Online version at https://www.minervamedica.it

The Journal of Sports Medicine and Physical Fitness 2023 mese;63(0):000-000
DOI: 10.23736/S0022-4707.23.14971-1

REVIEW
EXERCISE PHYSIOLOGY AND BIOMECHANICS

Acute physiological responses to eccentric cycling: a systematic review and meta-analysis

Renan V. BARRETO [1] *, Leonardo C. LIMA [2], Fernando K. BORSZCZ [3], Ricardo D. de LUCAS [3], Benedito S. DENADAI [1]

[1]Human Performance Laboratory, Department of Physical Education, São Paulo State University, Rio Claro, Brazil; [2]School of Physical Education and Sport of Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil; [3]Physical Effort Laboratory, Sports Centre, Federal University of Santa Catarina, Florianópolis, Santa Catarina, Brazil

*Corresponding author: Renan V. Barreto, Human Performance Laboratory, Department of Physical Education, São Paulo State University, 24A 1515, 13506900, Rio Claro, Brazil. E-mail: renan.vieira@unesp.br

ABSTRACT

INTRODUCTION: Eccentric cycling (ECC_{CYC}) has attracted considerable interest due to its potential applicability for exercise treatment/training of patients with poor exercise tolerance as well as healthy and trained individuals. Conversely, little is known about the acute physiological responses to this exercise modality, thus challenging its proper prescription. This study aimed to provide precise estimates of the acute physiological responses to ECC_{CYC} in comparison to traditional concentric cycling (CON_{CYC}).

EVIDENCE ACQUISITION: Searches were performed until November 2021 using the PubMed, Embase, and ScienceDirect databases. Studies that examined individuals' cardiorespiratory, metabolic, and perceptual responses to ECC_{CYC} and CON_{CYC} sessions were included. Bayesian multilevel meta-analysis models were used to estimate the population mean difference between acute physiological responses from ECC_{CYC} and CON_{CYC} bouts. Twenty-one studies were included in this review.

EVIDENCE SYNTHESIS: The meta-analyses showed that ECC_{CYC} induced lower cardiorespiratory (*i.e.*, $\dot{V}O_2$, $\dot{V}E$, and HR), metabolic (*i.e.*, [BLa]), and perceptual (*i.e.*, RPE) responses than CON_{CYC} performed at the same absolute power output, while greater cardiovascular strain (*i.e.*, greater increases in HR, Q, MAP, [norepinephrine], and lower SV) was detected when compared to CON_{CYC} performed at the same $\dot{V}O_2$.

CONCLUSIONS: The prescription of ECC_{CYC} based on workloads used in the CON_{CYC} sessions may be considered safe and, therefore, feasible for the rehabilitation of individuals with poor exercise tolerance. However, the prescription of ECC_{CYC} based on the $\dot{V}O_2$ obtained during CON_{CYC} sessions should be conducted with caution, especially in clinical settings, since there is a high probability of additional cardiovascular overload in this condition.

(*Cite this article as*: Barreto RV, Lima LC, Borszcz FK, De Lucas RD, Denadai BS. Acute physiological responses to eccentric cycling: a systematic review and meta-analysis. J Sports Med Phys Fitness 2023;63:000-000. DOI: 10.23736/S0022-4707.23.14971-1)

KEY WORDS: Oxygen consumption; Heart rate; Blood pressure.

Introduction

Eccentric exercise via motorized cycle ergometers, referred as eccentric cycling (ECC_{CYC}), has been attracting much interest due to its distinctive mechanical and physiological proprieties. During ECC_{CYC} sessions, one must resist (*i.e.*, attempt to brake) the backward moving pedals of the cycle ergometer by performing eccentric (*i.e.*, lengthening) contractions of the locomotor muscles.[1, 2] Due to the eccentric nature of this exercise modality, the energy requirement for mechanical work production (or "absorption") is reduced compared to traditional concentric exercises.[3-5] Accordingly, reduced cardiovascular, respiratory, and perceptual responses have been reported during ECC_{CYC} compared to concentric cycling (CON_{CYC}).[6-9]

These characteristics make ECC_{CYC} an attractive modality for exercise treatment of individuals with limited exercise tolerance such as older adults and patients with cardiopulmonary diseases.[8, 10, 11] Owing to the cardiopulmonary constraints, patients may be unable to sustain exercise workloads that provide sufficient stimulus to promote significant adaptations.[12] Hence, the rationale behind prescribing ECC_{CYC} for these populations is that, through ECC_{CYC}, patients would be able to accumulate greater amounts of muscle work over rehabilitation sessions without additional cardiopulmonary and/or psychophysiological burdens compared to those experienced during traditional exercise rehabilitation programs (commonly comprising CON_{CYC} sessions). However, prescribing ECC_{CYC} remains a challenging task since few studies have shed light on tolerance to maximal eccentric exercise[13, 14] and no study have investigated submaximal physiological anchors or intensity domains that should guide health professionals regarding the expected degree of homeostatic disturbance (measured as cardiorespiratory, metabolic, and/or perceptual responses) induced by exercising at a pre-determined eccentric workload.[15]

