



What are the Limiting Factors During an Ultra-Marathon? A Systematic Review of the Scientific Literature

by

Arkaitz Garbisu-Hualde¹, Jordan Santos-Concejero¹

This review aimed to analyse factors that limited performance in ultra-marathons and mountain ultra-marathons. A literature search in one database (PubMed) was conducted in February 2019. Quality of information of the articles was evaluated using the Oxford's level of evidence and the Physiotherapy Evidence Database (PEDro) scale. The search strategy yielded 111 total citations from which 23 met the inclusion criteria. Twenty one of the 23 included studies had a level of evidence 2b (individual cohort study), while the 2 remaining studies had a level of evidence of 5 (expert opinion). Also, the mean score in the PEDro scale was 3.65 ± 1.61 , with values ranging from 0 to 7. Participants were characterised as experienced or well-trained athletes in all of the studies. The total number of participants was 1002 (893 men, 86 women and 23 unknown). The findings of this review suggest that fatigue in ultra-endurance events is a multifactorial phenomenon that includes physiological, neuromuscular, biomechanical and cognitive factors. Improved exercise performance during ultra-endurance events seems to be related to higher VO_{2max} values and maximal aerobic speed (especially during submaximal efforts sustained over a long time), lower oxygen cost of transport and greater running experience.

Key words: trail running, VO_{2max} , performance, fatigue, endurance.

Introduction

Running events are within the most popular sports worldwide. Interestingly, these events are characterised by huge variability in terms of distance (sprints, middle-distance, long-distance), terrain in which they take place (track, road or cross-country), duration (one-day races, multi-day events), etc. It is unusual to achieve success in different running events due to differences in biomechanical, physiological and technical requirements of each distance and modality (Thompson, 2017).

There appears to be a longstanding consensus in the literature regarding factors that limit performance in races shorter than a marathon. These factors include maximal aerobic velocity, which is the velocity elicited at VO_{2max} (vVO_{2max}) (McLaughlin et al., 2010), VO_{2max} itself (Allen et al., 1985), the lactate threshold (Allen et

al., 1985; Coyle, 1995) and the oxygen cost of transport (Conley and Krahenbuhl, 1980).

When a running event involves longer distances than the classic marathon (42.195 m), it is considered an ultra-marathon (Millet and Millet, 2012). Additionally, when ultra-endurance races take place in mountainous environments, they are known as mountain ultra-marathons (Vernillo et al., 2014, 2015).

Since shorter distance races have been more popular than ultra-endurance races, most of the literature available has analysed performance related factors for races shorter than 42.2 km. The question arises whether the limiting factors in ultra-endurance events are similar to those described in shorter distances. Thus, the aim of this review was to analyse limiting factors in ultra-marathons and mountain ultra-marathons.

¹ - Department of Physical Education and Sport, University of the Basque Country UPV/EHU, Vitoria-Gasteiz (SPAIN).

Methods

Experimental Approach to the Problem

A literature search was conducted in February, 2019. The PubMed database was searched. This database was searched from inception to February 2019, with language limitations: only peer-reviewed articles in English were selected. Citations from scientific conferences were excluded.

Literature Search

In the database the title and abstract search fields were used. The following MeSH terms and key words, combined with the Boolean operators (AND, OR), were used: ("Running"[Mesh] AND ultra-marathon) OR ultra-marathon) AND "Athletic Performance"[Mesh] AND "Humans"[Mesh]. No additional filters or search limitations were used.

Inclusion Criteria

Studies were eligible for further analysis if the following inclusion criteria were met; a) studies were written in English; b) studies analysed ultra-marathon distances from 42.2 to 101 km. If any study analysed more than one distance, it was included in the review as long as at least one of the distances analysed fell into the range mentioned above.

