to sex is a complex one, largely due to a question of parity in trail and ultra-trail running participation, the sex gap in performance appears relatively constant with increasing distance when focusing on top level runners.

Long-distance running performance (up to the marathon) depends on the interaction between $\dot{V}O_{2max}$, the fraction of $\dot{V}O_{2max}$ sustained (F) on the covered distance that is closely linked to lactate threshold (LT), and running economy (RE) (e.g. [20, 21]). Endurance factors such as F or LT do not seem to be affected by sex (e.g. [22–25]). For instance, Davies and Thompson [22] reported that male and female athletes were able to sustain similar F over the marathon distance (82 and 79%, respectively). The most obvious physiological variable to explain running performance difference is the maximal oxygen uptake ($\dot{V}O_{2max}$). When expressed in $mlO_2 \cdot min^{-1} \cdot kg^{-1}$ (of body mass), $\dot{V}O_{2max}$ is considered as the main factors explaining sex differences in endurance

running performance [20, 26], mainly due to greater percentage of body fat and lower haematocrit levels in females [26, 27]. When $\dot{V}O_{2max}$ in males and females is adjusted to fat-free mass, some controversy exists in the literature, with some studies showing no sex differences [28–30] whereas other report a higher $\dot{V}O_{2max}$ in males [31, 32]. Lower O_2-carrying capacity is definitively one factor explaining the lower $\dot{V}O_{2max}$ in females [33]. As sex differences in $\dot{V}O_{2max}$ have largely been reviewed elsewhere [26, 31, 32, 34], the present review focuses on the other factors that differentiate males and females in endurance running. Thus, the aim of the present narrative review was to examine whether males and females differ in terms of running biomechanics, economy and physiological responses during short (< 1 h) and prolonged (i.e. several hours of running) running exercises. This narrative review offers a novel comprehensive and multidisciplinary (i.e. psychological, physiological, neuromuscular and biomechanical aspects) overview of the sex differences in endurance running. Article databases of the US National Library of Medicine (PubMed), ScienceDirect and SPORTDiscuss were searched using the search general (Gender or Sex differences) and specific terms (corresponding to the studied scientific area of each part). For instance, article databases focusing on the "Running economy" part were searched as follows: Gender OR Sex differences AND Running economy OR oxygen demand OR Energy cost of running OR Oxygen cost of running OR oxygen uptake OR metabolic efficiency. Any additional relevant literature was obtained from the reference lists of the published papers. This searching process has been applied for each part of the current review.

2 Biomechanics of Running

Many studies have been conducted to compare the running biomechanics of males and females (Table 1). Several parameters such as the studied population, footwear, running surface and speed may contribute to the disparity in the results observed between studies. In the absence of fatigue, differences in spatiotemporal, kinematic and kinetics parameters of the running pattern have been extensively studied, but primarily in experimental conditions at given absolute running speeds and for a short period of time rather than in endurance condition. The major sex differences are indicated in blue on Fig. 1.

2.1 Spatiotemporal Parameters

Sex differences in spatiotemporal parameters have been investigated over a large range of running velocities (from 7.5 to 24 km h^{-1}) [35–38]. For given absolute running speeds above 16 km h^{-1}, female runners present shorter absolute contact time, longer absolute flight time, shorter absolute stride length and higher stride frequency than males [36]. Because of shorter contact time and longer flight time, females present a lower duty factor, i.e. percentage of stride time spent on the ground, indicating that females are not a "scaled-down version of the male model" [36]. Interestingly, these sex differences seem to disappear at slower speeds (10–14 km h^{-1}), with the exception of contact time as females still present shorter contact time than males when the speed decreases [35]. At high absolute speeds, females probably have to adjust their biomechanics, in particular through adopting a high stride frequency as they are closer than males to their maximal speed. Indeed, once normalized to maximal velocity (from 60 to 90% of maximal velocity), sex differences in contact time and in duty factor tend to disappear and step frequency is actually lower in females [36]. Sex differences in body proportions might also explain part of the sex differences in spatiotemporal parameters. For instance, several studies reported shorter step length in females at various running speeds (from 7.5 to 24 km h^{-1}), but these differences vanished or even reversed once adjusted to stature or leg length [35, 36, 38, 39]. Furthermore, a significant positive association between contact time and body height, leg length and body mass has been found [37], but the extent to which morphological differences contribute to the sex influence on spatiotemporal parameters is not yet clear.

2.2 Running Kinematics and Muscle Electromyographic Activity

The multitude of variables studied and the diversity of the methods of running kinematics analysis make comparisons between studies quite challenging. However, a shared observation across studies is that sex differences mostly existed at the hip and knee level [40–51].

In recreational runners, females exhibited significantly greater hip adduction and internal rotation during the stance phase of running compared to males across a range of speeds [40, 42, 43, 49] and surface inclinations [42]. Sex differences in running kinematics at the hip level have been attributed to the fact that females have a wider pelvis [52] and possibly weaker hip abductor and external rotator muscle strength compared to males [49, 53]. Despite moderate correlations between hip, pelvis and trunk kinematics and hip abductors or external rotator strength in both males or females, hip strength parameters remain a substantial portion of the explained variance in running kinematics for both sexes [45]. Females have also been shown to present greater knee abduction during the stance phase of running compared to males [43, 44, 47–50]. Greater knee abduction has been associated with smaller rearfoot

Table 1 Overview of sex differences in running biomechanics

References	*n*	Footstrike	Footwear	Surface	Speed (km h^{-1}) and slope	Spatiotemporal parameters	Kinematics	Kinetics
Almonroeder and Benson [40]	14 M 18 F	Rearfoot	Std		14.4		Peak angles: Knee flex : = Knee add: = Knee IR: = Hip add: F+ Hip IR: F+	**MOMENT** Peak moment: Knee ext moment: F− PFJ stress: F− PFJ reaction Force: F−
Bazuelo-Ruiz et al. [41]	28 M 27 F	Rearfoot	Std		11.9		Peak angles: Knee flex: F+ Ankle dorsiflexion: F+	**GRF** Impact peak: = Active peak: F− Loading rate: F+ Peak braking force: = Peak propulsive force: F+
Chumanov et al. [42]	17 M 17 F	NS	NS		6.5, 9.7, 13 With 0, 10 and 15% uphill incline		For all speed and incline: Peak angles: Hip add: F+ Hip IR: F+ Lateral pelvic tilt: = Amplitudes: Hip add: F+ Hip rotation and lateral pelvic tilt: =	
Esculier et al. [193]	51 M 36 F	NS	Std		Preferred running speed* M: 11.2 F: 10.1	Stride length: F− Step width: F−	Peak angles: Knee flex: = Knee add: = Knee abd: =	**MOMENT** Peak moment: Medial TFJ forces: F− External knee flex: F− External knee add: =
Ferber et al. [43]	20 M 20 F	Rearfoot	NS		13.1	Contact time: =	Peak angles: Hip flex: = Hip add: F+ Hip IR: F+ Knee flex: = Knee abd: F+ Knee IR: =	**MOMENT** Peak moment: Hip ext, add and IR: = Knee ext, abd and IR: = **WORK** Negative work: Hip sagittal plane: = Hip frontal and trans planes: F+ Knee sagittal, frontal and trans planes: =