To date, ECC_{CYC} training protocols are mainly designed based on CON_{CYC} workloads, oxygen uptake ($\dot{V}O_2$), heart rate (HR), or rating of perceived exertion (RPE).[15] Information regarding the acute physiological responses to ECC_{CYC} sessions come from cross-sectional studies involving similar protocols of ECC_{CYC} and CON_{CYC} performed incrementally[7, 9, 13, 14] or at fixed power output (PO) or $\dot{V}O_2$.[16, 17] Evidence from eccentric and concentric bouts performed at the same external workload (*i.e.*, PO) indicate reduced energetic and cardiopulmonary demand during ECC_{CYC}. For instance, the expected difference of $\dot{V}O_2$ between ECC_{CYC} and CON_{CYC} was suggested by Hoppeler[11] to be ~4 times lesser. However, no study has systematically reviewed the literature and performed a meta-analysis to provide such reference values. Recent evidence also suggests that when both cycling modalities are performed at the same $\dot{V}O_2$, ECC_{CYC} induces greater cardiac overload.[18, 19] The greater workload performed eccentrically to match the $\dot{V}O_2$ produced during CON_{CYC} is suggested to induce greater autonomic drive and thermal stress, which were associated with greater cardiac overload.[18-20] Hence, a better knowledge of the acute physiological responses to ECC_{CYC} compared to CON_{CYC} may help in the designing of safe and effective exercise interventions. Therefore, the present review aimed to verify the differences in the physiological and perceptual responses to ECC_{CYC} and CON_{CYC} by employing a systematized search in the literature followed by a Bayesian meta-analysis.

Evidence acquisition

This study was part of a larger systematic review project investigating the acute and chronic physiological responses to ECC_{CYC} compared to CON_{CYC}. Hence, the search strategy and selection of studies included both cross-sectional and longitudinal studies that investigated the responses to ECC_{CYC} bouts and training protocols, respectively. The original protocol was prospectively registered within the Open Science Framework (https://osf.io/sa6g3). This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21]

Study eligibility

The eligibility criteria were based on PICO framework (Population, Intervention, Comparator, and Outcome). The *population* included male and female human subjects without restrictions on age, health condition, or level of physical fitness. As an *intervention*, the studies must have included a session of ECC_{CYC} lasting at least five minutes. The *comparator* consisted of a CON_{CYC} bout performed at similar PO or $\dot{V}O_2$ and with equal duration to the ECC_{CYC} bout. Studies that reported on *outcomes* related to physiological parameters (*e.g.*, $\dot{V}O_2$, HR, and RPE) during exercise were considered for inclusion. Additionally, only peer-reviewed original articles written in the English language were considered eligible. Studies that investigated acute physiological responses to single-leg ECC_{CYC} sessions or ECC_{CYC} performed with the upper limbs were excluded.

Information sources

Searches of the literature were conducted until February 2021 and updated in November 2021 using the electronic databases PubMed, ScienceDirect, and Embase. The reference list of the selected studies was checked, and relevant studies were included in the analysis. Relevant data and information from selected studies were requested from authors when they were not clearly presented.

Search strategy

The search strategy was designed to track all possible studies on the topic of "eccentric cycling". We used five known relevant studies for the development of the search strategy.[16, 17, 22-24] Possible search terms were identified by analyzing the titles and abstracts of the records. Search terms were also identified and verified using the PubMed database word frequency analysis tool.

The search strategy was verified by identifying the known relevant studies in the results of preliminary searches and by identifying new relevant studies, obtained through changing search terms. Hence, we used the following search syntax (or equivalent) to search through titles and abstracts of indexed documents: ("eccentric" OR "eccentrically" OR "negative work") AND ("cycling" OR "bicycle" OR "pedaling" OR "pedalling" OR "ergometer" OR "ergometry"). No temporal clipping was established.

Study selection

The study selection was carried out independently by two authors (RB and LL), using a freely available software - Rayyan QCRI (https://www.rayyan.ai/).[25] Following duplicate removal, irrelevant studies were discarded by reviewing titles and abstracts. Subsequently, full-text articles were read and evaluated according to the established eligibility criteria.

Data extraction

Two authors (RB and LL) independently extracted the data from each of the selected studies into an Excel spreadsheet (Microsoft, Redmond, WA, USA). The same authors then compared their spreadsheets and addressed the inconsistencies by discussion. When necessary, data were extracted from figures using the freely available software Web Plot Digitizer (https://automeris.io/WebPlotDigitizer).