Quality assessment

The Oxford's level of evidence (OCEBM Levels of Evidence Working Group 2011) and the Physiotherapy Evidence Database (PEDro) scale (de Morton, 2009) were used by two independent observers in order to assess the methodological quality of the articles included in the review. The Oxford's level of evidence ranges from 1a to 5, with 1a being systematic reviews of high-quality randomised controlled trials (RCT) and 5 being expert opinions. The PEDro scale consists of 11 different items related to scientific rigor. The items include random allocation, concealment of allocation, comparability of groups at baseline, blinding of subjects, researchers and assessors, analysis by intention to treat, and adequacy of the follow-up. Items 2-11 can be rated with 0 or 1, so the highest rate in the PEDro scale is 10, and the lowest, 0. Zero points are awarded to a study that fails to satisfy any of the included items, and 10 points to a study that satisfies all the included items.

Results

Studies Selected

The search strategy yielded 111 total citations as presented in Figure 1. From those 111 articles, 23 met the inclusion criteria. Excluded studies had at least one of the following characteristics: the article was not written in English, the distance covered in the race (no matter whether it was a single-day or a multi-day event) was higher than 101 km. The overall sample included 21 cohort studies and 2 experts' opinions (Table 1).

Level of Evidence and Quality of the Studies

Twenty one of the 23 included studies had a level of evidence 2b (individual cohort study). The 2 remaining studies had a level of evidence of 5 (expert opinion). Also, the mean score in the PEDro scale was 3.65 ± 1.61 , with values ranging from 0 to 7 (Table 1).

Characteristics of the Participants

Participants were characterised as experienced or well-trained athletes in all of the studies due to the training volume they had until the day of the race. A summary of participants' characteristics is presented in Table 2. The total number of participants was 1002 (893 men, 86 women and 23 unknown).

Physiological limitations

Sansoni et al. (2017) analysed the Procollagen type I N-terminal propeptide (PINP) pre- and post- in the Vigolana Trail (65 km) in 20 experienced ultra-marathon runners (experimental group). They found that PINP serum concentration was 50% greater in the experimental group at rest compared to controls ($p = 0.001$). In addition, when they compared pre- and post-race values, they observed a 15% decrease in PINP ($p = 0.020$) even though it remained higher than in the control group ($p = 0.017$).

Bonsignore⁽²⁰¹⁷⁾ compared changes in arterial compliance as well as body composition in runners participating in an 80-km ultra-marathon. They found no changes in any variable among participants of the same category (80 km race – these data were analysed for this review, and 195-km race – these data were excluded due to the unfulfillment of the inclusion criteria). When analysing data from pre- to post-race, there were some meaningful differences: diastolic blood pressure (mmHg) and large artery compliance

(mmHg) changed from 75.8 ± 9.6 to 74.2 ± 11.1 ($p = 0.008$) and from 16.1 ± 3.0 to 17.4 ± 4.0 ($p = 0.02$), respectively.

Chan-Dewar et al. (2010) made 16 male ultra-marathon runners undergo echocardiographic scans up to 24 h prior to an ultra-marathon (The Comrades Marathon, 89 km) and within 60 min after the race. After the race, they observed a small decrease in body mass, but more importantly, they observed a drop in systolic blood pressure (117 ± 11 to 105 ± 6 mmHg; $p < 0.05$).

Shave et al. (2002) carried out a study to analyse the cardiac function during an extended exercise bout (2-day Lowe Alpine Mountain Marathon) and they observed that left ventricular systolic function (stroke volume, ejection fraction and fractional shortening) was significantly ($p < 0.05$) reduced after the completion of the event. The left ventricular diastolic function was also significantly decreased as shown by the reduced early filling velocity ($p < 0.05$) and the decrease in the E:A ratio ($p < 0.05$).

Da Ponte et al. (2018) conducted a study to evaluate changes in cardiac troponin I levels (cTnI) and the main biomarkers of skeletal muscle damage after the *Supermartona dell'Etna* (43-km) in experienced ultra-endurance athletes. They found that cTnI increased significantly by +900.0% ($p < 0.001$) with high inter-individual variability after the race.

Martinez et al. (2018) evaluated the total kcal, the carbohydrate intake (% total energy), protein intake (% total energy) and lipids intake (% total energy) in experienced athletes competing at the *Ultra Mallorca Sierra de Tramuntana* (44 km marathon and 67 km trail). They found no differences in energy intake expressed as per hour of exercise.

