Differences in time to task failure and fatigability between children and young adults: A systematic review and meta-analysis.

Robin Souron[1,2], Marion Carayol[1], Vincent Martin[3,4], Enzo Piponnier[5], Pascale Duché[1], Mathieu Gruet[1]

[1] *Université de Toulon, Laboratoire IAPS (n°201723207F), Toulon, France*
[2] *Nantes Université, Movement - Interactions - Performance, MIP, UR 4334, F-44000 Nantes, France*
[3] *Université Clermont-Auvergne, Laboratoire AME2P (EA 3533), Clermont-Ferrand, France*
[4] *Institut Universitaire de France, Paris, France*
[5] *Université Côte d'Azur, LAMHESS (EA 6312), Nice, France*

All authors have read and approved this version of the manuscript. This article was last modified on 20th Jan 2022

For correspondence:
Robin.souron@univ-nantes.fr
Twitter: @RobinSouron

THIS IS A PREPRINT, NOT PEER REVIEWED, VERSION.

Please cite as: Souron, R., Carayol, M., Martin, V., Piponnier, E., Duché, P., & Gruet, M. (2022). Differences in time to task failure and fatigability between children and young adults: A systematic review and meta-analysis.

Abstract

Background. The transition from childhood to adulthood is characterized by many physiological processes which can impact physical exercise performance. Performance fatigability (i.e. decline in an objective measure of performance during and/or after exercise) and time to task failure (i.e. capacity for a participant to perform an exercise over an extended period of time until failure; TTF) are commonly used to capture exercise performance.

Objective. To determine the differences in fatigability and TTF between youth (including both children and adolescents, < 18 years old) and young adults, and to evaluate the influence of exercise modalities (i.e. exercise duration and type of exercise) on these potential differences.

Methods. Medline, SPORTDiscus and Cochrane Library were searched. The combination of terms related to the intervention (e.g. whole-body or isometric exercise), population (e.g. child, adolescent) and outcomes (e.g. fatigability, TTF) were used. This meta-analysis was registered on PROSPERO (CRD42020184549).

Results. Thirty-four studies were included. The meta-analyses revealed that both children (SMD –1.15; 95% CI –1.64 to –0.66; p < 0.001) and adolescents (SMD –1.26; 95% CI –2.34 to –0.18; p = 0.022) were less fatigable than adults. A subgroup meta-analysis revealed that children were less fatigable than adults during dynamic exercises (SMD –1.58; 95% CI –2.08 to –1.08; p < 0.001) with no differences during isometric ones (SMD –0.46; 95% CI –1.19 to 0.27; p = 0.22). While children had longer TTF than adults (SMD 0.89; 95% CI 0.15 to 1.63; p = 0.018), it was not the case for adolescents (SMD 0.75; 95% CI –0.12 to 1.62; p = 0.090). Subgroup meta-analyses revealed i) that children had longer TTF than adults for isometric (SMD 1.25; 95% CI 0.60 to 1.90; p < 0.001) but not dynamic exercises (SMD –0.27; 95% CI –2.82 to 2.28; p = 0.83), and ii) that TTF differences between children and adults were larger for short- (SMD 1.46; 95% CI 0.16 to 2.76; p = 0.028) than long-duration exercises (SMD 0.20; 95% CI –0.66 to 1.07; p = 0.64).

Conclusion. Children have higher endurance and are less fatigable than adults. These differences are influenced by the exercise modality, suggesting distinct physiological functioning during exercise between children and adults. The low number of studies comparing these outcomes between adolescents and adults prevents robust conclusions and warrants further investigations in this specific population.

1 – INTRODUCTION

There has been a growing interest in recent decades for the evaluation of exercise-induced fatigue in children, with numerous reports investigating potential child-adult differences regarding its magnitude and etiology [1, 2].

Fatigue is a multifactorial and complex concept, and a new taxonomy has been recently proposed to acknowledge some of its attributes that are performance and perceived fatigability. Those two attributes are closely interrelated and inseparable [3, 4]. Performance fatigability refers to a decline in an objective measure of performance (e.g. muscle force or power) during and/or after a given exercise while perceived fatigability refers to any detectable changes at rest or during exercise that regulate the integrity of the participant, e.g. motivation, pain [5]. Although linked but not interchangeable, fatigability should not be confused with another commonly-used term when exercise-induced fatigue is investigated, i.e. time to task failure (TTF). This term refers to the capacity for a subject to perform an exercise at a given percentage of a maximal parameter (e.g. muscle force, maximal aerobic power) over an extended period of time until failure.

Over the last three decades, several studies investigated differences in TTF (e.g. [6-13]) and fatigability (e.g. [9, 12, 14-17]) between youth (that considers both children and adolescents) and adults. Of note, the current literature has rarely considered the adolescents *versus* children and/or adults comparison for the evaluation of fatigability. While it seems that children and adolescents have lower level of fatigability and longer TTF than adults, the lack of consistency in the experimental procedures prevent an appropriate interpretation of the data. For instance, while some studies used experimental designs where the exercise duration (or the number of contractions in the case of intermittent exercises) was fixed, e.g. a 30-s sustained maximal voluntary contraction (MVC) [14, 18-21], many other studies used protocols with a pre-set amount of fatigue, e.g. the exercise stopped when the subject reached a decrease of 40% of the baseline force level [9, 13, 22-26], thus preventing any comparison of fatigability between youth (including both children and adolescents) and adults. Then, to allow a reliable comparison for the level of fatigability between youth and adults, studies should report an "isotime" measurement that includes only the portion of the fatiguing exercise that is available for all the subjects being analyzed, which is limited by the subject with the shortest TTF [27]. This specific method of analysis allows to compare youth *versus* adults at a similar exercise duration, without any consideration of the total TTF that could largely differ between these two populations [6, 9, 22-25, 28].

While various fatiguing protocols have been used to assess either TTF and/or fatigability in youth and adults, one should note that the exercise modality may influence the reported differences in these two concepts when these two populations are compared. First, the type of exercise, i.e. dynamic (e.g. cycling, running, jumping, isokinetic contractions) *versus* isometric exercises, should be considered when looking at potential between-group differences in fatigability and/or TTF. This issue has not been directly addressed so far and a critical review of the literature could help to better understand how the type of exercise could influence the potential differences in fatigability and TTF between youth and adults. This is an important question since large differences in physiological demands exist between these two types of exercise. For instance, performing either a dynamic or isometric exercise may modulate the influence of blood flow occlusion on exercise performance. Intramuscular pressure is dramatically increased during isometric compared to dynamic exercises [29]. This could lead to large variations in the stimulation of type III/IV metabo-nociceptive afferents, which project their inputs to various sites within the central nervous system then modulating exercise performance [30, 31]. The consideration of two populations with fundamental differences in physiological functioning [1, 32] may exacerbate the effect that blood flow occlusion may have on the level of fatigability and TTF depending on the type of exercise that is used. For instance, large differences in muscle mass may have a direct impact on intramuscular pressure and blood flow occlusion during exercise. Second, one may question the influence that exercise duration could have in the differences in TTF and fatigability between youth and adults, i.e. do differences in TTF and/or fatigability between children and adults are greater or lower for short or long-duration exercises? Indeed, exercise duration could influence the mechanisms responsible for impairments in exercise performance [33]. Longer exercise duration usually leads to a larger magnitude of fatigability (e.g. greater loss of maximal force), as reported for instance in running exercises [34]. Because the contribution of each energy systems (i.e. aerobic *versus* anaerobic metabolisms) in exercise performance may differ between youth and adults [35], it is tempting to suggest that differences in fatigability and TTF between youth and adults may be influenced by exercise duration. Such a question has never been studied so far, and a quantitative analysis of the current literature could help to shed light on this specific point.

The primary purpose of this study is to systematically review the literature regarding the differences in performance fatigability and TTF between youth (including children and adolescents) and young adults (18–35 years old) and to assess the influence of exercise modalities on these outcomes. The secondary aim of this review is to identify the physiological mechanisms underlying the reported differences between youth and adults, based on neuromuscular evaluation (i.e. central and peripheral components of fatigue).

2 – METHODS

2.1 – Literature search strategy

We looked for cross-sectional and longitudinal studies that compared TTF and fatigability between youth (i.e. including both children and adolescents) and young adults (18–35 years old). A distinction is made throughout the manuscript between children and adolescents, with the former and the latter referring to prepubescent and pubescent young individuals, respectively. We made this distinction based on objective criteria displayed in the articles, e.g. Tanner classification and/or peak height velocity. When no objective criteria were given, we arbitrary classified the data in the children category (knowing that it could include both prepubescent and pubescent young individuals). We used the following electronic databases: Medline (via PubMed), SPORTDiscus and Cochrane Library. Each database was searched from inception until June 5th, 2020. The search was conducted by combining terms related to the intervention (e.g. whole-body or isometric exercises), population (e.g. child, adolescent, prepubertal, pubertal) and outcomes (e.g. fatigability, isometric and/or dynamic force, power, endurance, number of contractions, time to exhaustion). There was a language restriction (English or French) and only accepted or published studies were considered. Details of the protocol and search strategy (see Document, Electronic Supplementary Material 1) for this systematic review were registered on PROSPERO (CRD42020184549).

2.2 – Selection of studies

The initial search was performed by two authors (RS and MG). The first step consisted in screening titles and abstracts. The articles that were judged to be outside the scope of this meta-analysis were removed. Following this first screening, and in the case the abstracts did not provide enough information, two authors (RS and MG) independently selected and reviewed all included articles. At this point, all duplicate studies were removed. The articles that met the inclusion criteria were read and eligible studies were included in the meta-analyses (Figure 1). Disagreements were solved by a third author (PD).

2.3 – Eligibility criteria – inclusion and exclusion

Studies were considered for review if they met the following PICOS criteria (i.e. Population, Intervention; Comparison group; Outcomes; Study type): i) comparison between youth (< 18 yrs) and adults (18–35 yrs); ii) existence of a fatiguing exercise protocol (i.e. dynamic or isometric); iii) assessment of fatigability (i.e. evaluated by changes in muscle force and/or power and/or velocity after the fatiguing exercise) and/or TTF (i.e. evaluated by a TTF in the case of continuous exercises or a number of repetitions in the case of intermittent exercises); iv) cross-sectional and longitudinal studies (in the case of longitudinal studies that assessed the effect of a training intervention, only baseline data were included). The exclusion criteria were the following: i) lack of a comparison group (i.e. adult group); ii) absence of investigation of the main outcomes of interest for the meta-analysis (i.e. isometric or dynamic muscle force, power output, maximal velocity, TTF, number of contractions); iii) adult group older than 35 years; iv) any publications written in another language than English or French.

2.4 – Quality assessment

The methodological quality assessment of all studies included in the meta-analysis was performed with a modified Newcastle-Ottawa Quality Assessment Scale for cross-sectional studies. This scale is based on three broad criteria that are specific to the study design, i.e. i) selection of study groups; ii) comparability and iii) outcome assessments. Similarly to a recent meta-analysis that investigated the differences in fatigability between healthy young and old subjects [36], we modified the original quality scale to meet the needs of our study design (see Document, Electronic Supplementary Material 2). First, the selection domain presents three sub-categories, i.e. the representativeness of the sample (is the sample representative of the average in the target population or was it a sample from selected group of users?), the sample size (is there a justification for sample size calculation?) and the ascertainment of participants' health status (is the participants' health status checked with medical report or specific questionnaire or is the participants' health status only basically reported?). As performed by Kruger et al. [36], the ascertainment of exposure section from the original scale has been adapted to our study design to have information on participants' health status. Second, the comparability domain allowed us to control for physical activity and fitness levels and to control for any additional factors that could have impacted the main outcomes (e.g. caffeine and alcohol consumption, strenuous physical activity before physical testing). Third, the outcome domain presents two sub-categories, i.e. the assessment of the main outcomes (are the main outcomes obtained after reliable fatiguing protocol and using validated measuring tools?) and the statistical test (is the statistical test used to analyze the data clearly described and appropriate?). The quality of the paper was rated by stars, ranking from zero to four for the selection domain, zero to two for the comparability domain and zero to three for the outcome domain, for a maximum of nine stars. The global quality scores were calculated based on the scoring algorithm proposed by McPheeters, Kripalani [37].

2.5 – Data extraction

For all studies included in the meta-analysis, study characteristics (i.e. authors, year, sample size, study design), participant demographics (i.e. age, sex), fatiguing exercise details (i.e. isometric or dynamic fatiguing task, muscle(s) involved in the exercise) and main outcomes (i.e. muscle force and/or power and/or velocity, TTF, number of contractions) were retrieved on a standardized Excel sheet. Corresponding authors were contacted when data were missing. Different meta-analyses were performed for the main outcomes (see the sections below).

2.5.1 – Time to task failure.