Table 1 (continued)

References	*n*	Footstrike	Footwear	Surface	Speed (km h^{-1}) and slope	Spatiotemporal parameters	Kinematics	Kinetics
Garcia-Pinillos et al. [35]	51 M 46 F	NS	NS		10, 11, 12, 13, 14, 15, 16	Contact time: F− at 10 to 16 km h^{-1} Flight time: = at 10 to 16 km h^{-1} Stride length: = at 10 to 13 km h^{-1} F− at 14 to 16 km h^{-1} Stride length (norm.): = at 10 to 14 km h^{-1} F− at 15 and 16 km.h^{-1} Step frequency: = at 10 to 13 km h^{-1} F+ at 14 to 16 km h^{-1}		
Gehring et al. [44]	16 M 16 F	Rearfoot	Std		10.8, 14.4, 18	Contact time: F−	Peak angles: Hip add: F+ Knee add: F−	**MOMENT** Peak moment: Hip add at Impact and Mid-stance: F+ Knee add at Impact and Mid-stance: = **WORK** Hip joint impulse: F+ Knee joint impulse: F+
Hannigan et al. [45]	37 M 23 F	NS	Std		Self-selected "easy" run pace* M: 12.6 F: 11.9		Amplitudes: Hip ext: F+ Hip add: = Hip IR: F+ Anterior pelvic tilt, Contralateral pelvic drop and Pelvic IR: =	
Hennig [194]	17 M 15 F	NS	Std		11.9	Contact time: =		**GRF** Impact peak: F− Active peak: =

Table 1 (continued)

References	*n*	Footstrike	Footwear	Surface	Speed (km h^{-1}) and slope	Spatiotemporal parameters	Kinematics	Kinetics
Isherwood et al. [60]	20 M 20 F	Rearfoot	Std		11.9	Contact time: F−	Peak angles: Hip flex and add: = Hip IR: F+ Knee flex, add: = Knee IR: F− Ankle eversion: = Ankle add: =	**GRF** Impact peak and active peak: = Loading rate: F+ Peak braking force and propulsive force: = **MOMENT** Peak moment: In the sagittal plane, for Hip, Knee and Ankle: F−
Keller et al. [63]	13 M 10 F	NS	Std		From 12.6 to maximal speed			**GRF** Active peak: F− at 18 km h^{-1} Loading rate: =
Malinzak et al. [46]	11 M 9 F	NS	Perso		M: 18.8 F: 18.4		Peak angles: Knee flex : F−	
Nelson et al. [36]	24 M 21 F	NS	NS		16.5 to 24.1	Absolute speed: Stride length, contact time and duty factor: F− Step frequency and flight time: F+ Stride length (normalized): F+ Relative speed: Stride length, step frequency and duty factor: F− Contact time: = Flight time: F+ Stride length (normalized): F−		
Nigg et al. [47]	47 M 46 F	Rearfoot	Std		12		Amplitudes: Pelvic tilt: F+ Hip add: F+ Knee abd: F+	
Phinyomark et al. [48]	220 M 263 F	NS	Std		Self-selected speed 8 to 12.1		Peak angles: Hip add: F+ Knee abd and ER: F+ Knee flex: F− Ankle eversion and dorsiflexion: F−	
Roche-Seruendo et al. [37]	52 M 45 F	NS	Perso		12	Contact time: = Flight time: = Step length: = Step frequency: =		

Table 1 (continued)

References	*n*	Footstrike	Footwear	Surface	Speed (km h^{-1}) and slope	Spatiotemporal parameters	Kinematics	Kinetics
Sakaguchi et al. [49]	11 M 11 F	NS	Std		12.6	Contact time: =	Peak angles: Hip add and IR: F+ Knee IR: = Knee abd: F+ Tibial IR: = Rearfoot eversion: F−	
Schache et al. [39]	22 M 22 F	NS	Perso		14.4	Stride time: F− Stride frequency: F+ Stride length: F− Stride length (normalized): = Contact time: F− Flight time: F−	Amplitudes: Pelvis (antero post tilt, obliquity and axial rotation): F+ Hip flex-ext and IR-ER: = Hip Add-abd: F+	
Sinclair et al. [50]	12 M 12 F	NS	Std		14.4	Contact time: =	Only significant differences are reported Peak angles: Hip flex: F− Knee abd and IR: F+ Ankle eversion: F+	**GRF** Vertical impact peak : = Loading rate: = Peak braking force and prop force: = Peak medial force and lateral force: =
Sinclair and Selfe [67]	15 M 15 F	Rearfoot	Std		14.4			**MOMENT** Peak moment: Knee extensor and abd: F+ PTJ contact force: F+ PTJ load rate: F+
Sinclair and Taylor [55]	20 M 20 F	NS	Std		14.4		Peak angles: Ankle eversion: F+ Tibial IR: F+ Amplitudes: Ankle eversion and Tibial IR: =	

Table 1 (continued)

References	*n*	Footstrike	Footwear	Surface	Speed (km h^{-1}) and slope	Spatiotemporal parameters	Kinematics	Kinetics
Takabayashi et al. [38]	12 M 12 F	Rearfoot	Barefoot		Individual transition speed from walking to running on a treadmill* M: 7.8 F: 7.3	Relative speed: Step frequency: = Step length: F− Step length (normalized): =	Only significant differences are reported Peak angles: Rearfoot plantarflexion: F+ Midfoot dorsiflexion and Abd: F+ Amplitudes: Rearfoot sagittal plane: F+ Midfoot sagittal plane: F+	
Willson et al. [51]	19 M 19 F	NS	Std		Between 12.7 and 14		Amplitudes: Hip add and ER: = Knee IR: F− Knee add: = Angle at mid stance: Hip add: F+ Hip ER: = Knee IR and add: =	

For kinematic variables, only peak and amplitude joint angles were reported. The results reported are based on the *p* value according to the significant level set in each studies

M males, *F* females, overground, treadmill, *GRF* ground reaction forces, *Std* standardized footwear (i.e. all participants wore the same pair of shoes), *Perso* personal shoes, *Flex* flexion, *Ext* extension, *Abd* abduction, *Add* adduction, *IR* internal rotation, *ER* external rotation, *TFJ* tibio-femoral joint, *PFJ* patello-femoral joint, *NS* not specified, * significant sex difference, *F*+ superior in females, *F*− inferior in females, = no sex difference