Data items

Relevant information regarding the publication (*i.e.*, author, year, journal, and digital object identifier [DOI]), population (*i.e.*, sample size, age, height, body mass, maximal oxygen uptake [$\dot{V}O_{2max}$], and health condition), intervention (*i.e.*, intensity, duration, pedal cadence, and type of the session), comparator (*i.e.*, ECC_{CYC} *vs.* CON_{CYC} at the same PO or $\dot{V}O_2$), and outcomes (*i.e.*, mean and standard deviation [SD] of the physiological parameter assessed during CON_{CYC} and ECC_{CYC} sessions and the inferential statistics parameters) was extracted from each study.

Following data extraction, the studies involving ECC_{CYC} and CON_{CYC} sessions performed at the same PO were separated from those investigating sessions performed at the same $\dot{V}O_2$. Thus, it was possible to identify the physiological variables assessed by at least three selected studies (for each condition of comparison) that was therefore viable to be meta-analyzed. Hence, for the analysis of the acute physiological responses to ECC_{CYC} compared to CON_{CYC} performed at the same PO, we selected variables of cardiorespiratory demand (*i.e.*, $\dot{V}O_2$, pulmonary ventilation per minute [$\dot{V}E$], and HR), metabolic demand (*i.e.*, blood lactate concentration [BLa]), and psychophysiological burden (*i.e.*, RPE). For the evaluation of acute physiological responses to ECC_{CYC} compared to CON_{CYC} performed at the same $\dot{V}O_2$ we selected cardiovascular variables (*i.e.*, cardiac output [Q], HR, stroke volume [SV], and mean arterial blood pressure [MAP]), norepinephrine blood concentration, and PO produced during the sessions.

Study quality assessment

The Physiotherapy Evidence-Based Database (PEDro) Scale was used to rate the methodological quality of the selected reports.[26] The PEDro Scale consists of 11 items related to the external (item 1) and internal (items 2-9) validity of the study and the statistical information presented (items 10-11). For each satisfied item, the report receives 1 point, except for the first item, which was not used to calculate the PEDro Score. Thus, the higher the study score (with 10 points being the maximum score), the higher the quality of the study.[26] The study quality assessment was carried out by two independent authors (RB and LL) and divergences were resolved by a third author (BD).

Effect size calculation

The effect size of interest was the mean difference in percentage units between control (*i.e.*, mean of the physiological variable obtained during a CON_{CYC} session) and experimental (*i.e.*, mean of the physiological variable obtained during an ECC_{CYC} session) conditions. Therefore, a positive effect size value means that the response of the analyzed physiological variable was % higher in CON_{CYC} compared to ECC_{CYC}, and *vice versa*. To calculate effect sizes from studies with more than one ECC_{CYC} session (*i.e.*, studies investigating the repeated bout effect), we used the data from the last ECC_{CYC} session for comparison with the control condition, since most (71%) of the selected studies[16, 18, 20, 27-38] included a familiarization period (1-4 sessions) before experimental sessions.

The precision of the effect sizes was given by the standard error (SE) of the difference between CON_{CYC} and ECC_{CYC} conditions. The SE was calculated by dividing the SD of the differences between conditions by the square root of the sample size. Within the meta-analytic model, the weight of each study was set by the inverse of the squared SE ($1/SE^2$). Thus, studies with less variability in responses and/or a greater number of participants exerted greater weight on the final meta-analyzed result.

The SDs of the difference between the control and experimental conditions were determined using the exact P values via t-statistics, F-values, raw data, or was extracted from figures. When it was not possible, the SDs of the difference were imputed by the mean correlation coefficient

(r) of the studies in which this determination was possible. A moderate correlation coefficient (r=0.50) was adopted for the imputation of the SDs when none of the alternatives described above were possible.

The mean difference and the SE were then converted to percentage units by dividing by the mean of CON_{CYC} condition and multiplying by 100.

Statistical analysis

The meta-analyses were conducted within a Bayesian framework using multilevel models. For all analyses, the identity of each effect was set as a random effect (*i.e.*, random-effects meta-analysis). Additional random effects (group levels) were used to account for the influence of the health condition of the participants and the duration and intensity of the sessions on the effect size. Meta-regressions were performed when the number of effects was greater than or equal to 10,[39] with the mean participants' $\dot{V}O_{2max}$ and the duration and intensity of the sessions as covariates (*i.e.*, fixed effects). Heterogeneity was presented as SD (tau - τ) between all effects (*i.e.*, each effect size observed in each study) and between subjects and studies characteristics set as group-level effects. Analysis was performed in the statistical software R (v4.0; R Core Team [2020], Vienna, Austria) in its graphical interface RStudio (v1.2.5). The package brms[40] was used for analysis, which allowed the adjustment of multilevel Bayesian models using Stan.[41]