The first meta-analyses compared TTF between children *versus* adults and adolescents *versus* adults. In the case of sustained prolonged exercises, the total time (in sec) was extracted for further analysis. In the case of intermittent exercises, and if the article only reported the total number of contractions until task failure, the data were extracted and transformed in time units (i.e. seconds). The resting time allowed between each intermittent contraction (e.g. 5 s ON/5 s OFF) was included in the calculation to obtain the total exercise duration. If these information (i.e. number of contractions, duration of the contraction, resting time allowed between contractions) were missing, the article was not included in these meta-analyses. Further, studies were excluded if the exercise was performed with a fixed duration (e.g. a sustained submaximal isometric contraction for 10 min) or a fixed number of contractions (e.g. 50 intermittent contractions with 5 s ON/5 s OFF). When more than one fatiguing exercise was performed in a similar study (e.g. sustained contraction at 20 and 60% MVC), the data obtained during the longest exercise was kept for quantitative analysis.

2.5.2 – Performance fatigability.

Additional meta-analyses compared the indices of fatigability (i.e. muscle force, power and/or velocity) between children *versus* adults and adolescents *versus* adults. The analyses were only performed for data extracted from studies that used an experimental design where the exercise duration or the number of contractions were fixed (e.g. a sustained maximal isometric contraction maintained for 2 min or a similar number of intermittent contractions performed by participants over a similar period of time). When a study did not meet these criteria (e.g. a study where exercise termination was set to a 30% decrease in maximal force, independently of the time to reach this target), the authors were contacted to know if they performed an "isotime" comparison (i.e. the analysis that includes only the portion of the exercise that is available for all the participants in the groups being analyzed, which is limited by the participant with the shortest TTF; [27]), or if they were willing to perform such analyses. In such case, these data were included in the meta-analyses. Otherwise, the article was excluded from the meta-analyses. Because huge differences exist in baseline maximal muscle force and power between children and adults, these meta-analyses solely included the studies that reported relative data (i.e. when the changes at the end of the fatiguing exercise were expressed as a percentage of the baseline value). When only absolute data (i.e. Newton for muscle force and Watts for muscle power) were reported, we contacted the authors and asked them to provide the relative data.

2.5.3 – Exercise modalities.

Separate subgroup meta-analyses were performed to investigate the potential influence of exercise modality on the reported differences in TTF and fatigability between children and adults (because of a too low number of studies, these analyses were not performed for the adolescents *versus* adults comparison). For that purpose, we dissociated the type of exercises that were performed, i.e. isometric *versus* dynamic (e.g. running, cycling, jumping, isokinetic contraction), to investigate its influence on the potential differences in fatigability and TTF between children and adults. We also investigated the potential influence of exercise duration on child-adult differences in TTF and fatigability. For this purpose, the median was calculated and the studies were classified either as long (i.e. duration > median) or short (i.e. duration < median) duration. The study with the duration equal to the median [24] was excluded for this subgroup analysis, thus 14 studies were included.

2.5.4 – Peripheral and central components of fatigue.

When available, data on central and peripheral factors of fatigue were also extracted as secondary outcomes to shed light on the potential differences in TTF and fatigability between children and adults. The following parameters were considered to investigate central factors of fatigue: i) voluntary activation level (VA), consisting in an electrical/magnetic stimulation superimposed to a maximal voluntary contraction (both the interpolated twitch technique and the central activation ratio were considered), ii) normalized electromyographic (EMG) signals recorded during a maximal force; iii) transcranial magnetic stimulation (TMS)-related parameters, i.e. motor evoked potentials (MEP, amplitude and/or area) and silent period duration to investigate corticospinal excitability and inhibition, respectively; iv) H- and T-reflexes to investigate spinal excitability. The following parameters were considered to investigate peripheral factors of fatigue: i) peak twitch (Pt) and doublet (Db), i.e. the mechanical response to a single or double electrical and/or magnetic stimulation, with its associated characteristics (e.g. half relaxation time, time to Pt) also being considered; ii) M-wave amplitude and/or area, i.e. the EMG response to a single electrical and/or magnetic stimulation; iii) low-to-high frequency fatigue ratio (LHF_R), i.e. the ratio of peak forces evoked by low and high-frequency doublets or stimulation trains (e.g. the ratio between Db evoked at 10 and 100 Hz).

2.6 – Data analysis

Descriptive statistics (mean, median, range) were used to describe studies characteristics and methodological quality of all the included studies.

Hedges' g were calculated [38] as the measure of standardized mean difference (SMD), i.e. the difference between the outcome mean values of the children or adolescents and the adult group divided by the pooled standard deviation [38, 39]. A negative SMD indicates less fatigability or TTF in children, whereas a positive SMD represents greater fatigability or TTF in adults. To assess the difference in outcomes of interest between children and adults, effect sizes were estimated by weighting SMDs by the inverse of their variance based on random effects models [40].

Heterogeneity was tested with Cochran's chi-square test (Q) to assess the consistency of associations. To quantify the extent of heterogeneity, we estimated the between-study variance (I^2). I^2 statistic describes the proportion of variability in SMDs due to the heterogeneity between studies ranging from 0% to 100% (with small heterogeneity: < 25%; moderate: 25 to 50%; high: ≥ 50%). Because heterogeneity was high ($I^2 > 50\%$), random effect models were used to incorporate heterogeneity in meta-analyses [41].

In addition, effect sizes were computed for subgroups of included studies based on dichotomized identified exercise modalities that may impact our main outcomes, i.e. type (isometric *versus* dynamic) and duration of exercise (< median *versus* ≥ median duration across studies). Publication bias was searched by funnel plot representation and Egger's [42] and Begg's [43] tests with $p < 0.10$ taken as an indication of publication bias. All statistical analyses were carried out by using Stata software version 11 (StataCorp, College Station, TX, USA).

3 – RESULTS

The process of study identification, screening, and evaluation of the eligibility of included studies is displayed by the PRISMA flow chart (Figure 1). The initial searches provided a total of 4468 articles. Following the removal of duplicates, the titles and abstracts of the remaining

3964 records were screened, with 3871 being excluded at this stage for not meeting the inclusion criteria. Then, full texts of 93 records were assessed for eligibility with a further 59 of these being removed for various reasons (i.e. lack of main outcomes, lack of adult group, same data set, inappropriate fatiguing exercise, no access to the full version of the article, lack of information that includes for instance studies reported only absolute rather than relative data for the fatigability domain). This leaves 34 records that were included in the meta-analyses. A detailed description of the characteristics of the meta-analyzed studies that investigated differences in TTF and fatigability between children, adolescents and adults is given in Tables 1 and 2, respectively.

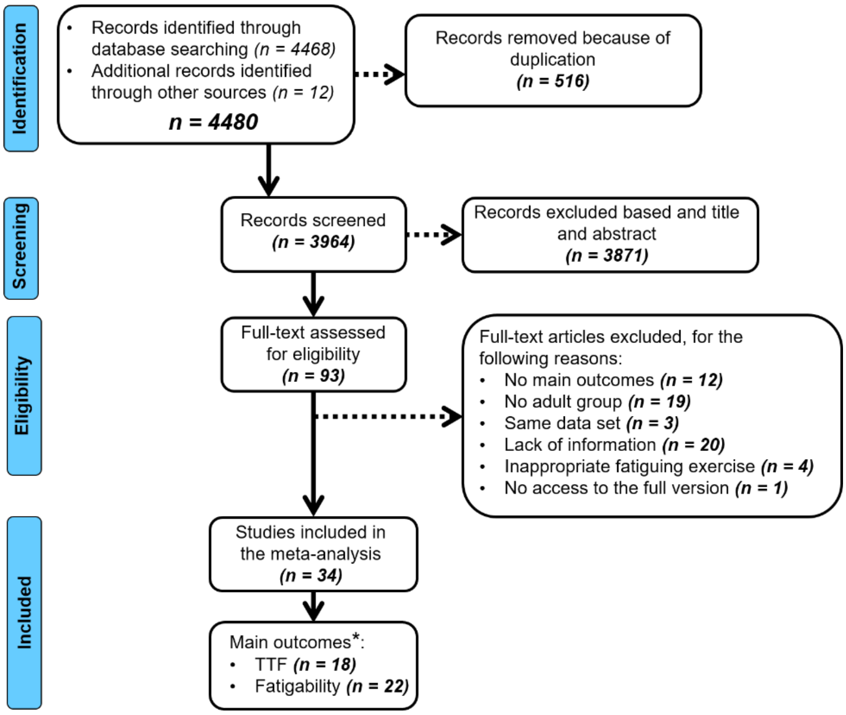

Fig. 1 PRISMA flowchart of included studies. **Some articles investigated TTF and fatigability in the same experimental design and were included in both meta-analyses.*

Table 1 Study characteristics – Fatigability

Study	Participant's age (n)			Fatiguing exercise *(criteria for exercise ending)*	Main outcome (investigated muscle)	% decrease			Statistical significance
	Ch	Ado	Adu			Ch	Ado	Adu	
ISOMETRIC EXERCISE									
Bontemps et al. [23]	10 (18)	–	22 (19)	5 s MVC/5 s rest *(↓ of 40% MVC)*	I_{MVC} (KE)	**38**	**–**	**49**	S
Halin et al. [21]	11 (15)	–	22 (12)	30-s sustained MVC	I_{MVC} (EF)	**29**	**–**	**35**	S
Hatzikotoulas et al. [19]	10 (15)	–	24 (15)	10-min sustained 20% MVC	I_{MVC} (PF)	**24**	**–**	**26**	NS
Piponnier et al. [26]	10 (19)	–	22 (23)	5 s MVC/5 s rest optimal length *(↓ of 40% MVC)*	IMVC (PF)	**36**	**–**	**22**	S
				5 s MVC/5 s rest long length *(↓ of 40% MVC)*		**34**	**–**	**25**	S
				5 s MVC/5 s rest short length *(↓ of 40% MVC)*		**35**	**–**	**26**	S
Piponnier et al. [25]	10 (22)	–	21 (22)	5 s MVC/5 s rest optimal length *(↓ of 40% MVC)*	I_{MVC} (KE)	**25**	**–**	**34**	S
				5 s MVC/5 s rest long length *(↓ of 40% MVC)*		**27**	**–**	**23**	NS
				5 s MVC/5 s rest short length *(↓ of 40% MVC)*		**24**	**–**	**22**	NS
Piponnier et al. [24]	10 (9)	14 (8)	24 (11)	5 s MVC/5 s rest *(↓ of 40% MVC)*	I_{MVC} (KE)	**20**	**25**	**32**	S
Ratel et al. [28]	10 (11)	–	24 (12)	5 s MVC/5 s rest *(↓ of 40% MVC)*	I_{MVC} (KE)	**22**	**–**	**30**	S
Willcocks et al. [17]	–	13 (6)	29 (6)	30 × 6 s MVC	I_{MVC} (KE)	**–**	**23**	**31**	NS
DYNAMIC EXERCISE									
Äyrämö et al. [48]	12 (8)	15 (8)	21 (8)	50-s all out run	I_{MVC} (PF)	**3**	**+7**	**16**	NS (Ch vs Adu) S (Ado vs Adu)
Birat et al. [50]	10 (12)	–	21 (12)	30-s Wingate test	MP (LL)	**35**	**–**	**52**	S
Bucheit et al. [88]	10 (10)	15 (6)	20 (7)	10 × 10-s all-out cycling sprint	MP (LL)	**6**	**6**	**5**	NS
De Ste Croix et al. [51]	12 (16)	–	30 (24)	50 CONC MVC	D_{MVC} (KE)	**39**	**–**	**60**	S
Dipla et al. [52]	11 (10)	15 (10)	24 (10)	4 × 18 KE-KF CONC MVC	D_{MVC} (KE)	**9**	**16**	**29**	S (Ch & Ado vs Adu)
					D_{MVC} (KF)	**NC**	**15**	**23**	S (Ch vs Ado & Adu)
Ftikas et al. [53]	10 (11)	–	24 (11)	10 × 10 max vertical jumps	I_{MVC} (KE)	**13**	**–**	**18**	S
Gorianovas et al. [18]	12 (11)	–	21 (11)	100 max drop jumps	I_{MVC} (KE)	**22**	**–**	**36**	NR
Hebestreit et al. [54]	10 (8)	–	22 (8)	30-s Wingate test	MP (LL)	**44**	**–**	**52**	S
Kanehisa et al. [95]	–	14 (26)	18-25 (27)	50 CON MVC	D_{MVC} (KE)	**–**	**36**	**48**	S
Lazaridis et al. [14]	10 (13)	–	25 (13)	10 × 10 max CMJ	I_{MVC} (KE)	**12**	**–**	**18**	S
Liamopoulou et al. [55]	10 (12)	–	25 (12)	10 × 10 max plyometric jumps	I_{MVC} (KE)	**14**	**–**	**22**	S

Marginson et al. [56]	10 (10)	–	22 (10)	8 × 10 max plyometric jumps	I_{MVC} (KE)	**14**	**–**	**26**	S
Pullinen et al. [16]	–	14 (6)	27 (6)	5 × 10 contractions 40% RM	I_{MVC} (KE)	**–**	**15**	**25**	NS
Weinstein et al. [57]	10 (11)	–	20 (10)	30-s Wingate test	MP (LL)	**33**	**–**	**47**	S

Data presented in bold black were given as relative results (PRE-POST changes in % of PRE) in the published article. Data presented in bold blue were calculated by the authors from the absolute results given in the article. In the cases where data were not fully presented in the manuscript, data were extracted from original figures using ImageJ software (ImageJ V.1.45 s, National Institute of Health, MD, USA).