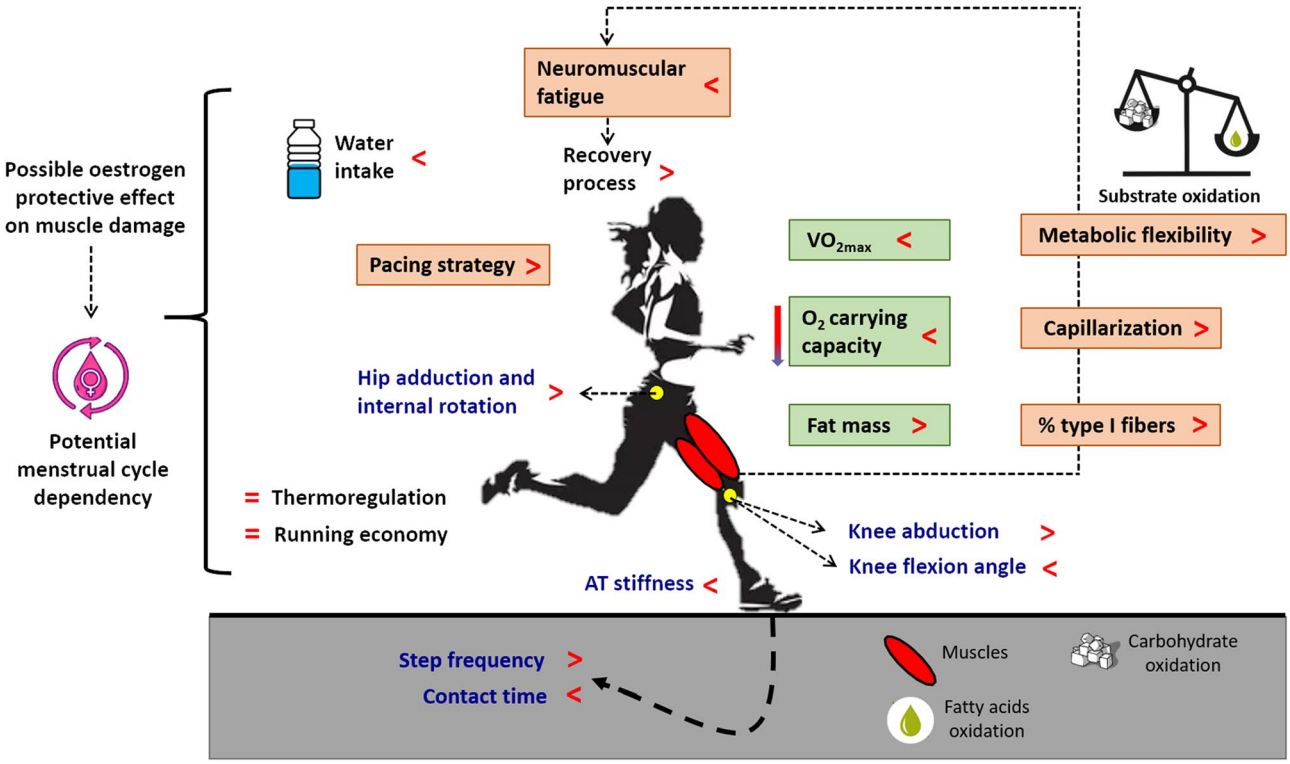


Fig. 1 This schematic representation of a female runner is an overview of the main psychological, physiological, neuromuscular and biomechanical sex differences in endurance running. Parameters that could give an advantage to males and to females in endurance running performance are boxed in green and orange, respectively. >: superior in females, <: inferior in females, =: no sex difference, *AT* Achilles tendon, O_2 oxygen, $\dot{V}O_{2max}$ maximal oxygen uptake

eversion to compensate for larger hip adduction, as typically seen in females [49], i.e. sex differences in kinematics at the hip level can explain differences at the knee level. In other words, greater knee abduction in females could also be a plausible consequence of morphological differences and especially the greater Q-angle (i.e. the acute angle formed by the vector for the combined pull of the quadriceps femoris muscle and the patellar tendon [54]) reported in females [43, 50]. Smaller knee flexion angles have been reported in females both at high running velocities (around 18 km h^{-1} [46]) and at preferred running speed among a very large sample of 483 (263 females and 220 males) recreational and competitive runners [48]. However, previous investigations showed no sex difference in knee sagittal plane motion between females and males [43, 50]. These discrepancies could be explained by the imposed speed (13 and 14.4 km h^{-1}) in previous studies [43, 50], where running speeds varied from 8 to 12 km h^{-1} in Phinyomark et al. [48]. At the ankle level, one study found smaller rearfoot eversion in female runners [49], whereas two other studies found greater rearfoot eversion in females [50, 55]. In these studies, as males and females ran at the same absolute speed, Takabayashi et al. [38] suggested that differences could be attributed to differences in body size and spatiotemporal parameters [38], as described in Sect. 2.1.

Given the identified sex differences in joint kinematics, research has been conducted to identify sex specificities in lower limb muscle activities. Unfortunately, sex comparisons have mostly been studied at given absolute running speeds and for very short periods of time (about 10 s). The neuromuscular strategies adopted may thus differ from those used in endurance running and racing conditions. In these experimental running conditions, females had a higher activation of the gluteus maximus [42, 51] than males at all speed (from 9.7 to 14 km h^{-1}) and incline (0, 10 and 15%) conditions and a larger increase in activity of the vastus lateralis than males as incline increased [42]. Females may thus use different neuromuscular strategies than males in case of increased task demand, i.e. changes in speed and incline [56]. At similar running speeds of around 18 km h^{-1}, Malinzak et al. [46] demonstrated a higher activation of the quadriceps but a lower activation of the hamstrings in recreational female athletes compared to males, which potentially induced a higher anterior knee shear force (i.e. perpendicular force applied by the quadriceps muscles on the tibia) in female runners. In contrast, a higher medial hamstring pre-activation has been reported

in downhill running at a slow running speed (7.5 km h^{-1} on a 15° declined treadmill) in female runners, which may contribute to better stabilization of the knee joint in this situation [57]. Similarly, an increased pre-activation of the peroneal muscle group was found in female runners during level running, and this was considered as a strategy to stabilize and protect the ankle joint [58]. As these studies only considered a small number of muscles, further analysis of the inter-muscular coordination in running was limited. However, in a recent study conducted in 60 females and 60 males [59], the concept of muscle synergies could be used based on the electromyographic recording of 13 lower limb muscles at running speeds ranging from 7.2 to 13.7 km h^{-1}. This study found sparse sex-specific modulations of the relative muscle contribution in running. During the stance phase, no sex differences were found in the contribution of the hip extensors, tensor fasciae latae and plantar flexors, yet females used the vastus medialis less during the weight acceptance. In this particular phase, the timing of the main peak of activity was similar but the synergy was narrower in females, implying a shorter time-duration of activation in females than in males. The authors suggested that the neuromotor strategy showed by females could reduce their fatigability during prolonged locomotion efforts. During the early swing, females used the rectus femoris less but the gluteus medius more whereas during the late swing, females used the tibialis anterior more compared to males.