Weakly-informative Student's-t prior distributions (df = 3, μ = 0, and σ = 10) were used for models fixed effects. Moderately informative half-normal prior distributions (μ = 0 and σ = 3 to 5) were used for the between group-level effects variances (*i.e.*, τ values). Model fitting was performed using Markov Chain Monte Carlo (MCMC) methods, more specifically the No-U-Turn sampler (NUTS) implemented in Stan (*i.e.*, a platform for statistical modeling and high-performance statistical computation). For each model, four chains were run in parallel with 4000 iterations and a warm-up of 1000 iterations. The convergence of the models was verified with Gelman-Rubin diagnostics ($\hat{R}$).[42]

To deal with repeated measures in the meta-analyses of studies with more than one effect for the same participant, variance-covariance matrices were calculated. When the information provided in the studies was insufficient to determine the correlation between the dependent effect sizes to perform the matrix calculation, a moderate correlation coefficient (r=0.50) was assumed between the effects derived from the same participants. Furthermore, sensitivity analyzes were performed also using the values of r = 0.30 and 0.70 in the calculation of matrices (Supplementary Digital Material 1: Supplementary Figure 1-7).

For meta-regressions in which the covariates were missing, we imputed the data during model fitting using a multivariate model as described elsewhere.[43]

All data were reported as posterior means with two-tailed 95% credible intervals (CrI). Furthermore, considering the complete posterior distributions, the probability (in %) of the effect being smaller (P<0) than zero (*i.e.*, greater response during ECC_{CYC}) was presented, that is, the area of the posterior distribution located below zero.

Transformations

To analyze the physiological responses to ECC_{CYC} and CON_{CYC} sessions performed at the same $\dot{V}O_2$, it was necessary to convert $\dot{V}O_2$ values obtained during the sessions (reported in units of $ml \cdot min^{-1}$, $l \cdot min^{-1}$, and $mL \cdot kg^{-1} \cdot min^{-1}$) for percentage values relative to $\dot{V}O_{2max}$.

For the analysis of RPE during ECC_{CYC} and CON_{CYC} sessions it was necessary to convert the RPE values assessed using different scales (0-10 and 6-20 scales) into a common scale (0-100 scale).

Evidence synthesis

Study selection

The searches in the databases yielded a total of 992 records (Figure 1). Following the exclusion of 364 duplicates, 628 titles and abstracts were screened. A total of 105 full-text articles were read and assessed for eligibility. Four additional articles were retrieved from reference lists. Finally, a total of 21 articles were included in this review.

Study characteristics

Table I summarizes the main characteristics of the included studies.[16-20, 27-38, 44-47] A total of 18 studies (86%) recruited healthy individuals[16-20, 27-31, 33-37, 45-47] and three studies (14%) recruited individuals with cardiopulmonary diseases.[32, 38, 44] Among the studies that evaluated healthy individuals, one study classified the participants as aerobically trained individuals.[20] Regarding the studies evaluating individuals with cardiopulmonary diseases, two recruited patients with chronic obstructive pulmonary disease,[32, 38] and one study recruited patients with chronic heart failure.[44]

All selected studies used continuous exercise protocols performed at a constant load/demand. The duration