Ado: adolescents; Adu: adult; BP: bench press; Ch: children; CON: concentric; D_{MVC}: dynamic maximal voluntary contraction; ECC: eccentric; EF: elbow flexors; I_{MVC}: isometric maximal voluntary contraction; KE: knee extensors; KF: knee flexors; LL: lower limbs; MP: muscle power; MVC: maximal voluntary contraction; n: number of participants; NC: no change; NR: not reported; NS: nonsignificant (i.e. $p > 0.05$); PF: plantar flexors; RM: maximum repetition; S: statistically significant (i.e. $p < 0.05$).

Table 2 Study characteristics – Time to task failure

Study	Ch	Ado	Adu	Fatiguing exercise *(criteria for exercise ending)*	Muscle group	Ch	Ado	Adu	Statistical significance
ISOMETRIC EXERCISE									
	Participant's age (n)					TTF (in s)			
Armatas et al. [22]	10 (13)	–	26 (13)	5 s MVC/5 s rest *(↓ of 50% MVC)*	KE	**563**	**–**	**348**	S
Bontemps et al. [23]	10 (18)	–	22 (19)	5 s MVC/5 s rest *(↓ of 40% MVC)*	KE	**404**	**–**	**159**	S
Hatzikotoulas et al. [9]	11 (10)	–	26 (11)	Sustained MVC *(↓ of 50% MVC)*	PF	**127**	–	**94**	S
Patikas et al. [12]	10 (14)	–	24 (14)	Sustained 20% MVC *(5 s < 95% target force)*	PF	**771**	–	**786**	NS
				Sustained 60% MVC *(5 s < 95% target force)*		**195**	–	**201**	NS
Piponnier et al. [26]	10 (19)	–	22 (23)	5 s MVC/5 s rest optimal length *(↓ of 40% MVC)*	PF	**156**	**–**	**135**	NS
				5 s MVC/5 s rest long length *(↓ of 40% MVC)*		**120**	**–**	**130**	NS
				5 s MVC/5 s rest short length *(↓ of 40% MVC)*		**170**	**–**	**160**	NS
Piponnier et al. [25]	10 (22)	–	21 (22)	5 s MVC/5 s rest optimal length *(↓ of 40% MVC)*	KE	**397**	**–**	**148**	S
				5 s MVC/5 s rest long length *(↓ of 40% MVC)*		**295**	**–**	**158**	S
				5 s MVC/5 s rest short length *(↓ of 40% MVC)*		**337**	**–**	**409**	NS
Piponnier et al. [24]	10 (9)	14 (8)	24 (11)	5 s MVC/5 s rest *(↓ of 40% MVC)*	KE	**529**	**426**	**266**	S (Ch & Ado vs Adu)
Ratel et al. [28]	10 (11)	–	24 (12)	5 s MVC/5 s rest *(↓ of 40% MVC)*	KE	**495**	**–**	**340**	S
Tanina et al. [10]	9 (14)	–	25 (14)	Sorensen back test *(> 2 cm reduction in height for 2 s)*	TE	**95**	**–**	**98**	NS
Woods et al. [47]	10 (18)	–	24 (21)	Intermittent 5 s submaximal contractions *(volitional exhaustion)*	KE	**688**	**–**	**632**	NS
Woods et al. [46]	10 (17)	–	24 (17)	Intermittent 5 s submaximal contractions *(volitional exhaustion)*	KE	**608**	**–**	**560**	NS
DYNAMIC EXERCISE									
Bar Yoseph et al. [7]	11 (18)	17 (18)	29 (8)	Incremental cycling exercise *(cadence < 60 rpm)*	LL	**670**	**692**	**690**	NS
				Incremental running exercise *(volitional exhaustion)*		**700**	**951**	**1013**	S (Ado & Adu vs Ch)
Berthoin et al. [8]	11 (9)	–	22 (8)	Cycling at 120% PMA *(volitional exhaustion)*	LL	**53**	–	**122**	S
Leclair et al. [11]	10 (15)	–	24 (15)	Constant load cycling exercise P50 *(cadence < 70 rpm)*	LL	**702**	**–**	**754**	NS
				Constant load cycling exercise P75 *(cadence < 70 rpm)*		**307**	**–**	**371**	
				Constant load cycling exercise P100 *(cadence < 70 rpm)*		**144**	**–**	**221**	S
				Constant load cycling exercise P110 *(cadence < 70 rpm)*		**96**	**–**	**147**	S
Murphy et al. [15]	10 (10)	–	26 (10)	3 × max CON MVC Low RM *(volitional exhaustion)*	KE	**274**	**–**	**253**	S
				3 × max CON MVC High RM *(volitional exhaustion)*		**213**	**–**	**193**	
Pullinen et al. [16]	–	14 (8)	31 (8)	3 × max contractions at 40% RM *(volitional exhaustion)*	KE	**–**	**48**	**48**	NS

Pullinen et al. [44]	–	14 (6)	27 (6)	1 × max contractions at 40% RM *(volitional exhaustion)*	KE	**–**	**46**	**42**	NS
Tibana et al. [45]	–	15 (15)	22 (15)	3 x max chest press w/ 30 s rest *(volitional exhaustion)*	UL	**–**	**96**	**88**	S
				3 x max chest press w/ 60 s rest *(volitional exhaustion)*		**–**	**163**	**156**	S
				3 x max chest press w/ 120 s rest *(volitional exhaustion)*		**–**	**292**	**282**	S

Data presented in bold black were directly given in time units (seconds) in the article. Data presented in bold blue were calculated by the authors from the number of contractions performed during the fatiguing exercise.

Ado: adolescents; Adu: adult; Ch: children; CON: concentric; KE: knee extensors; KF: knee flexors; LL: lower limbs; MVC: maximal voluntary contraction; n: number of participants; NS: nonsignificant; P50 and P75: intensities corresponded to 50 and 75% of the difference between maximal aerobic power and the power associated with the ventilatory threshold; P100 and P110: intensities corresponded to 100 and 110% of maximal aerobic power; PF: plantar flexors; RM: maximum repetition; S: statistically significant (i.e. $p < 0.05$); TE: trunk extensors; TTF: time to task failure; UL: upper limbs

3.1 – Quality assessment

Studies that met the inclusion criteria ranged between two and seven stars (out of a possible nine stars), with a mean score of 4.3 ± 1.2 and a median of 4 (see Table, Electronic Supplementary Material 3). Considering the classification proposed by McPheeters and colleagues [37], and regarding the risk of bias, 0% (0/29), 28% (8/29) and 72% (21/29) of the included studies had a good, fair and poor grade, respectively. For the comparability domain, 21% (6/29), 55% (16/29) and 24% (7/29) of the studies had a good, fair and poor grade, respectively. Finally, for the outcome domain, 17% (5/29), 76% (22/29) and 7% (2/29) of the studies had a good, fair and poor grade, respectively.

3.2 – Publication bias

Regarding TTF, no evidence of publication bias was identified by Begg's and Egger's tests ($p > 0.10$) or funnel plot representation (see Figure, Electronic Supplementary Material 4). However, Begg's and Egger's tests indicated evidence for small study-effects in fatigability with $p = 0.030$ and 0.025, respectively. Funnel plot representation (see Figure, Electronic Supplementary Material 5) showed a little asymmetry with a few studies with relatively small sample size reporting the largest effects on fatigability in favor of children as compared to adults. A risk of publication bias for fatigability suggests that our analyses may be biased in the sense of an overestimation of the fatigability differences between children and adults.

3.3 – Time to task failure

Two separate meta-analyses compared TTF between children *versus* adults and adolescents *versus* adults. The exercise duration of 12 out of 18 (67%) of the studies included in these meta-analyses [8, 15, 16, 22, 24-26, 28, 44-47] was derived from the total number of contractions performed until task failure. The TTF in seconds was directly provided in the other six studies [7-12]. The first meta-analysis indicated that TTF was longer in children when compared to adults (SMD 0.89; 95% CI 0.15 to 1.63; $p = 0.018$; *15 studies, n = 435;* Figure 2), with high heterogeneity of the results ($Q = 150.5$; $df = 14$; $p < 0.001$; $I^2 = 90.7\%$).

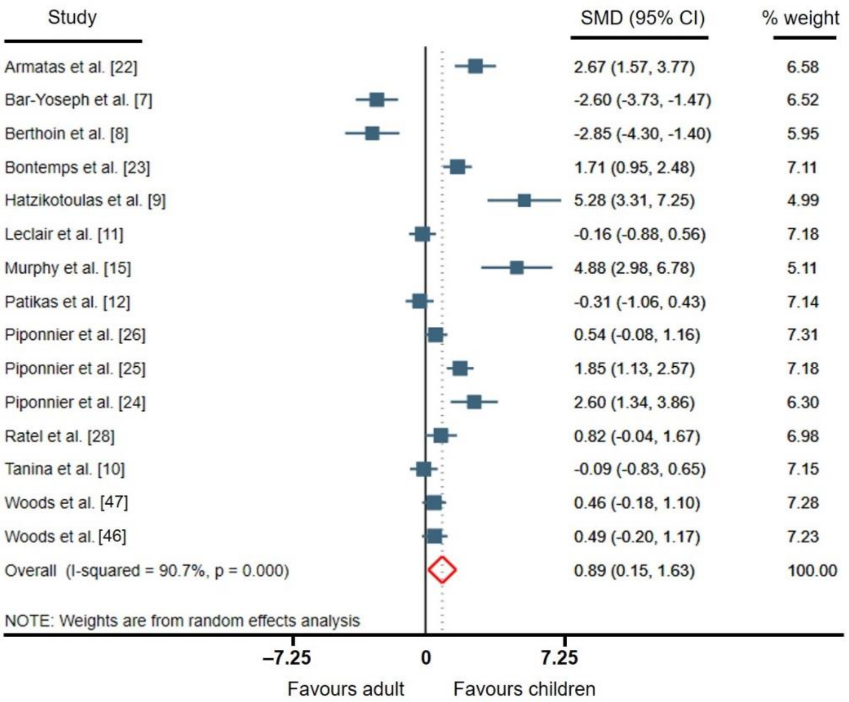

Fig. 2 Forest plot from the meta-analysis reporting TTF differences between children and adults.

Only five studies looked at TTF differences between adolescents and adults [7, 16, 24, 44, 45]. The second meta-analysis indicated no differences in TTF between adolescents and adults (SMD 0.75; 95% CI –0.12 to 1.62; p = 0.090; *5 studies*, *n = 103*; Figure 3), with high heterogeneity of the results (Q = 15.9; df = 4; p = 0.003; I^2 = 74.9%).

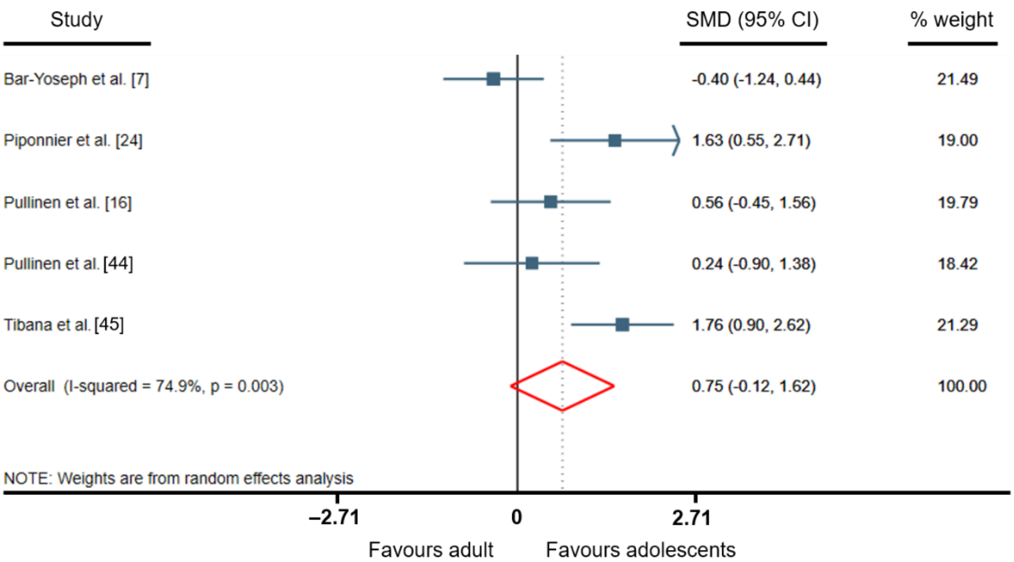

Fig. 3 Forest plot from the meta-analysis reporting TTF differences between adolescents and adults.