Overall, despite sex-specificities of the running kinematics, the reported differences in muscle activities, such as the female-specific protective joint strategies, are still controversial and unlikely to reduce the sex-related gap in performance. Further studies should focus on the sex differences in muscle synergies under endurance and competitive running conditions.

Most of these studies investigated running mechanics at the same absolute speed, putting female runners at a greater relative demand on their musculoskeletal system. Indeed, most of the previous literature on kinematics differences between male and female runners failed to establish a relationship with sex, often because of the lack of control for confounding factors such as running speed and participants' height and body mass. It is therefore necessary to conduct more studies with larger sample sizes allowing consideration of confounding factors in order to obtain a clearer picture of the real influence of sex on running biomechanics.

A recent study assessed sex differences in running biomechanics in a population of Chinese males and females [60]. The authors report similarities with sex differences in Western populations (e.g. increased hip and knee range of motion in females), but also differences in biomechanics (e.g. knee and ankle joint kinematics, vertical ground reaction force and plantar pressure) between Western and Chinese runners. Thus, the authors emphasized the fact that ethnicity should be considered when comparing running biomechanics in males and females, in particular by running shoe manufacturers. Another under-studied topic is the influence of females' breasts on their running biomechanics. A recent review [61] pointed out that, although there is some information on breast motion during walking or running, the previous breast-focused literature had "poor research design and inadequate biomechanical methods used to quantify complex three-dimensional breast motion". Brown and Scurr [62] found a slightly negative influence of breast mass on the marathon finish-time; however, no studies have been conducted so far to determine the influence of the biomechanics of females' breasts and trunk on their running performance. This specificity of females' morphology should also be considered in future studies examining sex difference in running biomechanics.

2.3 Running Kinetics and Muscle–Tendon Stiffness Regulation

At given running speeds up to 21.6 km h^{-1}, Keller et al. [63] did not report any sex difference in the changes in maximal vertical ground reaction force and loading rate (normalized by body weight) with speed. However, sex differences in the normalized force data have been reported in a larger group of recreational runners when running at the same absolute running speed of 11.9 km h^{-1} [41]. Females exhibited a significantly higher loading rate but a lower active peak force than males in both pre-fatigue and fatigue conditions. They also showed higher peak propulsive force (antero-posterior), but only before fatigue. Again, as this study was conducted at the same absolute running speed, greater peak propulsion force (measured on the antero-posterior axis) observed in females may have been due to the greater relative effort compared to males.

Joint moments and mechanical stress applied to lower limb joints have been compared to better understand potential sex differences in running-related injuries, rather than running performance [64]. Specifically, females appeared to be at greater prevalence [65] and incidence [66] to sustain patellofemoral joint pain compared to males. Conflicting results exist on sex differences in patellofemoral joint mechanical stress (PFJS) [40, 67, 68], probably due to different methods used to calculate it. In addition, contradictory results exist in sex differences when considering peak knee extension moment (normalized by body mass) in running since no difference [43], greater [67] or lower [40] moment in females have been reported. In the frontal plane, females have been shown to display greater normalized hip and knee adduction moment compared to males [44]. Similar to sex

differences in running kinematics, sex differences in kinetics have mainly been attributed to – yet not measured—morphological sex differences.

Running is a stretch–shortening cycle type activity in which higher Achilles tendon (AT) stiffness is expected to affect the storage of elastic energy during the braking phase, followed by its recoil during the subsequent push-off phase. Therefore AT stiffness is expected to affect RE [69–73]. Tendon structural quality and resistance to deformation, tendon collagen synthesis rate and hypertrophic effect of regular running exercise on the patellar and AT have been reported to be lower in females than in males [74, 75]. In particular, no significant hypertrophic effect on the patellar and AT was found in young and regularly trained female runners (at least 40 km of running mileage per week for the previous 5 years) as compared to untrained ones, whereas a significant gain was found in similarly trained males [75]. Both non-athletic [71] and trained female runners [73] have been reported with lower stiffness and hysteresis of AT than their male counterparts. Despite this AT difference, trained female and male runners had a similar RE (see Sect. 2.2), but this remains the only study on such a sex comparison. Other confounding factors should be considered, such as AT length and moment arm, but these factors were studied primarily in elite male runners [76]. Thus, further work is needed to determine in females the exact influence of a less stiff AT on their RE and running performance.

In addition to their effects on tendons, oestrogens are reported to reduce ligament stiffness. Although suggested as a potential risk factor for anterior cruciate ligament (ACL) injuries for female participants during sports activity [77], a causal link is refuted by other studies reporting no associated decrease in anterior knee stiffness [78]. ACL laxity also appears to be affected by the menstrual cycle, as evidenced by its increase reported in the late follicular phase, i.e. when the serum level of estradiol peaks and progesterone is low (e.g. [78, 79]). Once again, no associated change was found in anterior knee stiffness [78]. Within this framework, muscle stiffness being an important component of joint stability, it is noteworthy that Khowailed et al. [80] revealed different muscle activation strategies in running during different phases of the menstrual cycle. During the follicular phase, when oestrogen levels are low, females placed greater reliance on the quadriceps than on the hamstrings. During ovulation, when oestrogen level and knee laxity are high, increased hamstring pre-activation and co-activation during the braking phase have been observed. Thus, as oestrogen levels seem to influence the stretch–shortening cycle and potentially RE, running performance could possibly vary across the menstrual cycle.

3 Substrate Utilization and Running Economy

3.1 Substrate Utilization

Numerous original studies and review studies have analyzed sex differences in substrate utilization during exercise lasting from 60 to 120 min (e.g. [81–86]) at different intensities (from 35 to 75% $\dot{V}O_{2max}$). Comparing sexes in substrate use is methodologically challenging since this parameter is influenced by several factors such as training status, menstrual cycle phase, diet, age, etc. Controlling for age, diet and physical activity level (i.e. using $\dot{V}O_{2max}$ expressed relative to fat-free mass) would allow avoiding heterogeneity in the results when comparing exercise-induced metabolic responses between males and females [82]. Menstrual cycle phase has been reported to have a small impact on sex difference in substrate utilization [86]. Oral contraceptives have a slightly greater impact on substrate oxidation [86]. Together this implies that when the variance of these two factors is not controlled, sex differences in substrate utilization may be biased.