Rehrer et al. (1992) analysed the gastrointestinal (GI) distress in well-trained athletes participating in the *Swiss Alpine Marathon* (67 km). The authors reported a GI distress in 42% of men and 57% of women.

Brown et al. (2011) performed a study to determine the role of the COL5A1 gene genotypes during a 56 km ultra-marathon. The CC genotype of the COL5A1 was significantly associated with increased SR ROM (Brown et al., 2011), and it should be noted that a sit-and-reach ROM test that has been reported to have a negative

correlation with the oxygen cost of transport (Jones 2002). Similarly, Posthumus et al. (2011) reported that the TT genotype of the COL5A1 was associated with improved endurance running ability. The time to complete the race tended to be different ($p = 0.053$) among genotypes. Individuals with a TT genotype (341 ± 41 , $n = 21$) were significantly ($p = 0.014$) faster than individuals with a TC or a CC genotype (365 ± 39 , $n = 50$). The magnitude of the change in performance between those with TT genotype and those with either a TC or CC genotype was "moderate" (effect size = 0.61).

Lazzer et al. (2014) analysed different physiological variables in experienced ultra-trail runners taking part in a three-day race of 93 km (*Magraid* race). They found that lower oxygen cost of transport was related to greater muscular power and a lower footprint index, which suggests that greater ankle stability is likely to contribute to better performance in an ultra-endurance event.

Giovanelli et al. (2017) carried out an experiment in which they divided the subjects into two groups. One group served as a control, while the other one performed strength, explosive and plyometric exercises in cycles of 4 weeks (Giovanelli et al., 2017). The main finding was that the experimental group had lower oxygen cost of transport for all the analysed speeds ($-6.4 \pm 6.5\%$, $p = 0.005$, ES: 0.43, small at $8 \text{ km}\cdot\text{h}^{-1}$; $-3.5 \pm 5.3\%$, $p = 0.032$, ES: 0.48, small at $10 \text{ km}\cdot\text{h}^{-1}$; $-4.0 \pm 5.5\%$, $p = 0.020$, ES: 0.34, small at $12 \text{ km}\cdot\text{h}^{-1}$; $-3.2 \pm 4.5\%$, $p = 0.022$, ES: 0.035, small at $14 \text{ km}\cdot\text{h}^{-1}$).

Fornasiero et al. (2018) analysed the physiological profile of 23 runners during a 65 km mountain ultra-marathon with 4000 m cumulative elevation gain. They concluded that generally, athletes performed the race at a mean intensity of 140 ± 8.6 bpm or $77.1 \pm 4.4\%$ of HR_{max} . Additionally, they observed that athletes ran at an average of $63.2 \pm 9.1\%$ of their $\text{VO}_{2\text{max}}$ and that the great majority of the race time was ran in the Zone I ($85.7 \pm 19.4\%$).

Balducci et al. (2017) studied different physiological characteristics in 26 well-trained runners participating in the *Interlacs Trail* (75 km). The results of this study showed that performance in a heterogeneous group was correlated mainly with: maximal aerobic velocity ($v\text{VO}_{2\text{max}}$), the fraction of $v\text{VO}_{2\text{max}}$ at which the race was

sustained, knee extensors force and force loss.

McKune et al. (2005) aimed to determine alterations in serum concentrations of immunoglobulin isotopes and subclasses after a 90 km ultra-marathon. They found that all serum immunoglobulin concentrations before and after the race were among clinical normal ranges. Individually speaking immunoglobulin D concentration decreased immediately after the race (-51%, $p = 0.04$) and 24 hours later (-41%, $p = 0.04$), but differences three hours after did not show significant changes ($p = 0.15$). Seventy-two hours after the race the concentrations had returned to baseline. Immunoglobulin M decreased significantly 24 hours after the race (-23%, $p = 0.04$). In contrast, Immunoglobulin G, increased (+12%, $p = 0.05$) immediately after the race and took between 24 to 72 hours to return to baseline values.