Subgroup meta-analyses were performed to evaluate the influence of i) the type of exercise (i.e. isometric *versus* dynamic) and ii) the exercise duration on the reported differences in TTF. The first subgroup analysis revealed that children had longer TTF than adults for isometric exercises (SMD 1.25; 95% CI 0.60 to 1.90; $p < 0.001$; *11 studies, n = 342*; Figure 4), but no difference was found for dynamic exercises (SMD –0.27; 95% CI –2.82 to 2.28; $p = 0.83$; *4 studies, n = 93*; Figure 4). The heterogeneity of the results obtained for subgroup isometric (Q = 68.6; df = 10; $p < 0.001$; $I^2 = 85.4\%$) and dynamic (Q = 54.5; df = 3; $p < 0.001$; $I^2 = 94.5\%$) exercises analysis was high. For the second subgroup analysis, the mean duration (pooled data of children and adults participants) of the studies in the short-duration and the long-duration categories were 180 ± 89 s (range: 88–282 s) and 640 ± 164 s (range: 418–857 s), respectively. This analysis indicated that differences in TTF were significant between children and adults for short-duration exercises (SMD 1.46; 95% CI 0.16 to 2.76; $p = 0.028$; *7 studies, n = 209*; Figure 5) while it was not for long-duration ones (SMD 0.20; 95% CI –0.66 to 1.07; $p = 0.64$; *7 studies, n = 206*; Figure 5). The heterogeneity of the results obtained for the subgroup analysis relative to short- (Q = 80.4; df = 6; $p < 0.001$; $I^2 = 92.5\%$) and long-duration (Q = 48.9; df = 6; $p < 0.001$; $I^2 = 87.7\%$) exercises was high.

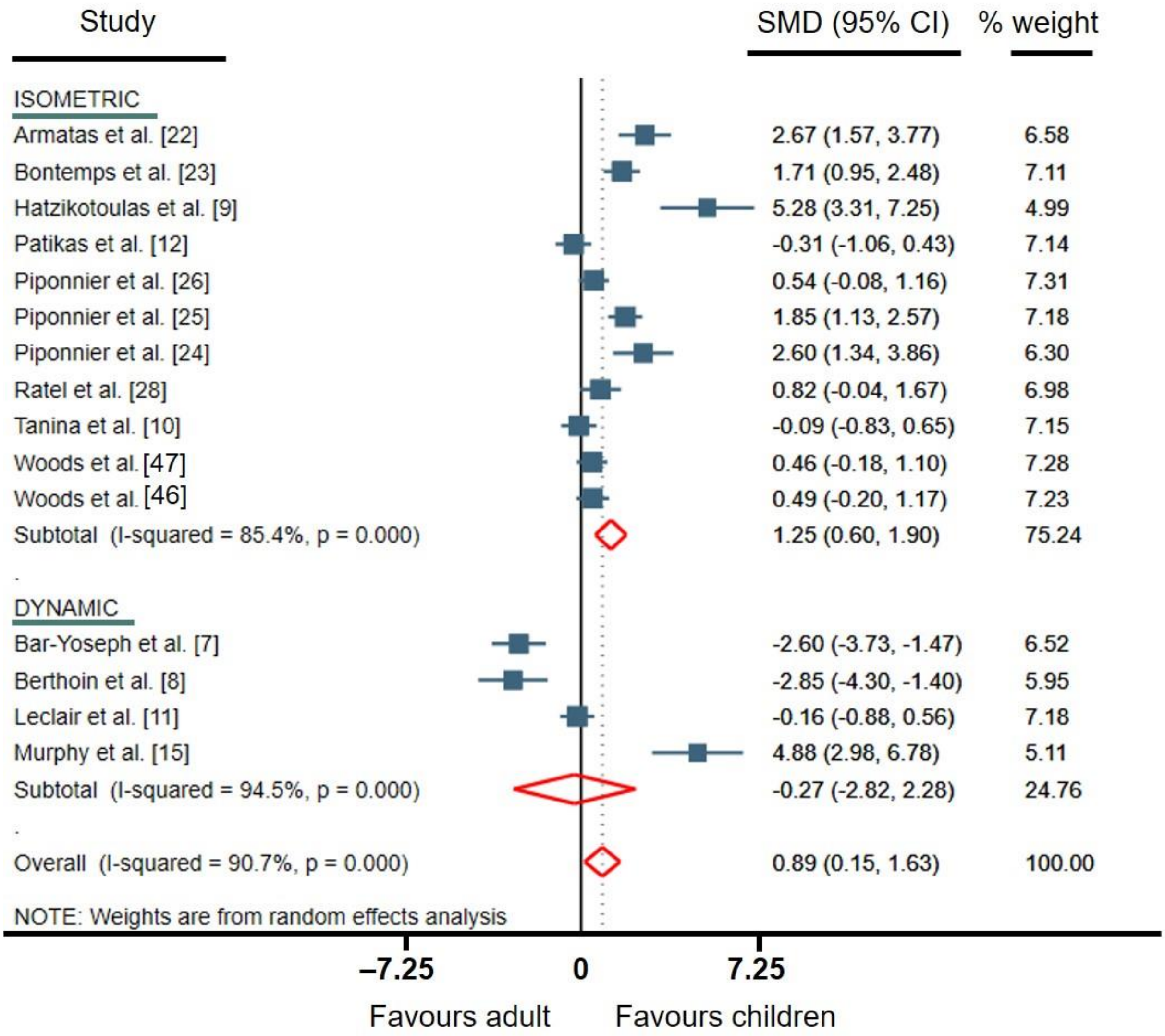

Fig. 4 Forest plot from the subgroup meta-analysis reporting the influence of exercise modality (i.e. isometric or dynamic) on TTF differences between children and adults.

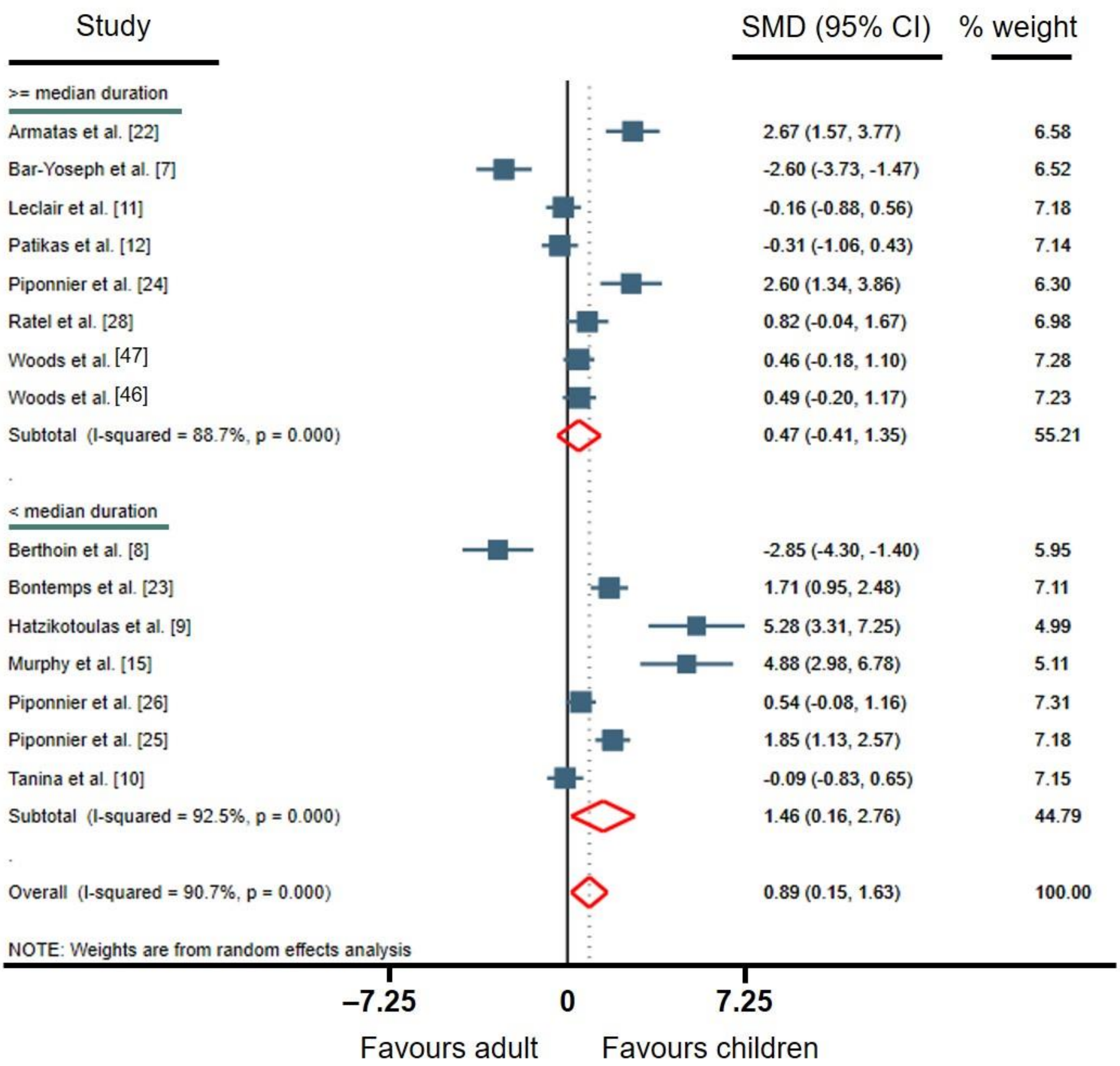

Fig. 5 Forest plot from the subgroup meta-analysis reporting the influence of exercise duration on TTF differences between children and adults.

3.4 – Fatigability

The meta-analyses that aimed to evaluate the differences in fatigability between children *versus* adults and adolescents *versus* adults included 19 and seven studies, respectively. The analyses revealed that children (SMD –1.15; 95% CI –1.64 to –0.66; $p < 0.001$; *19 studies*, $n = 489$; Figure 6) and adolescents (SMD –1.26; 95% CI –2.34 to –0.18; $p = 0.022$; *7 studies*, $n = 149$; Figure 7) were significantly less fatigable when compared to adults, with the heterogeneity of studies being high either for the children *versus* adults (Q = 103.1; df = 18; $p < 0.001$; I^2 = 82.5%) or adolescents *versus* adults (Q = 42.8; df = 6; $p < 0.001$; I^2 = 86.0%) comparisons.

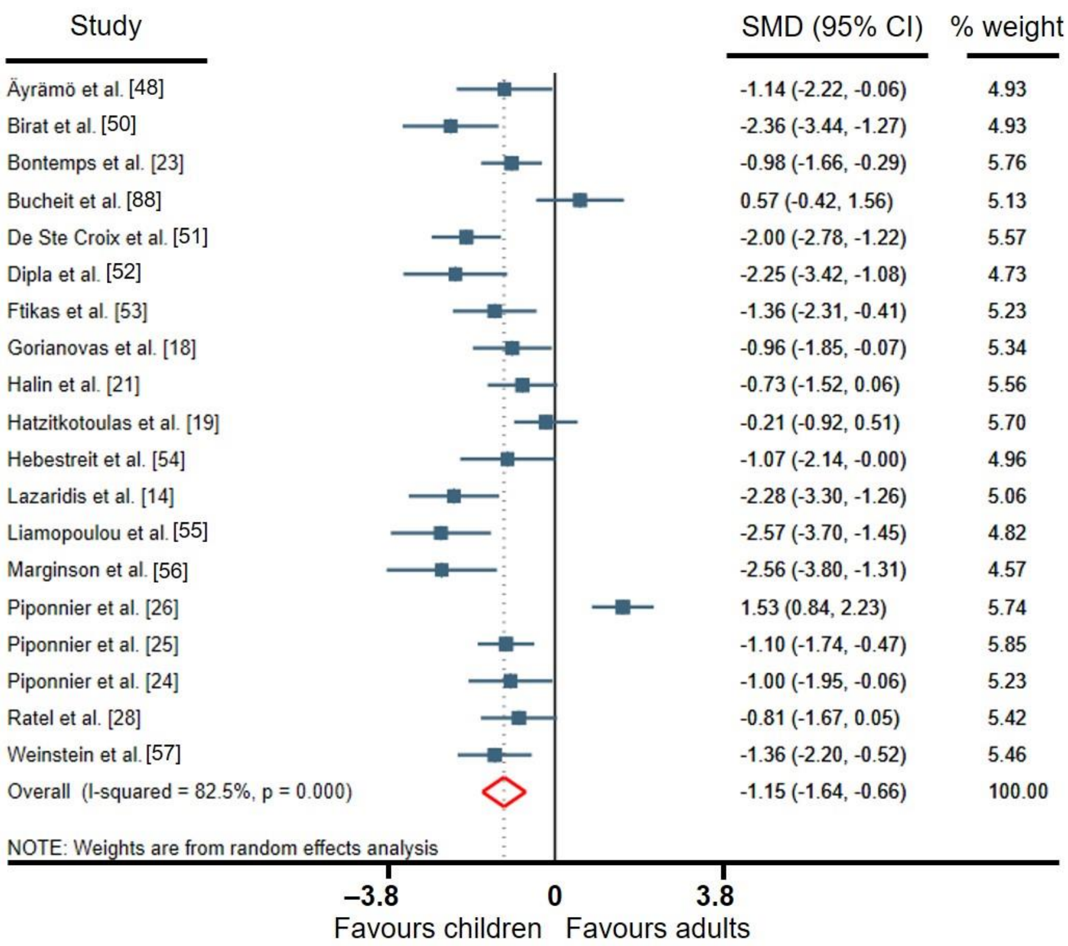

Fig. 6 Forest plot from the meta-analysis reporting differences in fatigability between children and adults.