When considering only the studies that presented as well controlled with regard to these factors, the overall conclusion is that females oxidize more lipid and less carbohydrate (CHO) and protein than males during prolonged exercise (at least until 120 min of exercise duration). Females have also greater metabolic flexibility since substrate oxidation is readily adjusted according to the availability of nutrients. In this regard, the respiratory exchange ratio (RER) has been reported to be lower in females during low-intensity, prolonged exercises, supporting a lower reliance on whole-body CHO oxidation (e.g. [86]). For instance, lower RER values were found for females (0.87) than for males (0.94) during a 15.5 km treadmill run at 65% $\dot{V}O_{2max}$ [84]. During an incremental treadmill run test to exhaustion performed in a large cohort of 157 males and 143 females, Venables et al. [87] showed that females displayed higher maximal rates of fat oxidation. In addition, females exercised at a higher $\%\dot{V}O_{2max}$, for which a CHO as dominant fuel is observed. Although less used than CHO and fat, protein provides approximately 5–8% of total energy in both sexes [29] during prolonged exercise. However, it should be noted that the protein catabolism seems to be lower in females, potentially due to the higher fatty acid oxidation [29, 30, 84, 88, 89]. Theoretically, this may constitute an advantage for females during ultra-endurance exercises (Fig. 1).

The higher metabolic flexibility observed in females constitutes a sex-specific difference that depends on several factors (and their interaction), including higher skeletal muscle insulin sensitivity as well as high levels of circulating and intramuscular fatty acids required for the oxidation

process (for a review, see [83]). Some authors have reported the crucial role of female sex steroid hormones (e.g. oestrogens) in the regulation of whole-body insulin sensitivity and substrate metabolism (e.g. [83, 86, 90]) at rest and during endurance exercise. Within the endogenous forms of oestrogens, 17-ß-estradiol and associated oestrogen receptors α are important in the regulation of substrate metabolism in skeletal muscle. Higher levels of 17-ß-estradiol are reported to spare glycogen stores and decrease liver glucose output and muscle uptake by shifting metabolism toward free fatty acids at certain (low to moderate) exercise intensities [28, 86, 91–93]. This metabolic hormonal action might thus contribute to enhanced performance capabilities of females compared to males for ultra-endurance exercise. Although lower RER values have been reported at submaximal running intensities (30–60% $\dot{V}O_{2max}$) in the luteal phase of the menstrual cycle [94, 95], other studies reported no significant differences throughout the menstrual cycle (e.g. [96]). Part of this discrepancy has been attributed to the complex balance between oestrogen and progesterone concentrations and their fluctuations during the menstrual cycle [82]. According to D'Eon et al. [92], the ratio of oestrogen/progesterone would be sufficiently elevated to lead to metabolic changes between the menstrual phases.

Although females and males do not differ in their glycogen stores and capacity for storage of glucose into glycogen [83, 84], females have a higher plasma fatty acid availability due to a greater number of intramyocellular lipid (IMCL) droplets (and not larger droplets) [97]. Moreover, female skeletal muscle is reported to be better able to store lipids and oxidize fatty acids during exercise, which would contribute to maintaining a high level of IMCL turnover [83]. During exercise, this dependence on lipid substrate to cover energy expenditure in females might be explained by a greater relative area of type I muscle fibers (see next section) characterized by higher oxidative capacity, capillary density and higher insulin sensitivity [98]. Indeed, Essén et al. [99] previously reported that IMCL content was 2.8-fold higher in type I fibers compared to type II fibers. Despite inconsistencies in the literature [82], higher IMCL use during submaximal exercise has been reported in females as compared to males, irrespective of training status [100–102].

The majority of studies focusing on sex differences in substrate oxidation have been conducted on a cycle ergometer rather than in running (see Table 1 in Tarnopolsky [86]). The differences in substrate oxidation observed between sexes highlights the importance of quantifying the cycle menstrual phase, oral contraception, training level and diet in females.

3.2 Running Economy

RE is known to be the most predictive variable of running performance within homogeneous groups of trained athletes (i.e. similar $\dot{V}O_{2max}$ values) (e.g. [21]). RE depends on several physiological, biomechanical, anatomical and neuromuscular (NM) attributes, supporting the importance of a holistic approach in RE determination (for reviews, see [103, 104]). Oxygen cost in $mlO_2\ kg^{-1}\ km^{-1}$ is derived from the mass-specific $\dot{V}O_2$, dividing the steady-state $\dot{V}O_2$ the resting value by the running speed. Given that substrate metabolized to provide energy may vary with exercise constraints such as intensity [105], duration [106], training and sex (e.g. [97, 107]), it has been proposed to express RE as gross energy cost [105] in $J{\cdot}kg^{-1}{\cdot}m^{-1}$ or $kcal{\cdot}kg^{-1}{\cdot}km^{-1}$. An enhanced/improved RE is associated with a decrease in this value.

During submaximal running tests (< 10 min), no scientific consensus exists on the differences in RE between trained or recreational male and female runners, with conflicting results strongly related to differences in methodological setting [73, 108–114]. $\dot{V}O_{2max}$ values, training background, running performance, body fat and quantification of RE have probably contributed to the lack of consensus on this issue. In this regard, sex-specific differences have often been observed when authors expressed RE from oxygen cost or submaximal $\dot{V}O_2$ (e.g. [23, 108, 112, 115]). Moreover, the majority of studies investigating sex differences in RE have used small sample sizes (e.g. $n < 30$) and/or comparisons across absolute speeds (rarely with relative intensities). In a study comparing RE between trained female and male runners, Fletcher et al. [73] did not show any sex difference at similar relative intensities (75, 85 and 95% of the speed at LT) when expressed in either energy cost or oxygen cost, or when using of an allometric scaling factor in order to take into account sex differences in body mass. These findings have been confirmed by the same research group with the inclusion of elite and trained male and female runners [113]. In addition, using a larger sample size ($n = 95$), Black et al. [109] recently reported no sex differences in RE in $kcal{\cdot}kg^{-1}{\cdot}km^{-1}$ at similar relative and absolute running speeds among females and males of equivalent standard. Considering these findings, no clear difference in RE responses exists between male and female runners even when applying different RE units.

In most of the articles focusing on RE responses in females, a qualitative analysis of menstrual cycle is lacking, and this might constitute an important methodological bias in RE evaluation. During endurance exercises, females generally use less CHO and have lower RER values [107, 116, 117]. These metabolic changes may depend on the phases of the menstrual cycle as well as short-term oral contraceptives and, in turn, affect the RE response in females. RE may also be naturally influenced by the specificity of each phase (e.g.

early, late follicular and mid-luteal phases), and, therefore, circulating hormone levels (i.e. oestrogen and progesterone). For instance, investigating three different times during the menstrual cycle in females taking oral contraceptives (i.e. constant doses of oestrogen and progestogen for 21 days), Giacomoni and Falgairette [118] reported an improved RE at low intensities (7–9 km h^{-1}) only during the late period of oral contraceptive use (i.e. days 19–21). In this regard, Dokumacı and Hazır [119] recently reported an improved RE (i.e. in terms of energy or oxygen cost) in the luteal phase compared to the follicular phase in female competitive athletes with no oral contraceptives. Conversely, two studies have indicated that the mid-luteal phase (high levels of oestrogen and progesterone) was associated with worse RE responses compared to early and late follicular phases [120, 121]. More work is needed to better understand the effects of the menstrual phase in RE, but these findings suggest that those effects must be considered.