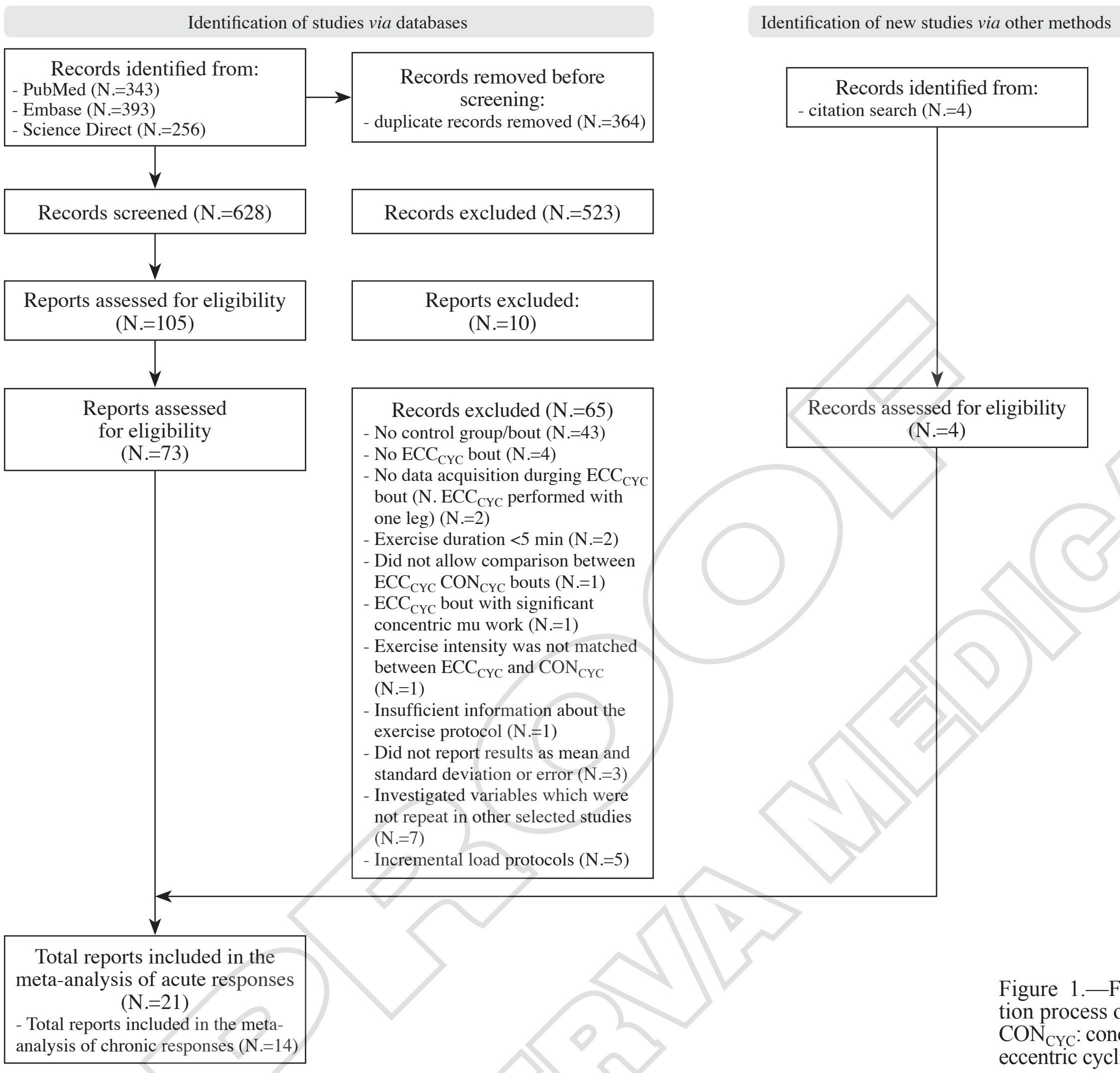

Figure 1.—Flow diagram of selection process of eligible studies. CON$_{CYC}$: concentric cycling, ECC$_{CYC}$: eccentric cycling.

of the sessions ranged from 5 to 45 min (mode =30 min). Thirteen studies (62%) investigated the acute physiological responses to ECC$_{CYC}$ and CON$_{CYC}$ performed at the same PO,[27, 28, 30-32, 34-36, 38, 44-47] five studies (24%) reported results from ECC$_{CYC}$ and CON$_{CYC}$ sessions performed at the same $\dot{V}O_2$,[18-20, 29, 37] and three studies (14%) performed both comparisons (*i.e.*, CON$_{CYC}$ performed once at the same PO and once at the same $\dot{V}O_2$ as ECC$_{CYC}$).[16, 17, 33]

Quality assessment

Scores on the PEDro Scale ranged between 5 and 6 points (mode =6 points; mean =5.52 points) (Table II).[16-20, 27-38, 44-47] Due to the nature of interventions (*i.e.*, cross-over design) and the discernible differences in pedal movement between modalities, blinding of the participants and assessors is considered unfeasible. Therefore, none of the selected studies scored on items 5, 6, and 7 of the PEDro Scale. Moreover, the order of the control and experimental sessions was not randomized in nine (43%) of the selected studies.[17, 20, 30, 31, 33-35, 44, 46] In these studies, the CON$_{CYC}$ session was performed firstly in order to avoid possible interference of eccentric exercise-induced muscle damage on subsequent cycling tests. Thus, the main sources of bias were the lack of order randomization of sessions and concealing allocation (criteria 2 and 3). Overall, the studies included in this review presented “fair” (*i.e.*, 4-5 points) to “good” (*i.e.*, 6-8 points) methodological quality.[48]