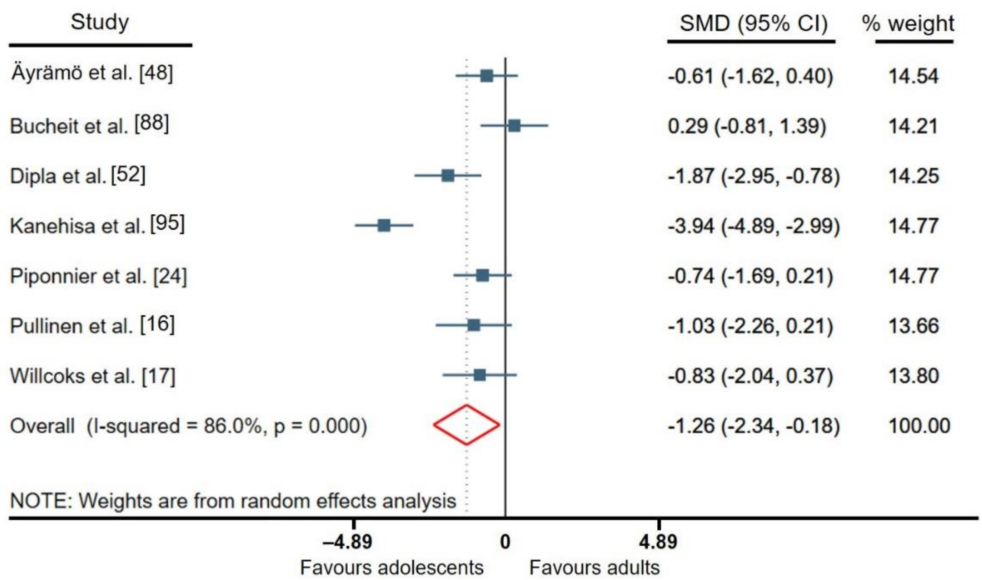

Fig. 7 Forest plot from the meta-analysis reporting differences in fatigability between adolescents and adults.

A subgroup analysis was performed to evaluate the influence of the type of exercise on the reported differences in fatigability between children and adults. This subgroup analysis was not performed on adolescents because of a too low number of studies. The subgroup meta-analysis reported that children were significantly less fatigable than adults during dynamic exercises (SMD –1.58; 95% CI –2.08 to –1.08; p < 0.001; *12 studies, n = 275*; Figure 8), but non-significant difference was found for isometric exercises (SMD –0.46; 95% CI –1.19 to 0.27; p = 0.22; *7 studies, n = 214*; Figure 8). The heterogeneity of the studies involved in isometric (Q = 41.8; df = 7; p < 0.001; I^2 = 83.2%) and dynamic (Q = 32.7; df = 10; p < 0.001; I^2 = 69.5%) exercises subgroups analyses was high.

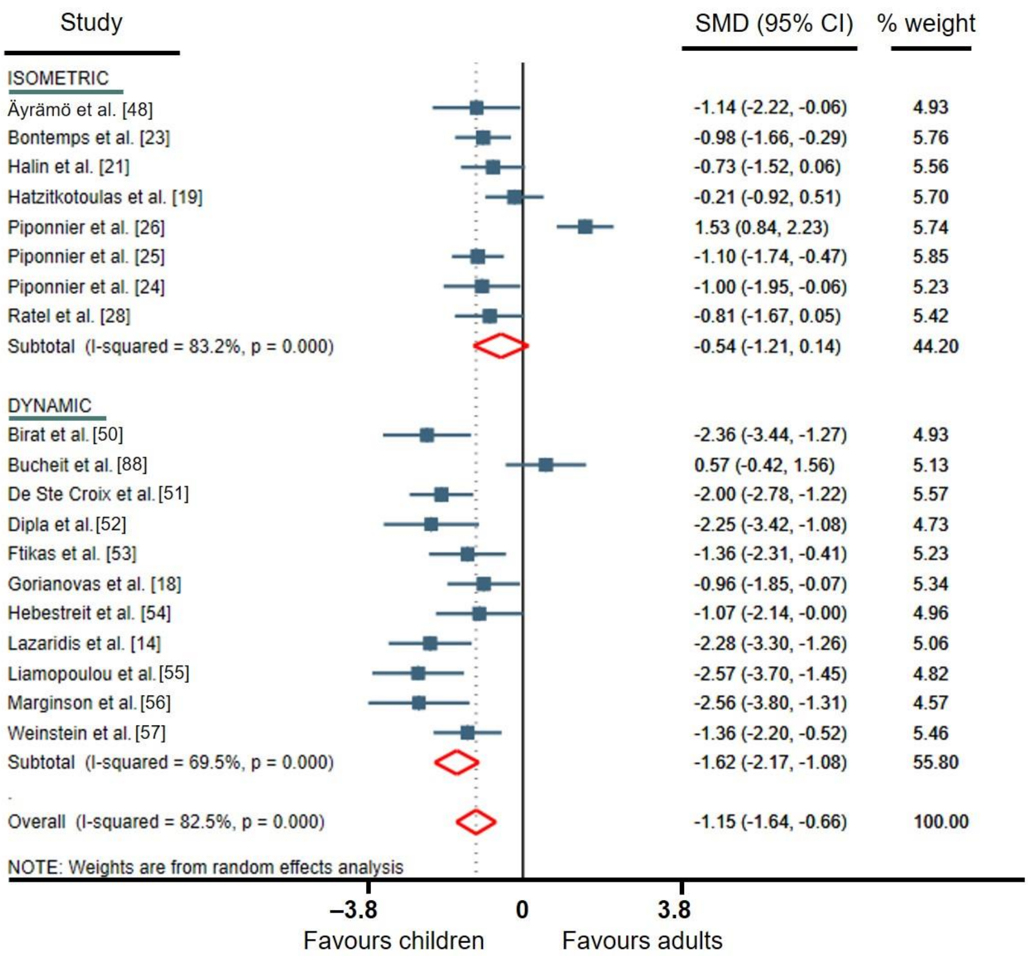

Fig. 8 Forest plot from the subgroup meta-analysis reporting the influence of exercise modality (i.e. isometric or dynamic) on fatigability differences between children and adults

3.5 – Secondary outcomes

Out of the 34 studies included in the meta-analyses, eight [9, 15, 23-26, 28, 48] used neurostimulation techniques to shed light on the central and peripheral factors that may explain the differences in TTF and fatigability between children and adults. Two additional studies [20, 49] that were not included in the previous meta-analyses (i.e. because relative data have not been provided by the authors) also investigated the central and peripheral components of fatigability in both children and adults after exercise. Detailed information on these studies is given in Table 3. Because of the small number of studies and the large heterogeneity in the methods used to investigate the peripheral and central factors underlying fatigability, no meta-analyses were performed.

3.5.1 – Central fatigue

Eight out of the ten studies investigated central fatigue, either using VA [9, 20, 23-26, 28], the EMG/M-wave ratio [23-26, 48] or H-reflexes [26, 48]. Six studies reported that VA was significantly more decreased at the end of the fatiguing exercise in children than in adults [20, 23-26, 28], while one study reported no significant differences in VA changes with fatigue between children and adults [9]. Three studies reported that the decrease in the EMG/M-wave ratio was significantly more pronounced in children than adults [23-25]. Two studies reported that changes in EMG/M-wave ratio were similar after the exercise between the two populations [26, 48], while one study reported no changes in EMG-M-wave ratio after fatigue for both children and adults [28]. Finally, two studies reported similar changes in H-reflexes after fatigue in children and adults [26, 48].

3.5.2 – Peripheral fatigue

All studies reported that Pt and Db were significantly more decreased after exercise in adults compared to children [9, 15, 20, 23-26, 28, 48, 49]. One study found a greater increase in the half relaxation time (measured from single nerve stimulation) in adults compared to children after exercise [15] while another reported similar changes [48]. Two studies investigated the time to peak twitch, with one reporting a greater decrease in adults after exercise [9] and the other one reporting similar changes between the two populations [48]. Eight studies investigated M-wave changes with fatigue. One study reported that M-wave decreased more in adults compared to children after exercise [15], while another study reported that M-wave increased in adults after fatigue while it was unchanged in children [26]. The other studies either reported a similar decrease in M-wave between children and adults [9, 48], or no changes in this parameter in both populations [23-26, 28]. Lower LFF was found in children compared to adults [23, 26, 49].

Table 3 Central and peripheral fatigue parameters

	Fatiguing exercise *(criteria for exercise ending)*	CENTRAL FACTORS			PERIPHERAL FACTORS					
		VA/CAR	EMG/M-wave	H-reflex	Pt	HRT	TPT	M-wave	Db	LHF_R
Äyrämö et al. [48]	50-s all out run	–	↑ Adu = Ch	↑ Adu = Ch	↓ Adu > Ch	↓ Adu = Ch	↓ Adu = Ch	↓ Adu = Ch	–	–
Bontemps et al. [23]	5 s MVC/5 s rest *(↓ of 40% MVC)*	↓ Ch > Adu	↓ Ch > Adu	–	↓ Adu > Ch	–	–	NC	↓ Adu > Ch	↓ Adu > Ch
Hatzikotoulas et al. [9]	Sustained MVC *(↓ of 50% MVC)*	↓ Ch = Adu	–	–	↓ Adu > Ch	–	↓ Adu > Ch	↓ Adu = Ch	–	–
Murphy et al. [15]	3 × max CON MVC *(volitional exhaustion)*	–	–	–	↓ Adu > Ch	↑ Adu > Ch	–	↓ Adu > Ch	–	–
Piponnier et al. [26]	5 s MVC/5 s rest *(↓ of 40% MVC)*	↓ Ch > Adu	↓ Ch = Adu	↓ Ch = Adu	↓ Adu > Ch	–	–	↑ Adu > Ch	↓ Adu > Ch	↓ Adu > Ch
Piponnier et al. [25]	5 s MVC/5 s rest *(↓ of 40% MVC)*	↓ Ch > Adu	↓ Ch > Adu	–	↓ Adu > Ch	–	–	NC	↓ Adu > Ch	–
Piponnier et al. [24]	5 s MVC/5 s rest *(↓ of 40% MVC)*	↓ Ch > Adu	↓ Ch > Adu	–	↓ Adu > Ch ↓ Adu > Ado	–	–	NC	–	–
Ratel et al. [28]	5 s MVC/5 s rest *(↓ of 40% MVC)*	↓ Ch > Adu	NC	–	↓ Adu > Ch	–	–	NC	–	–
Streckis et al. [20]	2-min sustained MVC	↓ Ch > Adu	–	–	↓ Adu > Ch	–	–	–	–	–
Streckis et al. [49]	100 drops jumps	–	–	–	↓ Adu > Ch	–	–	–	–	↓ Adu > Ch

Ado: adolescents; Adu: adult; CAR: central activation ratio; Ch: children; CON: concentric; Db: doublet; EMG: electromyography; HRT: half relaxation time; LHF_R: low-to-high frequency fatigue ratio; MVC: maximal voluntary contraction; Pt: peak twitch; TPT: time to peak twitch; VA: voluntary activation level

4 – DISCUSSION

This meta-analysis reveals that children have longer TTF and are less fatigable when compared to adults. Complementary analysis reveals that exercise modality (i.e. exercise duration and type of exercise) influences the differences reported in TTF and fatigability between children and adults. While this review points out the lack of studies that investigated differences in TTF and fatigability between adolescents and adults, the meta-analysis conducted on available data reported a higher fatigability in adults but no differences in TTF between these two populations.

4.1 – Children have higher endurance and lower fatigability when compared to adults

Longer TTF were reported in children for ten out of the 15 included studies [9, 15, 22-26, 28, 46, 47]. Seventeen out of the 19 studies that compared fatigability between children and adults observed a lower level of fatigability in children [14, 18, 19, 21, 23-25, 28, 48, 50-57]. Our results are in line with the current literature and statistically confirm that children have higher endurance capacities than adults (i.e. longer TTF) and are less fatigable (i.e. lower relative decrease in muscle performance at isotime). Physiological differences between children and adults may account for the observed differences [2].