4 Fatigue Resistance

NM function, RE and biomechanics are often measured in a non-fatigued state. However, our group and others have consistently shown in the last two decades using laboratory or field experiments (e.g. marathon, trail/ultra-trails), that fatiguing endurance running exercise drastically affects maximal strength, RE and running patterns. Some sex differences exist at these levels and are discussed below.

4.1 Neuromuscular Fatigue

NM fatigue has traditionally been defined as an exercise-induced reduction of maximal strength or power [122]. The causes can be peripheral (i.e., within the muscle) and/or central (i.e., proximal to the neuromuscular junction), and NM fatigue etiology in running depends on many factors such as exercise duration, intensity, altitude, and positive and negative slope [123]. Central fatigue reflects an inability to voluntarily activate muscles, and has been described as a protective mechanism acting to limit peripheral perturbations [124, 125]. In contrast to central fatigue, which occurs predominantly after very long and low intensity exercise, peripheral fatigue is greater at higher intensities, shorter duration exercise [126] including downhill running [127], and could impair (1) action potential transmission along the sarcolemma, (2) excitation–contraction coupling, and (3) actin–myosin interaction [123].

Sex differences in fatigability have been mostly investigated in laboratory conditions (for a review, see [128]). While females are less strong and less powerful than males, they were found to be less fatigable than males for sustained or intermittent isometric contractions performed at a similar relative intensity [129]. However, sex differences in fatigability are less clear following dynamic tasks as females have been reported to be either less than or as fatigable as males (see Fig. 1 in Hunter [128]). Among these studies, a lower fatigue index (i.e. smaller decline in each isokinetic variable) was found in females compared to males after a series of 30 maximal dynamic knee extension [130]. This finding could be of importance given that in a recent paper, Ehrstrom et al. [131] showed local endurance of the knee extensors was a good predictor of performance on a short trail running exercise (27 km with 1400 m of positive elevation) in trained male runners. On a fatiguing cycling task, Ansdell et al. [132] compared males and females after normalizing exercise intensity to critical intensity, and found that females displayed a greater relative critical intensity compared to males, yet contrary to their hypothesis, females had a longer time to task failure than males above critical power [132]. Females also exhibited lower strength loss and peripheral fatigue at exhaustion. However, sex differences in fatigability following prolonged running exercise is not well documented. After 2 h of laboratory treadmill running at a speed corresponding to their first ventilatory threshold, Glace et al. [133] reported that knee extensor/flexor strength measured in isokinetic conditions (60° s^{-1}) decreased in males only, while decreased hip strength was independent of sex.

Under real endurance racing conditions on short distances (< 40 km), Boccia et al. [134] reported no sex difference in the decrease in knee extension force after a half-marathon performed by moderately trained runners under real racing conditions. These authors also found that the origin of fatigue was independent of sex. After a graded 20-km race (± 350 m) in recreational males and female runners, sex differences were found in both the acute and delayed (up to 4 days) recovery period [135]. Females showed smaller functional decrements within the first 2 h and earlier full recovery than males. Indeed, only males showed decreases in maximal isometric knee extension force and maximal power in drop jump up to 4 days after the race. However, regarding the relative decrements (normalized by pre-values), no sex difference was found, so that the lower fatigue effects observed in females may be partly attributed to their lower initial strength levels.

Over a much longer distance, Temesi et al. [136] assessed NM fatigue in experienced male and female ultra-endurance trail runners matched by relative level of performance (i.e. same average percentage of performance as the winner of each sex) after a 110-km ultra-trail-running. In the ultra-trail study, female runners had (1) less peripheral fatigue in the plantar flexors and (2) a lower decrease in maximal force in the knee extensors when compared to their male counterparts. The authors suggested that females were more fatigue resistant following ultra-endurance running effort, which could partly explain why they manage to outperform males

in races of this format. A recent study from our group investigated sex differences in NM fatigue in trail running races of various distances (from 40 to 170 km) [137]. Male and female participants were matched by a relative level of performance using the same criteria as in Temesi et al. [136]. Greater knee extensor strength loss was found in males compared to females and, contrary to our hypothesis, this sex difference was independent of the race distance. Interestingly, we observed greater peripheral fatigue on plantar flexor muscles in males compared to females in races under 60 km but no sex difference in races above 100 km. This result could be partly due to sex differences in the "competition intentions" of the participants: with races < 60 km females reported that they performed the race in a more "pleasure mode" whereas males were more competitively oriented. This possibility should be considered when concluding on fatigability. In other words, less fatigue post-exercise does not necessarily mean a better resistance to fatigue, at least in non-elite runners.

4.2 Muscle Tissue Characteristics

Among the underlying mechanisms, males and females have distinct muscle properties. An obvious difference that mainly explains the difference in maximal strength is muscle mass, due to larger diameter muscle fibers in males rather than the number of fibers [138], this larger size being due to sex-related differences in human skeletal muscle gene (e.g. GRB10 and ACVR2B) expression [139]. This factor has been presented as partly explaining the sex differences in fatigability in most of the studies using single-joint exercise since stronger muscles tend to be less perfused because of higher blood flow occlusion resulting from higher intramuscular pressure. In order to overcome the occlusion effect, Ansdell et al. [140] compared NM fatigue in males and females across submaximal and short duration intermittent isometric contractions (i.e. they used a 3-s contraction duration with a duty cycle allowing to negate the influence of occlusion). After normalizing the intermittent exercise intensity by maximal force, lower force reduction and longer time to task failure was still found in females compared to males. However, this is not the only factor explaining the fatigability. Despite no sex differences in peak force, in power and shortening velocity of single fibers when normalized to muscle cell size (e.g. [141]), there is considerable evidence that females have a greater proportional area of type I fibers in several key muscles for locomotion and daily function [128]. Females also have greater capillarization [100] and lower glycolytic enzyme activity [142] when compared to males. Related to these important features, a better vasodilatory response to exercise has been reported for females. For example, vasodilatory responses of the femoral artery during dynamic knee extensor exercise were found to be greater in females than in males [143]. Overall, these results explain why females show attenuated impairments in contractile function compared to males [144], and are able to recover at a faster rate from repeated fatiguing exercise [145].