Knechtle et al. (2011a; 2011b) investigated the prevalence of exercise associated hyponatremia (EAH) in 145 male ultra-runners. Two of the finishers were classified as hyponatremic (1.4%), seven as hyponatremic (4.8%) and the remaining 136 as normonatremic (93.8%). Surprisingly, hyponatremic subjects did not drink more than non-hyponatremic subjects.

Noakes and Carter (1982) analysed changes in biochemical variables after a 56 km race in novice ($n = 5$) and experienced ($n = 18$) runners. The major finding was the difference between groups in plasma creatine kinase (CK) and aspartate aminotransferase (AST), with the non-experienced showing higher values for both measures. The only variable significantly higher in experienced runners was serum calcium.

Leonard and Leklem (2000) analysed plasma B₆ vitamin changes following a 50 km ultra-marathon. The main result of the study was a decrease in pyridoxal phosphate (PLP) concentration: 41.1 ± 14.2^{AB} (Pre-race), 28.2 ± 10.8^A (Post race) and 23.2 ± 9.9^B (Post 1 h) (A is significant to B, $p < 0.001$).

Schweltnus et al. (2011) analysed 49 runners participating in a 56-km race to identify the risk factors associated with muscle cramps (EAMC) in ultra-endurance runners. They found that runners within the EAMC group ran the first half of the race significantly faster (144.3 ± 20.2 min) than those in the CON group (157 ± 14.3 min; $p = 0.029$).

Cognitive limitations

Cona et al. (2015) explored cognitive functioning in athletes participating in the *Trans d'Havet* race (80 km), using two modified versions of two computerised tasks: the Inhibitory Control Task and a dual-task paradigm with emotional stimuli. They found that faster runners outperformed slower runners selectively in the *no-go* trials ($p < 0.001$), whereas they did not differ from slower runners in the *detect and go* trials. On the other hand, in the dual-task paradigm, authors reported that slower runners tended to have increased reaction times in ongoing trials when they had to monitor for pleasant and unpleasant prospective memory cues (both $p = 0.05$).

Neuromuscular and muscular limitations

Ker and Schultz (1996) hypothesised that increased demand on the respiratory muscles during an ultra-marathon could lead to prolonged fatigue. They measured the maximum inspiratory pressure (MIP) and values were compared to age matched normal individuals. The main result of the study was that no significant differences were found in MIP measured 3 days after the race between athletes that ran the race and age-matched individuals.

Discussion

The most important finding of this review is that a high-level performance in long-distance running is reliant on high VO_{2max} , high fraction of the VO_{2max} utilisation and low cost of oxygen transport. Similarly, it appears that around 50% of the increase in oxygen cost of transport during the stages of an ultra-marathon is related to changes in the footprint index (Lazzer et al., 2014). However, this contrasts with another study reporting that the cost of oxygen transport does not correlate with performance in ultra-endurance events (Balducci et al., 2017). Instead, other previous research suggests that the main performance limiting factor is vVO_{2max} (Balducci et al., 2017; Fornasiero et al., 2018). Similarly, it also seems that knee extensors force capability and fatigability appear to be determining factors considering ultra-endurance performance (Yokozawa et al., 2007).

Long endurance events lead to increases in pro-inflammatory markers and changes in endothelial function. This happens because of the

increased blood flow and shear stress in order to satisfy the increased oxygen demand of the heart and skeletal muscles (Chan-Dewar et al., 2010). Horita and Ishiko (1987) found a longer time from onset of the QRS complex to peak systole and early diastole after the race, with an increase in electromechanical delay. This could be due to

reduced skeletal muscle excitability, reduction in cytosolic Ca²⁺ concentration, reduced myofibrillar Ca²⁺ sensitivity and/or metabolic derangement. Chan-Dewar et al. (2010) proposed that the same mechanisms could be responsible for the myocardial delay.

Table 1

Physiotherapy Evidence Database (PEDro) ratings and Oxford evidence levels of the included studies.