First, differences in muscle fiber types distribution between children and adults could explain part of the differences in fatigue resistance capacity during exercise. The type of muscle fibers composing a muscle influences its resistance to fatigue, with muscles mainly proportioned in type II fibers being less resistant [58, 59]. Although the evidences on age-related muscle typology are scarce so far and obtained on small sample sizes, it has been suggested that children have a higher proportion of slow-twitch type I fibers than adults, as reported by the ~65-70% type I fibers proportion in the vastus lateralis in children *versus* ~47-57% in adults [60, 61]. This is associated with a greater muscle oxidative capacity, as demonstrated in the forearm flexor muscles by a higher rate of post-exercise recovery in phosphocreatine and a faster rate of aerobic ATP production [62]. Similar results were reported in the gastrocnemius muscle [63]. This could have a major influence on fatigue resistance especially during intermittent fatiguing exercise where the recovery in energy substrates plays a key role, i.e. children have a greater ability to replenish their phosphocreatine stores. Also, differences in mitochondrial function and density could favor the children to better liberate and capture oxygen and/or use it [32, 64]. Nine out of the 15 meta-analyzed studies that investigated TTF differences between children and adults used experimental designs with intermittent fatiguing protocols [15, 22-26, 28, 46, 47]. All of these nine studies reported longer TTF in children, with only three studies reporting the differences to be non-significant. Interestingly, five [7, 8, 10-12] of the six studies that used continuous fatiguing protocols found no differences in exercise duration between children and adults (see Table 2). This confirms that differences in metabolic profiles between children and adults could play a major role on the fatiguing resistance capacity especially when intermittent designs of exercise are used.

Second, the higher muscle mass involved during exercise in adults could account for the observed differences in muscle endurance and fatigability. Higher intramuscular pressure could occur during exercise in adults, thus increasing vascular occlusion and limiting metabolite removal and energy substrate replenishment [62, 65], potentially leading to lower TTF. These peripheral alterations could interact with psychophysiological mechanisms that may play a fundamental role in determining the premature exercise ending in adults. A higher metabolic by-products accumulation (e.g. H+ accumulation [66]) would increase the activation of metabosensitive group III/IV muscle afferents [67]. These afferents project their input to various sites within the central nervous system [68, 69]. The central integration of afferent feedbacks (together with the increased corollary discharge, e.g. [70]) may lead to increased sensations (e.g. effort, pain) involved in exercise termination [30, 71]. One could speculate that the greater metabolic perturbations in adults would increase these sensations at a higher rate than in children thus leading to a premature exercise ending. These differences in perception of effort (usually reported in these studies into a single "Gestalt" perception, including other sensations like fatigue, discomfort as suggested in the seminal definitions of perceived exertion e.g. [72, 73]) between children and adults have been addressed in a review [2], with a common observation that children rate their effort lower than adults [74-77]supporting our previous assumption. However, this argument must be balanced with the fact that youth tend to score lower ratings of perceived effort during exercise [78]. In the latter study, the median maximum rating for leg exertion in children after cycling was only slightly greater than half the maximum possible value of 10 using the Borg CR10 scale [72]. This observation has been confirmed by others [74, 79, 80]. This low-rating tendency could be due to the fact that children are unable to correctly understand the scale or properly gauge their perceived exertion because of a lack of previous experiences [78].

The differences in metabolic profile between children and adults could also give some clues to the observed differences in fatigability. The exercise duration has a direct influence on fatigability, with longer exercise inducing greater decrement muscle in performance [81]. Then, it would have been incorrect to analyze fatigability data for experimental designs that used exercises of different duration. We thus performed isotime analysis to increase the robustness of our interpretation [27]. For the same exercise duration, it is likely that children prevented the recruitment of high-threshold motor units, partly explaining the lower level of fatigability at isotime. This argument could be valuable for submaximal and maximal exercises if one considers that children have a greater activation deficit that adults. As reported in Table 3, a greater decrement in VA was observed in children after exercise, suggesting that children exhibited more central fatigue than adults. This may be in favor of a specific neural regulation in children during fatiguing exercises that could partly explain our results at isotime. In addition to the common argument of a lower capacity for spatial recruitment in children than in adults, i.e. lesser type-II motor-unit utilization [82], one should also consider differences in temporal recruitment with differences in firing rates of the active motor units between children and adults. Direct evidences for this latter point are lacking so far, and the emergence of novel investigation technique (e.g. high-density electromyography) could help to obtain a more precise overview of differences in motor unit recruitment between children and adults. Last, the low activation level in children could allow the organization of motor units rotation [83], which is much more difficult when the level of activation are high.

Further, because of their specific muscle phenotype, adults develop peripheral alterations at a higher rate when compared to children for the same relative exercise duration (see figures 2 in [23, 24, 28]) or at exercise termination (see the Pt-related data in Table 3), providing another possibility for the higher level of fatigability recorded at isotime in adults.

While the meta-analyses confirmed that children are i) less fatigable and ii) able to sustain exercise at a given intensity longer than adults, one could speculate that the role of some specific physiological functioning, e.g. muscle metabolism, involved in the performance would vary as a function of the exercise modality, i.e. type of exercise (isometric *versus* dynamic) and exercise duration (short *versus* long-duration exercise), and that it could play a major role in the reported differences in TTF and fatigability between children and adults.

4.2 – Differences in TTF and performance fatigability between children and adults depend on the modality of exercise

Sustained or intermittent isometric contractions at a single joint are common to evaluate TTF and fatigability. However, the conclusions derived from these contraction modalities do not necessarily apply for dynamic exercises where the physiological demands and the muscle mass involved in the exercise are different [84, 85]. Considering the major changes in body size and physiological function over the course of growth and development [86, 87], one may expect an influence of the type of exercise on the observed differences in TTF and fatigability between children and adults.

Among the 15 studies that looked at TTF differences between children and adults, 11 used an isometric modality [9, 10, 12, 22-26, 28, 46, 47] while four used a dynamic modality that included running and cycling exercises [7, 8, 11] as well as concentric MVC [15]. We found that children had longer TTF than adults when isometric exercises were performed with no differences for dynamic exercises. Eight out of the 11 isometric studies used intermittent fatiguing protocols. We can speculate that the use of intermittent exercises favored the children in sustaining the exercise for a longer duration, thanks to their higher muscle oxidative activity and their faster regulation of blood acid-base balance. Interestingly, two out of the three studies that used continuous isometric fatiguing protocols showed no differences in TTF between children and adults [10, 12]. The nature of the exercise (i.e. intermittent *versus* continuous) could explain the absence of differences between children and adults for the four studies that used dynamic exercises. Indeed, three out of these four studies used continuous exercises and showed either no changes [11] or higher TTF in adults [7, 8], while the one that used an intermittent design showed higher TTF in children [15]. Overall, these results support the idea that differences in exercise duration between children and adults are more detectable when intermittent exercises are used. One should note, however, the large imbalance in the number of studies included in the quantitative analyses that used isometric (n = 11) *versus* dynamic (n = 4) exercises which could have prevented detecting possible differences between children and adults for this latter exercise modality.

Among the 19 included studies in fatigability analyses, seven used isometric exercises [19, 21, 23-26, 28] and 12 used dynamic exercises that included running [48], cycling [50, 54, 57, 88] and jumping [14, 18, 53, 55, 56] efforts as well as repeated concentric MVCs [51, 52]. The results revealed that children were less fatigable than adults when performing dynamic rather than isometric exercises. This finding is not consistent with TTF analyses which did not reveal any differences in TTF for dynamic exercises. While any attempt to give a physiological explanation for this result would remain hazardous, one could nevertheless suggest that the use of isotime comparison to compute fatigability in our meta-analysis is a candidate. Isotime data for most children were reported away from the end of the exercise. For instance, isotime comparisons in a study from our group [25] were made at the 10th MVC which corresponded to the lowest number of contractions performed by one adult participant while the mean number of contractions was 40±18 (range: 15–79) in children, suggesting that most children were still far from exercise termination. While these two outcomes (i.e. TTF and fatigability) are commonly used interchangeably to inform on exercise-related performance (e.g. [89]), our results evidenced that they are not. TTF considers the time to exhaustion which rely on physiological mechanisms but also on psychological and motivational ones [90]. Fatigability, as evaluated in this meta-analysis, informs on what happened on the early-middle phase of the exercise, far from exhaustion for most participants.

We also investigated whether differences in TTF were impacted by the exercise duration. Children are more likely to engage in very short bursts of intense physical activity interspersed with varying intervals of low to moderate intensity [91]. This is consistent with our results showing higher between-group differences, favoring children i) for short compared to long-duration exercises and ii) for intermittent exercises. The classification of short *versus* long-exercise duration indirectly reflects the exercise intensity that was performed during the exercise. Six out of the seven studies classified in the short-duration category used high intensity and maximal exercises [8, 9, 15, 23, 25, 26] and five out of the seven studies classified in the long-duration category used moderate and submaximal intensities [7, 11, 12, 46, 47]. Higher oxidative capacities in children could have favored a most effective recovery between intense exercise bouts explaining why they lasted longer than adults. Moreover, the perception of effort reported in children is often lower than in adults for short/intense bouts of exercise (i.e. up to 10 min) [2, 92]. This is likely due to differences in the way by which peripheral and central signals are integrated [92]. Then, the perception of effort may increase at a higher rate in adults for short-duration and high-intensity exercises, contributing to earlier exercise termination, possibly explaining why children performed better for short- than long-duration exercises. Finally, differences in thermoregulation processes have been reported between children and adults (see [93] for a review). For instance, children present a lower rate of sweating than adults that is known to have a negative influence on body temperature regulation during prolonged exercise. This could lead to a higher metabolic demand relative to body mass in children, thus lowering the exercise economy [94] and impacting exercise performance for long-duration exercises, especially involving whole-body tasks.

Overall, both the type of exercise and exercise duration can modulate the reported differences in fatigability and TTF between children and adults. Beyond these two modalities, it seems that the intermittent *versus* continuous design of exercise plays a significant role in these differences.

4.3 – Physiological changes during maturation influence the exercise-related performance

Because significant changes occur in physiological systems during the transition from childhood to adulthood, there is a necessity to make a clear distinction between children and adolescents in the literature to have a precise overview of their potential differences in exercise-related performance especially when compared to adults.

Differences in TTF and fatigability between adolescents and adults were investigated in only five [7, 16, 24, 44, 45] and seven [17, 24, 44, 48, 52, 88, 95] studies, respectively. Our analysis showed a longer but not significant ($p = 0.09$) TTF in adolescents together with a lower level of fatigability, when compared to adults. Only few studies compared children, adolescents and adults within the same experimental design. The results regarding TTF are controversial. Some authors reported longer TTF in children and adolescents when compared to adults, and a trend ($p = 0.05$) for longer TTF in children than adolescents [24]. Others reported longer TTF in adolescents and adults than children during running exercises (with no differences during cycling) [7]. Eight studies investigated differences in fatigability between the three populations, some of them being not included in the statistical analyses because of methodological concerns [96, 97]. Overall, adolescents are more fatigable than children [24, 52, 96-98] but less than adults.

This confirms that growth and maturation influence the level of fatigability likely because of specific neuromuscular changes that are attributed to the puberty [83]. First, adolescents engage a higher muscle mass during the exercise [99]. This could be the origin of greater metabolic perturbations, especially because of greater intramuscular pressure during exercise. Differences in muscle typology (i.e. higher proportion of type II muscle fibers in adolescents, e.g. [100]) or in energy metabolism (i.e. lower oxidative activity for ATP synthesis in adolescents, e.g. [101]) contribute to the higher level of fatigability observed in adolescents. Second, adaptations within the central nervous system during the maturation process could contribute to these differences. Children are less able to voluntarily recruit their motor units during exercise, likely due to an immaturity of the corticospinal pathway [102]. Besides this lower recruitment capacity, they would recruit a higher relative proportion of slow-twitch fibers and would benefit from a more organized and efficient motor unit rotation [83]. Because of the limited number of studies that investigated how peripheral and central modulations could differentially impact the exercise-related performance between children and adolescents, these arguments remain speculative. Only two studies investigated in the same experimental design the neural and peripheral functioning in response to exercise in children, adolescents and adults.

Our group recently reported that Pt amplitude was reduced in adolescents after an intermittent isometric exercise while it was not in children [24], suggesting that contractile properties and/or excitation-contraction coupling was preserved in children while altered in adolescents (see Table 3). In contrast, VA decreased at a similar level after exercise in children and adolescents, while it remained unchanged in adults, suggesting that the greater central fatigue in children and adolescents likely account for their lower degree of peripheral alterations than adults. These isolated results strengthen the hypothesis of an evolution in the maturation of the central nervous system during growth, with the tolerance of the central nervous system to peripheral alterations increasing during puberty [58]. Besides this pioneer theory claiming that peripheral functioning is preserved by central regulation in children, one should also consider that the explanation could directly come from the muscle functioning, i.e. the fatigue-resistant muscles of the children do not develop a large amount of fatigue independently of any central influence. Another study investigated the peripheral and central factors of fatigue after a 50-s maximal run [48] and confirmed the aforementioned observations. Of note, a large delay (i.e. 6–12 min) separated the end of the exercise and the beginning of neuromuscular testing in the latter study [48]. Considering the rapid recovery of neuromuscular function that occurs within the first 2-min after exercise [103-105], these latest results should be interpreted with caution.