In addition to directly explaining the sex-related difference in fatigability at the muscle level, the attenuated metabolic disturbance related to the greater proportional area of type I may also lead to attenuated afferent feedback (groups III and IV). This may induce less inhibitory inputs to the motoneuronal pool, and thereby less central fatigue. Indeed, greater levels of fatigue observed in males have been associated with greater central deficits, but these studies were using maximal efforts and it is not known if this is also true for submaximal contractions [128].

In conclusion, as generally reported following single-joint fatiguing tasks, females appear less fatigued following trail and ultra-trail races. A greater proportion of type I muscle fibres and higher muscle capillarization (i.e. less muscle de-oxygenation) in females compared to males are possible explanations for lower fatigability in females, and could be of advantage for females over ultra-endurance running performance (Fig. 1). Although the results obtained with the scale on "the competitive intention" of the runners must be treated with caution (i.e. the scale has not undergone a validation process), the fact that females (non-elite) have been showed to be less competition oriented than males could also at least partly explain sex differences in fatigability following such trail running races.

4.3 Muscle Fiber Damage, Inflammation and Delayed-Onset Muscle Soreness

Endurance running races induce metabolic stress and include thousands of ground impacts and subsequent eccentric muscle actions that are likely to induce very focal and limited ultrastructural muscle damage. In the most severe case, less than 10% of the sarcomeres appeared damaged [146], which clearly differ from those induced by pure eccentric muscle actions [147]. The subsequent ultrastructural recovery process involves oedema, remodelling/inflammation, and delayed-onset muscle soreness (DOMS) [148, 149]. The ultrastructural damage is expected to be less or even absent in trained runners [150, 151]. Importantly, (1) neither the degree nor the timing of exercise-induced muscle damage (EIMD) per se correlates well with the DOMS sensation [152, 153], and (2) the timing of DOMS disappearance usually occurs prior to complete structural and functional recoveries [149]. The only study that has directly addressed in humans (via muscle biopsies) the effect of sex on ultrastructural muscle damage and/or inflammation up to 6 days after an eccentric exercise reported no sex difference in muscle damage, yet an attenuated inflammatory response in females as compared to males [154]. In our own study

of the sex differences after a graded 20-km running race [135], DOMS were recorded for the major lower limb muscles. Independently of sex, DOMS was reported at day 2 for the quadriceps muscle group, but only in female runners for the hamstrings, suggesting that possible sex differences are muscle-group dependent. At day 4, despite the disappearance of DOMS, males still had functional deficits in MVC and drop jump test. Female runners also had functional deficits in DJ, but no longer reported DOMS and had already recovered in MVC.

Sorichter et al. [155] have summarized the literature on the identification, usefulness and limits of indirect markers of ultrastructural muscle damage widely used in males and females. Aside from DOMS, the most reported indirect indicators include myoglobin (Mb) and lactate dehydrogenase (LDH) plasma levels as well as serum creatine kinase (CK) activity [156]. According to Goodman et al. [157], the increased serum levels of CK and Mb after an endurance run might result from free radical-induced cell membrane damage and/or transiently increased permeability rather than from mechanical ultrastructural damage. Part of these perturbations are likely to decrease with training (e.g. Margaritis et al. [158]). However, owing to high inter-individual variability none of these indirect markers accurately reflect the magnitude of muscle damage. This appears clearly in the extremely large range of CK concentration values (1500–264,300 IU L^{-1}) reported among finishers of ultra-trail running events, but no differences between sexes have been reported [136, 159]. These methodological limits apply to the serum CK [160], which is still widely used as a marker of the sex difference in the exercise-induced muscle damage [161].

As reviewed by Enns and Tiidus [162], sex and oestrogen are reported as potentially attenuating indices of exercise-induced skeletal muscle damage by influencing the inflammation and repair processes. Although the underlying mechanisms are not yet fully elucidated in humans, oestrogens are thought to exert their protective effects by: (1) acting as an antioxidant, thus limiting oxidative damage; (2) acting as a membrane stabilizer by intercalating within membrane phospholipids; and (3) binding to oestrogen receptors, thus governing downstream muscle repair processes, including the activation and proliferation of muscle satellite cells. Supporting the oestrogen protective effect in runners, lower resting serum CK values are reported in female compared to male athletes [161] and in eumenorrheic compared to amenorrhoeic female athletes [163], whereas no sex effect was found in the peak values after a marathon [164] in moderately trained runners. Illustrating the limitations of using indirect markers of muscle damage and inflammation, the downhill running study of Oosthuyse and Bosch [165] found that DOMS peaked after 24 h in males and females, but the time to disappearance of CK and DOMS then differed by sex. Compared with males, females showed earlier restoration of the pre-run CK activity level (at 48 vs. 72 h) but longer-lasting DOMS (up to 72 vs. 48 h).

In conclusion, despite the lack of direct assessment of sex differences in the running-induced ultrastructural muscle damage, the reported time-evolution of indirect markers of muscle inflammation (such as plasmatic CK activity and DOMS) during the recovery period suggest less damage or at least earlier structural recovery in female runners.

4.4 Change in Running Biomechanics and Economy with Fatigue

An altered RE has been repeatedly reported after prolonged road and trail exercises in male runners (e.g. [166–170]), but only a few studies have been conducted in trained or recreational female runners [133]. After a 2-h treadmill run session at a given relative intensity, Glace et al. [133] showed an increase in oxygen cost in male but not in female distance runners. In male athletes, the exacerbated increase in oxygen cost was related to their greater muscle fatigue characterized by the larger strength decrement of the knee extensors (see Sect. 4.1). To the best of our knowledge, only two other studies have examined sex differences with regard to RE change with fatigue, albeit with shorter running bouts. Similar changes in RE were found for males and females following (1) a 1-h run at marathon pace [171] and (2) a 5-km run at 80–85% of $\dot{V}O_{2max}$ [172]. These three experiments were conducted on a treadmill in laboratory conditions. A recent study from our group reported an increase in RE following trail running races from 40 to 170 km; however, no significant sex difference were observed in the changes in RE measured on both flat (+3.1 vs. +8.7% in females vs. males, respectively) and uphill (+1.4 vs. +6.9% in females vs. males, respectively) conditions [137]. Further investigations are warranted to further examine sex differences in RE in the ecological context using models of prolonged road and trail run exercises.