TABLE I.—*Study characteristics.*

Study	Population	Intervention			Physiological variables assessed during cycling bouts
		Session type	Duration	Intensity (ECC_{CYC} / CON_{CYC})	
Chasland *et al.*[44]	CHF patients (N.=11)	Constant load	5 min	70% PPO / Same PO	$\dot{V}O_2$, $\dot{V}E$, RER, HR, MAP, and BLa
Clos *et al.*[27]	Healthy individuals (N.=15)	Constant load	30 min	60% PPO / Same PO	$\dot{V}O_2$, HR, EMG, RPE, and muscle pain
Dufour *et al.*[16]	Healthy individuals (N.=11)	Constant load	6 min	270 W / Same PO and same $\dot{V}O_2$	$\dot{V}O_2$, HR, SV, Q, SBP, DBP, MAP, BLa, [epinephrine], [norepinephrine], and EMG
Eiken *et al.*[20]	Aerobic trained individuals (N.=8)	Constant load	~20 min	60% PPO / Same $\dot{V}O_2$	$\dot{V}O_2$, HR, RPE, and body temperature
González-Bartholin *et al.*[28]	Healthy individuals (N.=10)	Constant load	30 min	50% PPO / Same PO	$\dot{V}O_2$, HR, and RPE
Hesser *et al.*[45]	Healthy individuals (N.=7)	Constant load	6 min	16, 33, 49, 98, and 147 W / Same PO	$\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, Bf, Vt, RER, and HR
Isacco *et al.*[29]	Healthy individuals (N.=12)	Constant load	45 min	35% $\dot{V}O_{2max}$ / Same $\dot{V}O_2$	$\dot{V}O_2$, RER, HR, and energy expenditure
Kan *et al.*[30]	Healthy individuals (N.=30)	Constant load	20 min	20% PPO assessed during 10 maximal concentric revolutions at 60 rpm / Same PO	HR, pre-frontal cortex oxygenation, and cognitive demand variables
Kuipers *et al.*[31]	Healthy individuals (N.=6)	Constant load	30 min	80% $\dot{V}O_{2max}$ / Same PO	$\dot{V}O_2$, HR, and BLa
Nickel *et al.*[32]	COPD patients (N.=10)	Constant load	30 min	50% PPO / Same PO	$\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, Bf, SpO_2, HR, SBP, DBP, MAP, RPE, and dyspnea
Okamoto *et al.*[33]	Healthy individuals (N.=15)	Constant load	30 min	60% PPO / Same PO and same $\dot{V}O_2$	$\dot{V}O_2$, HR, SBP, and DBP
Peñailillo *et al.*[34]	Healthy individuals (N.=10)	Constant load	30 min	60% PPO / Same PO	$\dot{V}O_2$, HR, BLa, RPE, and EMG
Peñailillo *et al.*[35]	Healthy individuals (N.=11)	Constant load	10 min	65% PPO / Same PO	$\dot{V}O_2$, HR, muscle oxygenation and hemodynamics, vastus lateralis fascicle behavior, and EMG
Peñailillo *et al.*[36]	Healthy individuals (N.=10)	Constant load	5 min	30-80% PPO / Same PO	$\dot{V}O_2$, HR, and RPE
Perrey *et al.*[17]	Healthy individuals (N.=6)	Constant load	6 min	$\dot{V}O_2$ corresponding to 70% ΔVT-$\dot{V}O_{2max}$ during maximal CON test / Same PO and same $\dot{V}O_2$	$\dot{V}O_2$, HR, RPE, and EMG
Plante and Houston[46]	Healthy individuals (N.=8)	Constant load	15 min	70% PPO / Same PO	$\dot{V}O_2$ and HR
Rakobowchuk *et al.*[18]	Healthy individuals (N.=12)	Constant load	45 min	54% HR_{peak} / 54% HR_{peak}	$\dot{V}O_2$, HR, SV, SBP, DBP, MAP, BLa, and muscle oxygenation
Ritter *et al.*[19]	Healthy individuals (N.=10)	Constant load	45 min	50% HR_{peak} / 50% HR_{peak}	$\dot{V}O_2$, $\dot{V}E$, Bf, Vt, HR, SV, Q, SBP, DBP, MAP, and [norepinephrine]
Rogers *et al.*[37]	Healthy individuals (N.=11)	Constant load	45 min	54% HR_{peak} / 54% HR_{peak}	$\dot{V}O_2$, HR, SBP, DBP, BLa, and [norepinephrine]
Rooyackers *et al.*[38]	COPD patients (N.=12)	Constant load	6 min	50% PPO / Same PO	$\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, HR, and arterial [K^+]
Walsh *et al.*[47]	Healthy individuals (N.=13)	Constant load	30 min	RPE 10-12 / RPE 10-12	HR and RPE

Bf: breath frequency; BLa: blood lactate; CON_{CYC}: concentric cycling; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; ECC_{CYC}: eccentric cycling; EMG: electromyography; HR: heart rate; HR_{peak}: peak heart rate; MAP: mean arterial blood pressure; PO: power output; PPO: peak power output; Q: cardiac output; RER: respiratory exchange ratio; RPE: rate of perceived exertion; SBP: systolic blood pressure; SpO_2: arterial oxygen saturation; SV: systolic volume; $\dot{V}CO_2$: carbon dioxide elimination; $\dot{V}E$: pulmonary ventilation; $\dot{V}O_2$: oxygen uptake; $\dot{V}O_{2max}$: maximal oxygen uptake; Vt: tidal volume; VT: ventilatory threshold.