4.4 – Limitations

Some limitations pertaining to our analyses must be acknowledged. First, most outcomes displayed a moderate to high level of heterogeneity, likely due to differences in experimental procedures, e.g. type of exercise (isometric *versus* dynamic, long *versus* short duration, intermittent *versus* continuous), muscles involved (e.g. lower *versus* upper limbs) and population characteristics. These high levels of heterogeneity are, however, common in this kind of quantitative analyses (e.g. [36]). A step towards a standardization of experimental protocols to evaluate TTF and fatigability in children, adolescents and adults could help in making the results of individual studies more homogeneous to establish more robust conclusions. Second, the overall quality of the studies included in the meta-analysis was low (mean quality score of 4.3 ± 1.2 stars out of a maximum of 9 stars) which could have led to a biased estimation of the between-group differences in TTF and fatigability. For instance, the overall score of the comparability domain was low (e.g. 0.9 ± 0.7 stars out of a maximum of 2 stars) meaning that physical activity status in some studies was not rigorously controlled. This is an important observation because the level of physical activity influences TTF and fatigability [106, 107] and varies during childhood [108]. Most of the included studies monitored the level of physical activity by the mean of self-report that involved questionnaires or brief interviews. These subjective measures can misjudge the absolute level of physical activity [109]. Objective measures (e.g. accelerometers) can increase the precision of this important outcome. Only a minor proportion (~12%) of the included studies used objective measures to capture the level of physical activity [7, 54, 57, 88], and one of them did not matched the participants for similar level of physical activity [88]. Third, a risk of publication bias was suggested for fatigability indicating that our analyses could overestimate fatigability differences between children and adults. Last, we excluded some studies because of the lack of information (e.g. absence of standard deviation [97, 110], no access to the Pre- *versus* Post-exercise relative changes [96], no access to the contraction duration during intermittent exercises [98, 111]) and their inclusion could have slightly influenced the results obtained in the meta-analyses.

5 – CONCLUSIONS AND PERSPECTIVES

While there is an interest in the existing literature for the evaluation of differences in TTF and fatigability between children and adults, this is the first systematic review and meta-analysis that pooled all these studies to provide a quantitative overview. Overall, our analyses revealed that children are able to sustain an exercise longer than adults, and that children are less fatigable than adults. This meta-analysis also reported that these differences were influenced by the exercise modality, i.e. the type of exercise (i.e. isometric *versus* dynamic) and the duration of the exercise. We also suggested that the design of the exercise (i.e. intermittent *versus* continuous) could have a major influence on the differences in exercise-related performance between children and adults. Fundamental differences in physiological functioning between children and adults are likely to explain the longer TTF and lower fatigability reported in children. While differences may also exist between children and adolescents, the low number of studies so far prevent a robust interpretation. In particular, it can be speculated that differences in maturation of the central nervous system that directly interact with peripheral function could explain why children and adolescents performed differently during exercise. However, the evidence is low, and further studies using novel experimental techniques in these populations (e.g. transcranial magnetic stimulation, high-density electromyography) should be considered to gain novel insights into the interplay that could exist between peripheral and central mechanisms throughout maturation. Here are some practical recommendations that could increase the robustness of data interpretation when TTF and performance fatigability (together with neuromuscular underpinning mechanisms) are evaluated in children, adolescents and adults:

1) Monitoring the level of physical activity by objective measures (e.g. accelerometry) and pairing participants according to this outcome.
2) Performing isotime analysis when fatigability is the main outcome.
3) Recording both TTF and fatigability to obtain global information on exercise-related performance, since these two outcomes are not interchangeable.
4) Combining various methods to gain insights into the specific role of the central nervous system in children' fatigability.
5) Combining, when possible, different exercise modalities within the same study to capture the whole facet of the differences in TTF and fatigability between children, adolescents and adults.

REFERENCES

1. Patikas DA, Williams CA, Ratel S. Exercise-induced fatigue in young people: advances and future perspectives. Eur J Appl Physiol. 2018; 118(5):899-910
2. Ratel S, Duché P, Williams CA. Muscle fatigue during high-intensity exercise in children. Sports Med. 2006;36(12):1031-65.
3. Gruet M. Fatigue in Chronic Respiratory Diseases: Theoretical Framework and Implications For Real-Life Performance and Rehabilitation. Front Physiol. 2018;9:1285.
4. Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. Neurology. 2013 Jan 22;80(4):409-16.
5. Enoka RM, Duchateau J. Translating Fatigue to Human Performance. Med Sci Sports Exerc. 2016 Nov;48(11):2228-38.
6. Barker AR, Welsman JR, Fulford J, Welford D, Armstrong N. Quadriceps Muscle Energetics during Incremental Exercise in Children and Adults. Med Sci Sports Exerc. 2010;42(7):1303-13.
7. Bar-Yoseph R, Porszasz J, Radom-Aizik S, Stehli A, Law P, Cooper DM. The effect of test modality on dynamic exercise biomarkers in children, adolescents, and young adults. Physiol Rep. 2019;7(14):e14178.
8. Berthoin S, Allender H, Baquet G, Dupont G, Matran R, Pelayo P, et al. Plasma lactate and plasma volume recovery in adults and children following high-intensity exercises. Acta Paediatr. 2003;92(3):283-90.
9. Hatzikotoulas K, Patikas D, Ratel S, Bassa E, Kotzamanidis C. Central and Peripheral Fatigability in Boys and Men during Maximal Contraction. Med Sci Sports Exerc. 2014;46(7):1326-33.
10. Tanina H, Nishimura Y, Tsuboi H, Sakata T, Nakamura T, Murata K-y, et al. Fatigue-related differences in erector spinae between prepubertal children and young adults using surface electromyographic power spectral analysis. J Back Musculoskelet Rehabil. 2017;30(1):1-9.
11. Leclair E, Mucci P, Borel B, Baquet G, Carter H, Berthoin S. Time to exhaustion and time spent at a high percentage of VO2max in severe intensity domain in children and adults. J Strength Cond Res. 2011;25(4):1151-8.
12. Patikas D, Kansizoglou A, Koutlianos N, Williams CA, Hatzikotoulas K, Bassa E, et al. Fatigue and recovery in children and adults during sustained contractions at 2 different submaximal intensities. Appl Physiol Nutr Metab. 2013;38(9):953-9.
13. Piponnier E, Martin V, Bontemps B, Chalchat E, Julian V, Bocock O, et al. Child-adult differences in neuromuscular fatigue are muscle-dependent. J Appl Physiol. 2018 Aug 9.
14. Lazaridis S, Patikas DA, Bassa E, Tsatalas T, Hatzikotoulas K, Ftikas C, et al. The acute effects of an intense stretch-shortening cycle fatigue protocol on the neuromechanical parameters of lower limbs in men and prepubescent boys. J Sports Sci. 2018;36(2):131-9.
15. Murphy JR, Button DC, Chaouachi A, Behm DG. Prepubescent males are less susceptible to neuromuscular fatigue following resistance exercise. Eur J Appl Physiol. 2014;114(4):825-35.
16. Pullinen T, Mero A, Huttunen P, Pakarinen A, Komi PV. Resistance exercise-induced hormonal response under the influence of delayed onset muscle soreness in men and boys. Scand J Med Sci Sports. 2011;21(6):e184-94.
17. Willcocks RJ, Fulford J, Armstrong N, Barker AR, Williams CA. Muscle metabolism during fatiguing isometric quadriceps exercise in adolescents and adults. Appl Physiol Nutr Metab. 2014;39(4):439-45.
18. Gorianovas G, Skurvydas A, Streckis V, Brazaitis M, Kamandulis S, McHugh MP. Repeated bout effect was more expressed in young adult males than in elderly males and boys. Biomed Res Int. 2013; 2013:218970.

19. Hatzikotoulas K, Patikas D, Bassa E, Hadjileontiadis L, Koutedakis V, Kotzamanidis C. Submaximal Fatigue and Recovery in Boys and Men. Int J Sports Med. 2009;30(10):741-6.
20. Streckis V, Skurvydas A, Ratkevicius A. Children are more susceptible to central fatigue than adults. Muscle Nerve. 2007;36(3):357-63.
21. Halin R, Germain P, Bercier S, Kapitaniak B, Buttelli O. Neuromuscular response of young boys versus men during sustained maximal contraction. Med Sci Sports Exerc. 2003;35(6):1042-8.
22. Armatas V, Bassa E, Patikas D, Kitsas I, Zangelidis G, Kotzamanidis C. Neuromuscular Differences Between Men and Prepubescent Boys During a Peak Isometric Knee Extension Intermittent Fatigue Test. Pediatr Exerc Sci. 2010;22(2):205-17.
23. Bontemps B, Piponnier E, Chalchat E, Blazevich AJ, Julian V, Bocock O, et al. Children Exhibit a More Comparable Neuromuscular Fatigue Profile to Endurance Athletes Than Untrained Adults. Front Physiol. 2019;10:119.
24. Piponnier E, Martin V, Bourdier P, Biancarelli B, Kluka V, Garcia-Vicencio S, et al. Maturation-related changes in the development and etiology of neuromuscular fatigue. Eur J Appl Physiol. 2019;119(11/12):2545-55.
25. Piponnier E, Martin V, Chalchat E, Bontemps B, Julian V, Bocock O, et al. Effect of Muscle–Tendon Unit Length on Child–Adult Difference in Neuromuscular Fatigue. Med Sci Sports Exerc. 2019;51(9):1961-70.
26. Piponnier E, Ratel S, Chalchat E, Jagot K, Bontemps B, Julian V, et al. Plantar flexor muscle-tendon unit length and stiffness do not influence neuromuscular fatigue in boys and men. Eur J Apply Physiol. 2020;120(3):653-64.
27. Nicolò A, Sacchetti M, Girardi M, McCormick A, Angius L, Bazzucchi I, et al. A comparison of different methods to analyse data collected during time-to-exhaustion tests. Sport Sci Health. 2019;15(3):667-79.
28. Ratel S, Kluka V, Vicencio SG, Jegu AG, Cardenoux C, Morio C, et al. Insights into the Mechanisms of Neuromuscular Fatigue in Boys and Men. Med Sci Sports Exerc. 2015;47(11):2319-28.
29. Lind AR. Cardiovascular adjustments to isometric contractions: static effort; in Handbook of Physiology, The Cardiovascular System, Peripheral Circulation and Organ Blood Flow (Supplement 8). Comprehensive Physiology. 2011:947-66.
30. Amann M, Blain GM, Proctor LT, Sebranek JJ, Pegelow DF, Dempsey JA. Implications of group III and IV muscle afferents for high-intensity endurance exercise performance in humans. J Physiol. 2011;589(Pt 21):5299-309.
31. Hureau TJ, Romer LM, Amann M. The 'sensory tolerance limit': A hypothetical construct determining exercise performance? Eur J Sport Sci. 2018;18(1):13-24.
32. Ratel S, Blazevich AJ. Are prepubertal children metabolically comparable to well-trained adult endurance athletes? Sports Med. 2017;47(8):1477-85.
33. Brownstein CG, Millet GY, Thomas K. Neuromuscular responses to fatiguing locomotor exercise. Acta Physiol. 2020;231(2):e13533.
34. Temesi J, Besson T, Parent A, Singh B, Martin V, Brownstein CG, et al. Effect of race distance on performance fatigability in male trail and ultra-trail runners. Scand J Med Sci Sports. 2021;31(9):1809-21.
35. Ratel S, Tonson A, Le Fur Y, Cozzone P, Bendahan D. Comparative analysis of skeletal muscle oxidative capacity in children and adults: a 31P-MRS study. App Physiol Nutr Metab. 2008;33(4):720-7.
36. Kruger RL, Aboodarda SJ, Samozino P, Rice CL, Millet GY. Isometric versus Dynamic Measurements of Fatigue: Does Age Matter? A Meta-analysis. Med Sci Sports Exerc. 2018;50(10):2132-44.