While many studies have investigated sex differences in running biomechanics under acute conditions (see Sect. 2.2), the literature is very limited on sex differences in the alteration of running biomechanics following a fatiguing task. Bazuelo-Ruiz et al. [41] reported a reduced ankle dorsiflexion angle at touchdown in females only after a succession of three consecutive tasks at high intensities (shuttle-run, running up and downstairs, and jumps), this parameter being associated with a decrease in loading rate and vertical impact peak force. These authors suggested a potential adaptative strategy to optimize shock attenuation and thus prevent running injuries. However, these results should be interpreted with caution since the fatiguing protocol was quite unusual. After a 110-km trail running race, Giandolini et al. [173] reported that males adopted a flatter

pattern (i.e. a decreased foot/ground angle) and increased step frequency contrary to females, who landed with a more dorsiflexed ankle accentuating their rear-foot strike pattern. Changes in males were considered as a compensatory adjustment to possibly greater decreased muscle capacity compared to females [173]. Although female adaptations to fatigue observed in the studies of Bazuelo-Ruiz et al. [41] and Giandolini et al. [173] seem to go in opposite directions (concerning the alteration of ankle angle with fatigue), the fatiguing tasks differed considerably between the two studies and could explain the discrepancies in the results. As also suggested by the sex-dependent DOMS sensations per muscle after a graded running race [135] (see Sect. 4.3), it appears that males and females adjust their running pattern differently, which suggests sex-relative biomechanical adaptations. Under laboratory conditions, no sex differences were reported in running biomechanical parameters previously associated with the aetiology or exacerbation of patellofemoral joint pain after a run on a treadmill at 3.5 m s^{-1} until reaching a RPE of 17 out of 20 [68]. These studies compared males and females following different modalities of exercise and under different methodological approaches. Further studies are needed to better investigate potential sex differences in biomechanical alterations following prolonged running exercise.

5 Other Factors Influencing Running Performance

5.1 Thermoregulation

Whether sex differences exist in thermoregulation was uncertain until recently [174], i.e. it was not known if thermoregulatory differences between males and females were due to sex per se or to other differences such as body size or aerobic fitness. Indeed, a correlation between $\dot{V}O_{2max}$ (lower in females) and the ability to maintain lower core temperatures during exercise in the heat has been found, potentially related to skin blood flow. Females may generate less heat in high ambient temperatures because of lower muscle mass and smaller body size but may be disadvantaged as their lower $\dot{V}O_{2max}$ can result in faster increases in body temperature. Notley et al. [175] concluded that, contrary to popular belief, sex does not significantly impact exercise thermoregulation [175]. A review by Yanovich et al. [176] confirmed the lack of sex differences and concluded that females were not at greater risk of heat illness, provided the usual risk-management techniques are in place (pacing, clothing, hydration, acclimation). It has been reported that female athletes used more heat illness prevention strategies than male athletes [177]. It is noteworthy that the American College of Sports Medicine does not provide specific guidelines or strategies for the female athlete. However, it has been argued that a sex difference in thermoregulation may depend on the percentage of humidity and exercise intensity [178]. Indeed, Shapiro et al. [179] found that core temperature increased less in females than in males for hot/humid environments (due to larger surface area to body mass ratio and more efficient sweating suppression), whereas the opposite was true in hot/dry climates (due to lower overall sweating capacity in females despite a higher density of sweat glands). Although thermoregulatory responses vary over the cycle, Notley et al. [175] suggested that there was no additional thermoregulatory concern for female athletes if an oral contraceptive was used or at any phase of the menstrual cycle phase. It is not known if potential sex differences exist in the time-course of acclimation.

It has also been suggested that performance was less affected by warm weather in females than in males during a 161-km ultra-marathon [180], although no sex difference was found in marathons. The opposite may actually be true since performance is more negatively affected for slower populations of runners on that distance [181]. Importantly, because of their smaller body size, lower heat generation, and less sweat loss (i.e. better efficiency in sweating that may decrease the total amount of so-called "wasted sweating" in a humid environment), the water intake required to maintain hydration and thermal balance is attenuated in females. Since hydration guidelines have been developed using data mainly collected in studies with males, they should be interpreted with caution when applied to females [176]. This is particularly important in ultra-endurance exercises since over-hydration may induce gastro-intestinal distress.

5.2 Pacing

Several studies, including a large study with data from 14 US marathons encompassing ~ 92,000 performances [182], have shown that females tend to have a more even pacing strategy in marathon races [183]. A similar finding has been found in half-marathons [184], 10-km races (at least in fast runners [185]) or even shorter races such as 5-km cross-country race when males and females have similar relative performance [186]. It has been suggested that sex difference in pacing partly reflects a sex difference in decision making [185] rather than greater susceptibility to glycogen depletion [186]. Interestingly, the sex differences in pacing were also found to be true for top runners. A study collected finishing and split times in 673 males and 549 females across nine Olympic and World Championship marathons and found that females slowed less and were more likely to run a negative split than males [187]. In addition, in a study from Trubee et al. [188], the more even pacing strategy in females was

found to be an even greater advantage during warm weather conditions.

The number of studies on sex differences in pacing strategy related to ultramarathon is low and there is no clear consistency among the results. Indeed, females showed lower relative starting speeds and higher finishing speeds than males on a 100-km race [189], yet no sex differences in pacing strategy [190] or even better preservation of mean speed throughout the race have been found in males [191] on 24-h races. It has been advised that, given the possibility of a "herd principle", comparison of competition dynamics between sexes must be further explored in ultra-marathon.

The level of performance and age may be confounding factors in pacing strategies although, again, the results are not that clear. As stated in the present section, sex differences in pacing on 10-k races were mostly found in good runners [185], whereas they occurred across all finishing time groups in the marathon [182]. Deaner et al. [182] also showed that sex differences in pacing occurred across age groups. On the contrary, it has been found that females showed no differences in pace variability across ages, whereas younger (< 30 years) and older (> 60 years) males showed a greater variability in pacing than other age groups [192].

6 Conclusion

Through this narrative review, we have identified a number of sex differences in running related to biomechanical, physiological and NM aspects, some of which potentially play a role in endurance running performance (Fig. 1). In particular, the current literature reports that females show (1) greater hip and knee joint motion in non-sagittal planes and (2) greater lower limb muscle activation, compared to their male counterparts at a given absolute speed. However, most of these sex differences disappear when normalized either by maximal aerobic velocity or anthropometry. Despite those sex differences in running biomechanics, males and females do not differ in terms of RE, suggesting that both sexes optimize their running pattern to adjust to their characteristics. During prolonged exercise, females use more fatty acids than males, which allows them to save carbohydrates. In addition, attenuated NM fatigue, particularly less peripheral impairments on plantar flexor muscles, is observed in females compared to males following endurance and ultra-endurance running bouts. The fact that oestrogen seems to have some protective effects may indicate that females could be less prone to damage induced by repetitive eccentric muscle actions. Yet these differences do not allow females to outrun males in endurance and ultra-endurance running exercises. It is also still not clear whether prolonged running affects males and females differently in terms of running biomechanics and economy. Sex differences in a fatigued condition are a clearly under-investigated research area and further direct physiological and biomechanical comparisons between males and females following prolonged running are warranted. Considering that females used different pacing (i.e. more even) strategies than males, other psychological and/or sociological parameters that could affect performance or help to understand sex differences in running participation also need to be explored.

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