Study	PEDro ratings*											Total	Evidence level
	1	2	3	4	5	6	7	8	9	10	11		
Sansoni et al. (2017)	yes	0	0	0	0	0	0	0	0	1	1	2	2b
Bonsignore et al. (2017)	yes	0	0	1	0	0	0	1	1	1	1	5	2b
Chan-Dewar et al. (2010)	yes	0	0	1	0	0	0	1	1	1	1	5	2b
Shave et al. (2002)	yes	0	0	1	0	0	0	1	1	1	1	5	2b
Da Ponte et al. (2018)	yes	0	0	0	0	0	0	1	1	0	1	3	2b
Martinez et al. (2018)	yes	0	0	0	0	0	0	1	1	0	1	3	2b
Rehrer et al. (1992)	yes	0	0	0	0	0	0	1	1	1	1	4	2b
Brown et al. (2011)	yes	0	0	1	0	0	0	1	1	1	1	5	2b
Lizzer et al. (2014)	yes	0	0	0	0	0	0	1	1	0	1	3	2b
Giovanelli et al. (2017)	yes	1	1	1	0	0	0	1	1	1	1	7	2b
Fornasiero et al. (2018)	no	0	0	0	0	0	0	1	1	1	1	4	2b
Balducci et al. (2017)	yes	0	0	0	0	0	0	1	1	1	1	4	2b
McKune et al. (2005)	yes	0	0	0	0	0	0	0	1	0	1	2	2b
Knechtle et al. (2011a)	yes	0	0	0	0	0	0	1	1	0	1	3	2b
Knechtle et al. (2011b)	yes	0	0	0	0	0	0	0	1	1	1	3	2b
Noakes et al. (1982)	yes	0	0	0	0	0	0	1	1	1	1	4	2b
Leonard and Leklem (2000)	yes	0	0	1	0	0	0	1	1	1	1	5	2b
Millet et al. (2002)	yes	0	0	0	0	0	1	1	1	1	1	5	2b
Cona et al. (2015)	yes	0	0	0	0	0	0	1	1	1	1	4	2b
Millet (2011)	no	0	0	0	0	0	0	0	0	0	0	0	5
Millet and Millet (2012)	no	0	0	0	0	0	0	0	0	0	0	0	5
Schwellnus et al. (2011)	yes	0	0	1	0	0	0	1	1	1	1	5	2b
Ker et al. (1996)	yes	0	0	0	0	0	0	1	1	1	1	4	2b