Meta-analyses of the differences between CON_{CYC} and ECC_{CYC} performed at the same PO

Oxygen uptake

Twelve studies measured $\dot{V}O_2$ during CON_{CYC} and ECC_{CYC} sessions (N. participants =124). The mean effect size indicated that $\dot{V}O_2$ was greater (μ [95% CrI]) 54.08% [47.62%, 60%] during CON_{CYC} compared to ECC_{CYC} sessions (τ [95% CrI] =14% [10.5%, 19.5%]) performed at the same PO (Figure 2).[16, 27, 28, 31-36, 44-46] The resulting posterior distribution showed a probability of (P<0) 0% of $\dot{V}O_2$ to be higher during ECC_{CYC} compared to CON_{CYC} sessions performed at the same PO.

TABLE II.—*Physiotherapy Evidence Database (PEDro) Score.*

Study	PEDro Scale											Total score
	1	2	3	4	5	6	7	8	9	10	11	
Chasland *et al.*[44]	1	0	0	1	0	0	0	1	1	1	1	5
Clos *et al.*[27]	0	1	0	1	0	0	0	1	1	1	1	6
Dufour *et al.*[16]	0	1	0	1	0	0	0	1	1	1	1	6
Eiken *et al.*[20]	0	0	0	1	0	0	0	1	1	1	1	5
González-Bartholin *et al.*[28]	0	1	0	1	0	0	0	1	1	1	1	6
Hesser *et al.*[45]	0	1	0	0	0	0	0	1	1	1	1	5
Isacco *et al.*[29]	1	1	0	1	0	0	0	1	1	1	1	6
Kan *et al.*[30]	0	0	0	1	0	0	0	1	1	1	1	5
Kuipers *et al.*[31]	0	0	0	1	0	0	0	1	1	1	1	5
Nickel *et al.*[32]	1	1	0	1	0	0	0	1	1	1	1	6
Okamoto *et al.*[33]	0	0	0	1	0	0	0	1	1	1	1	5
Peñailillo *et al.*[34]	0	0	0	1	0	0	0	1	1	1	1	5
Peñailillo *et al.*[35]	0	0	0	1	0	0	0	1	1	1	1	5
Peñailillo *et al.*[36]	0	1	0	1	0	0	0	1	1	1	1	6
Perrey *et al.*[17]	0	0	0	1	0	0	0	1	1	1	1	5
Plante and Houston[46]	0	0	0	1	0	0	0	1	1	1	1	5
Rakobowchuk *et al.*[18]	1	1	0	1	0	0	0	1	1	1	1	6
Ritter *et al.*[19]	1	1	0	1	0	0	0	1	1	1	1	6
Rogers *et al.*[37]	0	1	0	1	0	0	0	1	1	1	1	6
Rooyackers *et al.*[38]	0	1	0	1	0	0	0	1	1	1	1	6
Walsh *et al.*[47]	0	1	0	1	0	0	0	1	1	1	1	6