37. McPheeters ML, Kripalani S, Peterson NB, Idowu RT, Jerome RN, Potter SA, et al. Closing the quality gap: revisiting the state of the science (vol. 3: quality improvement interventions to address health disparities). Evid Rep Technol Assess. 2012; 1-475.
38. Hedges L, Olkin I. P. 369 in Statistical methods for meta-analysis. New York Academic Press, New York, USA; 1985.
39. Morris SB, DeShon RP. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. Psychol Methods. 2002;7(1):105.
40. Shadish WR, Haddock CK. Combining estimates of effect size. The handbook of research synthesis and meta-analysis. 2009;2:257-77.
41. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-60.
42. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34.
43. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994:1088-101.
44. Pullinen T, Mero A, Huttunen P, Pakarinen A, Komi PV. Resistance exercise-induced hormonal responses in men, women, and pubescent boys. Med Sci Sports Exerc. 2002;34(5):806-13.
45. Tibana RA, Prestes J, Nascimento Dda C, Martins OV, De Santana FS, Balsamo S. Higher muscle performance in adolescents compared with adults after a resistance training session with different rest intervals. J Strength Cond Res. 2012;26(4):1027-32.
46. Woods S, Dotan R, Jenicek N, Falk B. Isometric-based EMG threshold in girls and women. Eur J Appl Physiol. 2020;120(4):907-14.
47. Woods S, Dotan R, Jenicek N, Maynard J, Gabriel D, Tokuno C, et al. Isometric-based test improves EMG-threshold determination in boys vs. men. Eur J Appl Physiol. 2019;119(9):1971-9.
48. Äyrämö S, Vilmi N, Mero AA, Piirainen J, Nummela ARI, Pullinen T, et al. Maturation-related differences in neuromuscular fatigue after a short-term maximal run. Hum Mov. 2017;18(3):17-25.
49. Streckis V, Skurvydas A, Ratkevicius A. Twelve-to thirteen-year-old boys are more resistant to low-frequency fatigue than young men. Pediatr Exerc Sci. 2005;17(4):399-409.
50. Birat A, Bourdier P, Piponnier E, Blazevich AJ, Maciejewski H, Duché P, et al. Metabolic and Fatigue Profiles Are Comparable Between Prepubertal Children and Well-Trained Adult Endurance Athletes. Front Physiol. 2018;9:387.
51. De Ste Croix MB, Deighan MA, Ratel S, Armstrong N. Age- and sex-associated differences in isokinetic knee muscle endurance between young children and adults. Appl Physiol Nutr Metab. 2009;34(4):725-31.
52. Dipla K, Tsirini T, Zafeiridis A, Manou V, Dalamitros A, Kellis E, et al. Fatigue resistance during high-intensity intermittent exercise from childhood to adulthood in males and females. Eur J Appl Physiol. 2009;106(5):645-53.
53. Ftikas C, Sfyriou E, Stefanopoulos P, Kotzamanidou M, Bassa E, Lazaridis S. The effect of a stretch-shortening cycle fatigue test on the dynamic characteristics of lower limbs in adult men and pre-pubescent boys. JPES. 2010;27(2):27-32.
54. Hebestreit H, Mimura K, Bar-Or O. Recovery of muscle power after high-intensity short-term exercise: comparing boys and men. J Appl Physiol. 1993;74(6):2875-80.
55. Liamopoulou P, Ioannidis T, Lazaridis S. Effect of age on indirect symptoms of muscle damage after fatigue exercise. EJMAS. 2015.
56. Marginson V, Rowlands AV, Gleeson NP, Eston RG. Comparison of the symptoms of exercise-induced muscle damage after an initial and repeated bout of plyometric exercise in men and boys. J Appl Physiol. 2005;99(3):1174-81.

57. Weinstein Y, Inbar O, Mor-Unikovski R, Luder A, Dubnov-Raz G. Recovery of upper-body muscle power after short intensive exercise: comparing boys and men. Eur J Appl Physiol. 2018;118(8):1555-64.
58. Hamada T, Sale DG, MacDougall JD, Tarnopolsky MA. Interaction of fibre type, potentiation and fatigue in human knee extensor muscles. Acta Physiol Scand. 2003;178(2):165-73.
59. Barclay CJ. Mechanical efficiency and fatigue of fast and slow muscles of the mouse. J Physiol. 1996;497 (Pt 3):781-94.
60. Lexell J, Sjöström M, Nordlund AS, Taylor CC. Growth and development of human muscle: a quantitative morphological study of whole vastus lateralis from childhood to adult age. Muscle Nerve. 1992;15(3):404-9.
61. Sjöström M, Lexell J, Downham DY. Differences in fiber number and fiber type proportion within fascicles. A quantitative morphological study of whole vastus lateralis muscle from childhood to old age. Anat Rec. 1992;234(2):183-9.
62. Ratel S, Tonson A, Le Fur Y, Cozzone P, Bendahan D. Comparative analysis of skeletal muscle oxidative capacity in children and adults: a 31P-MRS study. App Physiol Nutr Metab. 2008;33(4):720-7.
63. Taylor D, Kemp G, Thompson C, Radda G. Ageing: effects on oxidative function of skeletal muscle in vivo. Detection of mitochondrial diseases: Springer; 1997. p. 321-4.
64. McCormack SE, McCarthy MA, Farilla L, Hrovat MI, Systrom DM, Grinspoon SK, et al. Skeletal muscle mitochondrial function is associated with longitudinal growth velocity in children and adolescents. J Clin Endocrinol Metab. 2011;96(10):E1612-E8.
65. Kappenstein J, Ferrauti A, Runkel B, Fernandez-Fernandez J, Müller K, Zange J. Changes in phosphocreatine concentration of skeletal muscle during high-intensity intermittent exercise in children and adults. Eur J Appl Physiol. 2013;113(11):2769-79.
66. Blain GM, Mangum TS, Sidhu SK, Weavil JC, Hureau TJ, Jessop JE, et al. Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans. J Physiol. 2016;594(18):5303-15.
67. Amann M, Sidhu SK, Weavil JC, Mangum TS, Venturelli M. Autonomic responses to exercise: group III/IV muscle afferents and fatigue. Auton Neurosci. 2015 Mar;188:19-23.
68. Craig A. Pain mechanisms: labeled lines versus convergence in central processing. Annu Rev Neurosci. 2003;26(1):1-30.
69. Craig AD. Distribution of brainstem projections from spinal lamina I neurons in the cat and the monkey. J Comp Neurol. 1995;361(2):225-48.
70. Amann M, Blain GM, Proctor LT, Sebranek JJ, Pegelow DF, Dempsey JA. Group III and IV muscle afferents contribute to ventilatory and cardiovascular response to rhythmic exercise in humans. J Appl Physiol. 2010;109(4):966-76.
71. Kayser B. Exercise starts and ends in the brain. Eur J Appl Physiol. 2003;90(3-4):411-9.
72. Borg G. Borg's perceived exertion and pain scales. Champaing, IL: Human kinetics. 1998;104.
73. Robertson RJ, Noble BJ. Perception of physical exertion: methods, mediators, and applications. Exerc Sport Sci Rev. 1997;25:407-52.
74. Bar-Or O. Age-related changes in exercise perception. Physical Work and Effort G Borg (ED). 1977:255-6.
75. Bar-Or O. Rating of perceived exertion in children. Advances in pediatric sports sciences. 1989:151-68.
76. Ratel S, Williams CA, Oliver J, Armstrong N. Effects of age and mode of exercise on power output profiles during repeated sprints. Eur J Appl Physiol. 2004;92(1-2):204-10.

77. Ratel S, Williams CA, Oliver J, Armstrong N. Effects of age and recovery duration on performance during multiple treadmill sprints. Int J Sports Med. 2006;27(1):1-8.
78. Huebner M, Zhang Z, Therneau T, McGrath P, Pianosi P. Modeling trajectories of perceived leg exertion during maximal cycle ergometer exercise in children and adolescents. BMC Med Res Methodol. 2014;14:4.
79. Barkley JE, Roemmich JN. Validity of the CALER and OMNI-bike ratings of perceived exertion. Med Sci Sports Exerc. 2008;40(4):760-6.
80. Lamb KL. Children's ratings of effort during cycle ergometry: an examination of the validity of two effort rating scales. Ped Exerc Sci. 1995;7(4):407-21.
81. Millet GY. Can Neuromuscular Fatigue Explain Running Strategies and Performance in Ultra-Marathons? Sports Med. 2011;41(6):489-506.
82. Dotan R, Mitchell C, Cohen R, Klentrou P, Gabriel D, Falk B. Child—adult differences in muscle activation—a review. Ped Exerc Sci. 2012;24(1):2-21.
83. Ratel S, Martin V. Is there a progressive withdrawal of physiological protections against high-intensity exercise-induced fatigue during puberty? Sports. 2015;3(4):346-57.
84. Carroll TJ, Taylor JL, Gandevia SC. Recovery of central and peripheral neuromuscular fatigue after exercise. J Appl Physiol. 2017;122(5):1068-76.
85. Enoka RM, Stuart DG. Neurobiology of muscle fatigue. J Appl Physiol. 1992;72(5):1631-48.
86. Cooper DM, Kaplan MR, Baumgarten L, Weiler-Ravell D, Whipp BJ, Wasserman K. Coupling of ventilation and CO 2 production during exercise in children. Pediatric Res. 1987;21(6):568-72.
87. Cooper DM, Leu S-Y, Galassetti P, Radom-Aizik S. Dynamic interactions of gas exchange, body mass, and progressive exercise in children. Med Sci Sports Exerc. 2014;46(5):877.
88. Buchheit M, Duche P, Laursen PB, Ratel S. Postexercise heart rate recovery in children: relationship with power output, blood pH, and lactate. Appl Physiol Nutr Metab. 2010;35(2):142-50.
89. Clark BC, Collier SR, Manini TM, Ploutz-Snyder LL. Sex differences in muscle fatigability and activation patterns of the human quadriceps femoris. Eur J Appl Physiol. 2005;94(1):196-206.
90. Pageaux B. Perception of effort in exercise science: definition, measurement and perspectives. Eur J Sport Sci. 2016;16(8):885-94.
91. Bailey RC, Olson J, Pepper SL, Porszasz J, Barstow TJ, Cooper DM. The level and tempo of children's physical activities: an observational study. Med Sci Sports Exerc. 1995;27(7):1033-41.
92. Bar-Or O, Rowland TW. Pediatric exercise medicine: from physiologic principles to health care application: Human Kinetics; 2004.
93. Notley SR, Akerman AP, Meade RD, McGarr GW, Kenny GP. Exercise thermoregulation in prepubertal children: a brief methodological review. Med Sci Sports Exerc. 2020;52(11):2412.
94. Rowland T. Thermoregulation during exercise in the heat in children: old concepts revisited. J Appl Physiol. 2008;105(2):718-24.
95. Kanehisa H, Okuyama H, Ikegawa S, Fukunaga T. Fatigability during repetitive maximal knee extensions in 14-year-old boys. Eur J Appl Physiol Occup Physiol. 1995;72(1-2):170-4.
96. Chen TC, Chen HL, Liu YC, Nosaka K. Eccentric exercise-induced muscle damage of pre-adolescent and adolescent boys in comparison to young men. Eur J Appl Physiol. 2014;114(6):1183-95.

97. Ratel S, Bedu M, Hennegrave A, Doré E, Duché P. Effects of age and recovery duration on peak power output during repeated cycling sprints. Int J Sports Med. 2002;23(6):397-402.
98. Faigenbaum AD, Ratamess NA, McFarland J, Kaczmarek J, Coraggio MJ, Kang J, et al. Effect of rest interval length on bench press performance in boys, teens, and men. Ped Exerc Sci. 2008;20(4):457-69.
99. Van Praagh E, Doré E. Short-term muscle power during growth and maturation. Sports Med. 2002;32(11):701-28.
100. Glenmark B, Hedberg G, Kaijser L, Jansson E. Muscle strength from aldolescence to adulthood—relationship to muscle fibre types. Eur J Appl Physiol Occup Physiol. 1994;68(1):9-19.
101. Berg A, Keul J. Biochemical changes during exercise in children. Young athletes Champaign, IL: Human Kinetics. 1988:61-78.
102. Nezua A, Kimura S, Uehara S, Kobayashia T, Tanaka M, Saito K. Magnetic stimulation of motor cortex in children: maturity of corticospinal pathway and problem of clinical application. Brain Dev. 1997;19(3):176-80.
103. Froyd C, Millet GY, Noakes TD. The development of peripheral fatigue and short-term recovery during self-paced high-intensity exercise. J Physiol. 2013;591(5):1339-46.
104. Mira J, Lapole T, Souron R, Messonnier L, Millet GY, Rupp T. Cortical voluntary activation testing methodology impacts central fatigue. Eur J Appl Physiol. 2017; 117(9):1845-1857.
105. Gruet M, Temesi J, Rupp T, Levy P, Verges S, Millet GY. Dynamics of corticospinal changes during and after high-intensity quadriceps exercise. Exp Physiol. 2014;99(8):1053-64.
106. Buchowski MS, Simmons SF, Whitaker LE, Powers J, Beuscher L, Choi L, et al. Fatigability as a function of physical activity energy expenditure in older adults. Age. 2013;35(1):179-87.
107. Murphy SL, Smith DM. Ecological measurement of fatigue and fatigability in older adults with osteoarthritis. J Gerontol A Biol Sci Med Sci. 2010;65(2):184-9.
108. Guinhouya B, Samouda H, De Beaufort C. Level of physical activity among children and adolescents in Europe: a review of physical activity assessed objectively by accelerometry. Public Health. 2013;127(4):301-11.
109. Prince SA, Adamo KB, Hamel ME, Hardt J, Gorber SC, Tremblay M. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. Int J Behav Nutr Phys Act. 2008;5(1):1-24.
110. Gaul CA, Docherty D, Cicchini R. Differences in anaerobic performance between boys and men. Int J Sports Med. 1995 Oct;16(7):451-5.
111. Soares JM, Mota P, Duarte JA, Appell HJ. Children are less susceptible to exercise-induced muscle damage than adults: a preliminary investigation. Ped Exerc Sci. 1996;8(4):361-7.