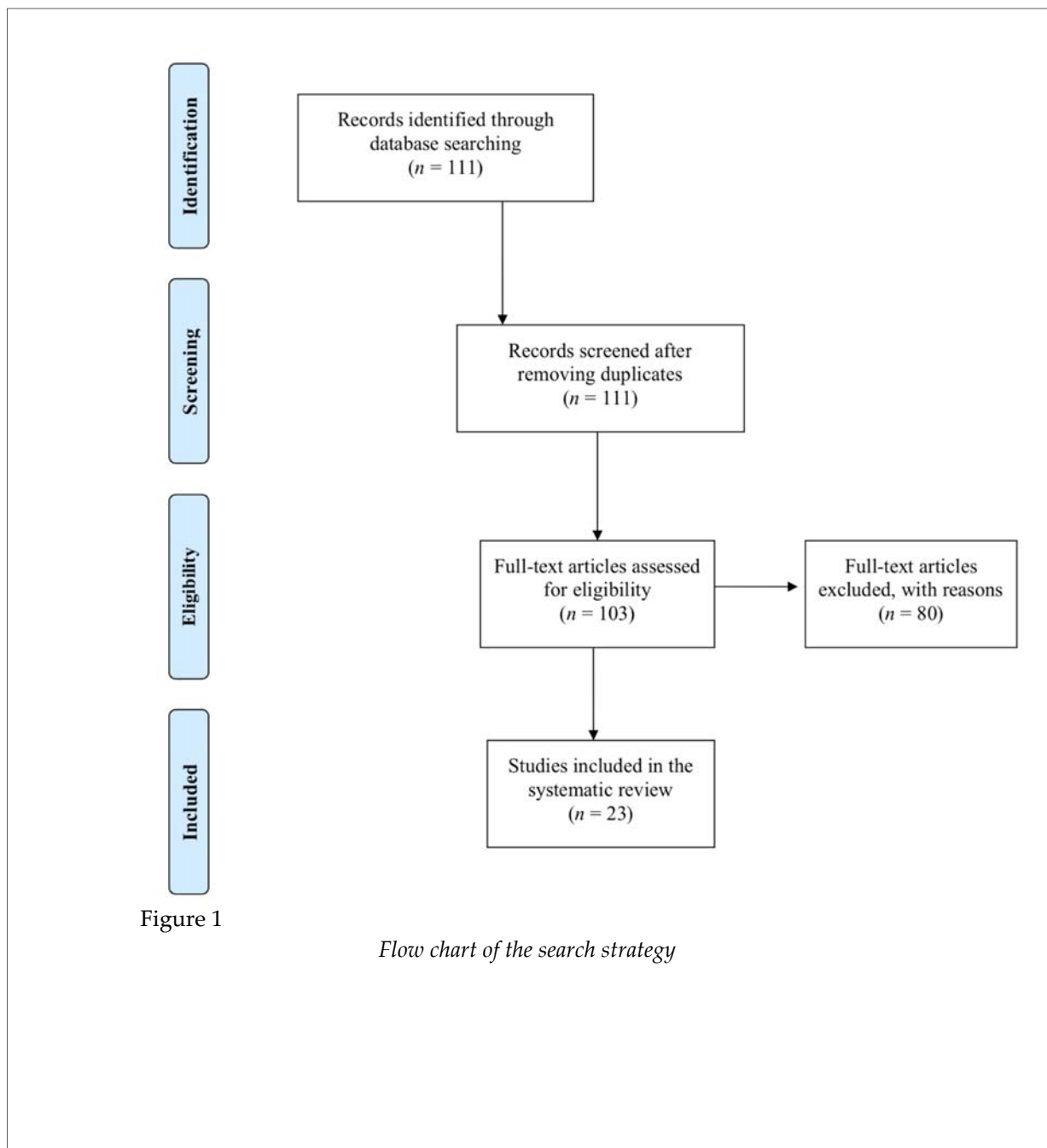
Items in the PEDro scale: 1 = eligibility criteria were specified; 2 = subjects were randomly allocated to groups; 3 = allocation was concealed; 4 = the groups were similar at baseline regarding the most important prognostic indicators; 5 = blinding of all subjects; 6 = blinding of all therapists who administered the therapy; 7 = blinding of all assessors who measured at least 1 key outcome; 8 = measures of 1 key outcome were obtained from 85% of subjects initially allocated to groups; 9 = all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least 1 key outcome were analysed by "intention to treat"; 10 = the results of between-group statistical comparisons are reported for at least 1 key outcome; 11 = the study provides both point measures and measures of variability for at least 1 key outcome.

Table 2

Included studies

Study	Number (M/F)	Age	Level	Main Outcome
Sansoni et al. (2017)	20 (20/0)	38.8 ± 7.2	E	Bone turnover
Bonsignore et al. (2017)	21 (15/6)	39.8 ± 8.3	WT	Arterial compliance
Chan-Dewar et al. (2010)	19 (16/3)	41 ± 9	WT	Electro-mechanical delay
Shave et al. (Study 1) (2002)	11 (11/0)	42 ± 11	WT	Cardiac disfunction and cTnT
Shave et al. (Study 2) (2002)	26 (26/0)	41 ± 10	WT	Cardiac disfunction and cTnT
Da Ponte et al. (2018)	22 (22/0)	46.1 ± 10.8	WT	Cardiac and muscle biomarkers
Martinez et al. (trail) (2018)	109 (98/11)	35 ± 8.4	WT	Macronutrient and water intake
Martinez et al. (marathon) (2018)	53 (41/12)	36.6 ± 8.0	WT	Macronutrient and water intake
Rehrer et al. (1992)	170 (158/12)	40 (M) / 35 (F)	WT	Gastro-intestinal disturbance
Brown et al. (TT) (2011)	21 (16/5)	38.5 ± 9.6	WT	COL5A1
Brown et al. (TC) (2011)	32 (25/7)	42.5 ± 9.3	WT	COL5A1
Brown et al. (CC) (2011)	18 (10/8)	40.6 ± 9.2	WT	COL5A1
Lazzer et al. (2014)	11 (11/0)	40.5 ± 8.4	E	Metabolic cost of transport
Giovanelli et al. (2017)	25 (25/0)	38.2 ± 7.1	WT	Strength training and Economy
Fornasiero et al. (2018)	23 (17/6)	40.2 ± 7.3	WT	Physiological profile
Balducci et al. (2017)	26 (26/0)	41.7 ± 9.5	WT	Performance factors
McKune et al. (2005)	11(6/5)	43 ± 10	E	Immunoglobulin types
Knechtle et al. (2011a)	95 (95/0)	44.5 ± 10.0	WT	Hyponatremia
Knechtle et al. (2011b)	157 (157/0)	45.7 ± 9.6	E	Hyponatremia
Noakes et al. (1982)	23 (Unkown)	28 ± 1 / 25 ± 4	E / N	Serum Biochemical parameters
Leonard and Leklem (2000)	11 (8/3)	43.7 ± 8.6	WT	Plasma B-6 vitamin
Millet et al. (2002)	9 (9/0)	41.6 ± 5.9	WT	Knee extensor fatigue
Cona et al. (2015)	30 (30/0)	43 ± 8.6	WT	Cognitive function
Millet (2011)	-	-	-	-
Millet and Millet (2012)	-	-	-	-
Schwellnus et al. (EAMC) (2011)	20 (19/1)	40.8 ± 11.7	WT	Muscle cramps
Schwellnus et al. (CON) (2011)	29 (23/6)	40.2 ± 9.2	WT	Muscle cramps
Ker et al. (1996)	10 (8/2)	38.2 ± 7.9	WT	Respiratory muscle fatigue

WT = Well-trained; E = Experienced; N = Novice



The same stress could cause some alterations in biomarkers as well. Da Ponte et al. (2018) reported that after an uphill ultra-marathon there was an increase in cardiac and skeletal muscle blood biomarkers of injury. They deduced that effort length and intensity prevailed over the contraction type. Cardiac muscle's behaviour during this uphill ultra-marathon, due to the predominance of repeated and simultaneous concentric contractions of the muscle, a higher cardiac afterload and vascular resistance,

resembled a higher-pressure situation (Kim et al., 2013). Cardiac troponin is a marker of cardiac damage, which means that an uphill ultra-marathon required a great effort from our body, regardless of age, training and performance status, but the increase in cardiac troponin does not seem to have any correlation with athletes' race times. In addition to this, Waśkiewicz et al. (2012) supported that after an ultra-marathon such as the 24 h Polish run, there was a remarkable effect on hypoxia-induced

biomarkers.

Another biomarker used is vitamin B₆, which is an important cofactor for enzymes involved in the conversion of amino acids to glucose (Leonard and Leklem, 2000). This vitamin has different forms, for example, pyridoxal 5'-phosphate. Leonard and Leklem's (2000) investigation is in contrast with other studies (Hofmann et al., 1991; Leklem and Shultz, 1983; Manore et al., 1987) that reported increased plasma pyridoxal 5'-phosphate post-exercise. The explanation for this apparent contradiction is that the experiment was much more stressful for the body than previous ones. During exercise muscle is the main source of vitamin B-6 and as the duration of exercise increases and the liver tends to increase gluconeogenesis, consequently requirements for the liver pyridoxal 5'-phosphate increase (Leklem and Shultz, 1983). Leonard and Leklem (2000) hypothesised that during endurance exercise the body's homeostatic control mechanism may be to release pyridoxal 5'-phosphate during the first moments of exercise for subsequent usage by the liver and/or muscle.

Ultra-endurance events also have been reported to lead to alterations in immunoglobulin levels. McKune et al. (2005) found that after an exercise bout, non-systemic immunoglobulins were flushed out of secondary lymph "storages" and/or entered the circulation because of the increased lymphatic flow. They noted that those increases in Immunoglobulin G concentration may be related to antibody switching. Yet immunoglobulin D measurements are not in agreement with Petibois et al. (2003). However, McKune et al. (2005) observed that during the early stages of the immunoglobulin response, small concentrations of Immunoglobulin D were found in plasma, as naive B cells underwent maturation and isotype switching from Immunoglobulin M to Immunoglobulin G. Thus, Immunoglobulin D represents a marker of naive B cells and if its concentration decreases it means the initiation of an immunoglobulin isotype switching.

Although physiological factors concerning ultra-marathon performance are important, there are more factors to consider. Outstanding athletes are more able to make decisions and extrapolate relevant information in order to anticipate future events and outcomes

(Williams et al., 1999). Overall, the external focus of attention appears to be more beneficial for a successful performance (Castaneda and Gray, 2007). For all these reasons, Cona et al. (2015) performed a test to assess the cognitive functioning of runners. Their results showed that faster runners had a greater capacity to inhibit a dominant, but inappropriate, response. Thus, they had enhanced motor inhibition, and that might be crucial for performance. Motor inhibition may play a key role in some physical skills, such as agility for example (Verburgh et al., 2014).

Magnitude and cause of fatigue depend on the exercise under consideration (Enoka and Stuart, 1992). Alterations in neuromuscular function produced by prolonged running, cycling and skiing were reviewed by Millet and Lepers (2002, 2004). They focused on the strength loss in knee extensors after exercise bouts lasting from 30 minutes to several hours and they found that isometric strength loss happened in a non-linear manner. Less is known about the decrease in peak power, but it has been reported that the decrease in counter-movement jump performance was around 45-60% of the knee extensors isometric MVC decrease after prolonged running (Millet et al., 2000, 2002; Petersen et al., 2007). Central fatigue largely contributes to muscle fatigue during long distance running (Martin et al., 2010; Millet et al., 2000, 2003; Racinais et al., 2007; Saldanha et al., 2008). Millet (2011) proposed what he called "*The Flush Model*", in order to explain how neuromuscular fatigue works. According to that author, during a self-paced 24 h treadmill run, the power output decreases during the first 16 h, and after that it remains stable (Millet, 2011). The level of muscle activation is thought to be progressively reduced to maintain the RPE below the maximum tolerated level (Millet, 2011).

The Flush Model was created to explain fatigue in ultra-marathon running and it consists of four components: (i) a ball that represents the RPE and can increase or decrease based on (ii) the filling rate and the water evacuated via (iii) a waste pipe. Finally, there is a (iv) security reserve too.

The filling rate is influenced by several factors, such as the running pace at the beginning of the race. Basically this initial pace gives an initial filling rate and the faster the speed, the faster the filling rate (Ulmer, 1996). The volume of

water in the tank does not only depend on the filling rate, because it is possible to start running with more water in the tanks than usual (i.e. with a higher RPE) if athletes had not had enough rest during the night before the race, which according to Millet (2011), is one of the most effective ways to reduce the RPE, together with psychological (Raglin, 2007) and even nutritional strategies (Millet, 2011). Lastly, regarding the security reserve and why runners decide to adjust intensity, athletes decide to stop when the task is too difficult or demands too much effort (Noakes et al., 2005).

Conclusion

The findings of this review suggest that fatigue during ultra-endurance events is a multifactorial phenomenon that includes physiological, neuromuscular, biomechanical and cognitive factors. On the other hand, improved exercise performance during ultra-endurance events seems to be related to higher $\text{VO}_{2\text{max}}$ values and $v\text{VO}_{2\text{max}}$ (especially during submaximal efforts sustained over a long time), lower oxygen cost of transport and greater running experience.

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Corresponding author:

Dr. Jordan Santos-Concejero,

Faculty of Education and Sport, Department of Physical Education and Sport,
University of the Basque Country UPV/EHU,
Portal de Lasarte 71, 01007, Vitoria-Gasteiz, SPAIN.
Telephone: +34 945013538
E-mail: jordan.santos@ehu.eus