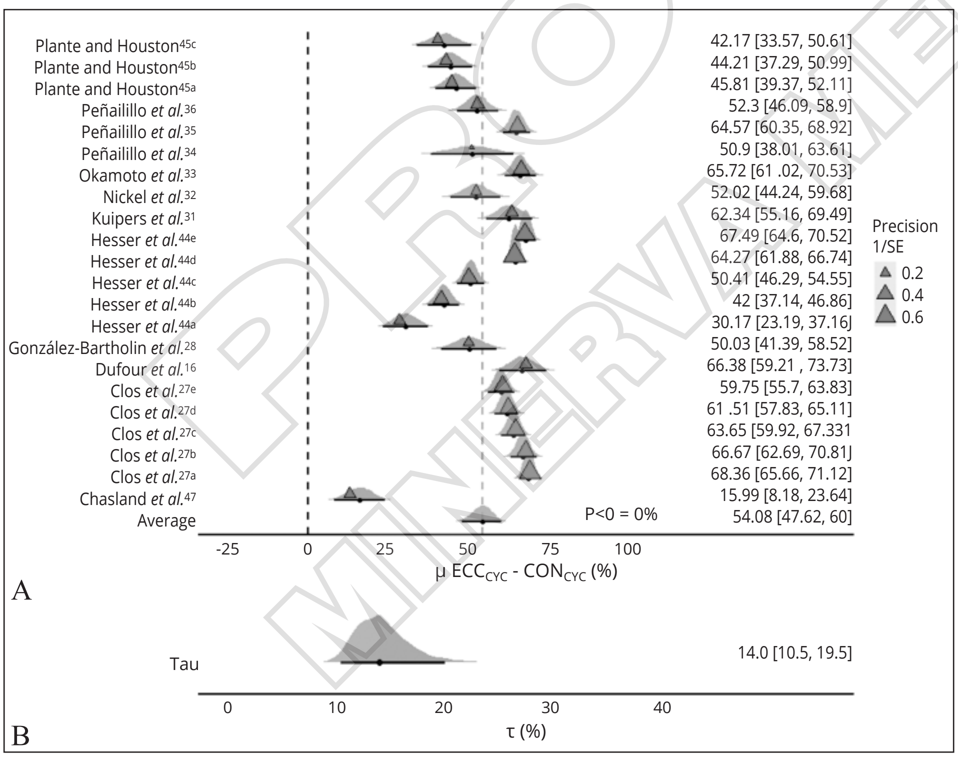

Figure 2.— Forest plot of effect sizes (% mean difference) between oxygen uptake during concentric and eccentric cycling sessions performed at the same power output of all effects and the population estimated average effect (A) and heterogeneity between all effects (B). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[16, 27, 28, 31-36, 44-46]

The meta-regression revealed that the difference between $\dot{V}O_2$ during CON_{CYC} and ECC_{CYC} sessions was greater at higher intensities, mainly for individuals with higher $\dot{V}O_{2max}$, but was not influenced by the duration of sessions (Figure 3). Specifically, for every extra 10 mL/kg/min in the subjects' $\dot{V}O_{2max}$, the percentage difference

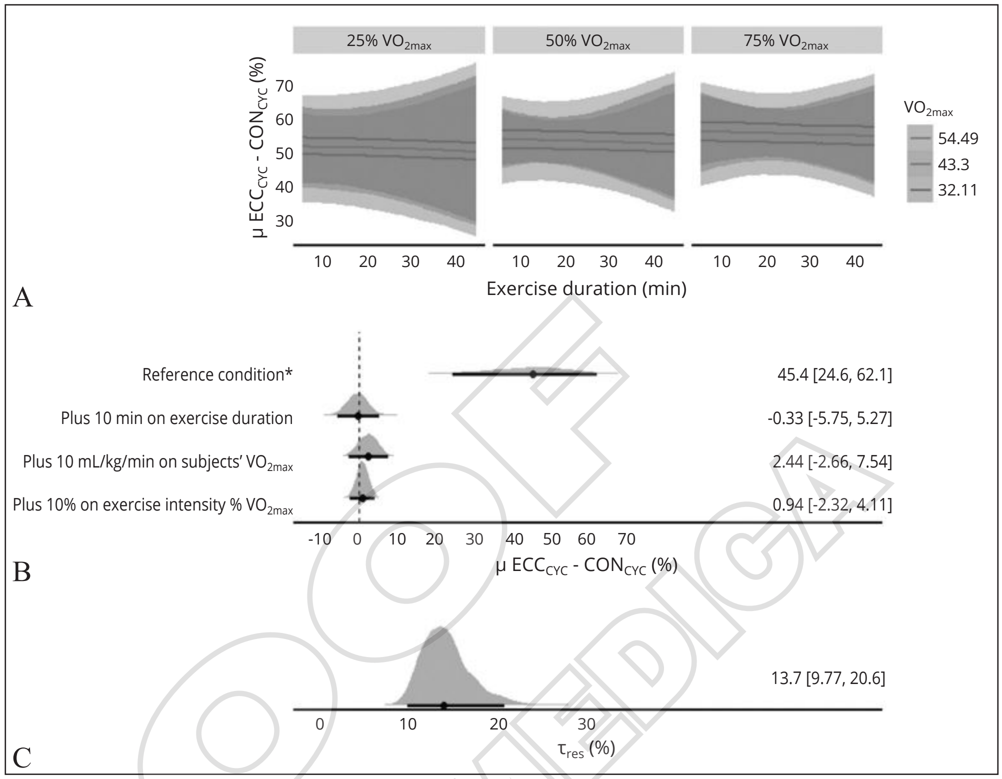

Figure 3.—Meta-regression posterior means and credible intervals of conditional effects on % mean difference between oxygen uptake during concentric and eccentric cycling sessions performed at the same power output with exercise intensity and duration, and subjects' maximal oxygen uptake as covariates (A), reference condition and modifying effects (B), and the residual heterogeneity between effect sizes (C). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively.
CON_{CYC}: concentric cycling; ECC_{CYC}: eccentric cycling; $\dot{V}O_{2max}$: maximal oxygen uptake; τ_{res}: residual heterogeneity.
*Reference condition: exercise duration =5 min; subjects $\dot{V}O_{2max}$ =18.8 mL/kg/min; and exercise intensity =17.3% $\dot{V}O_{2max}$.

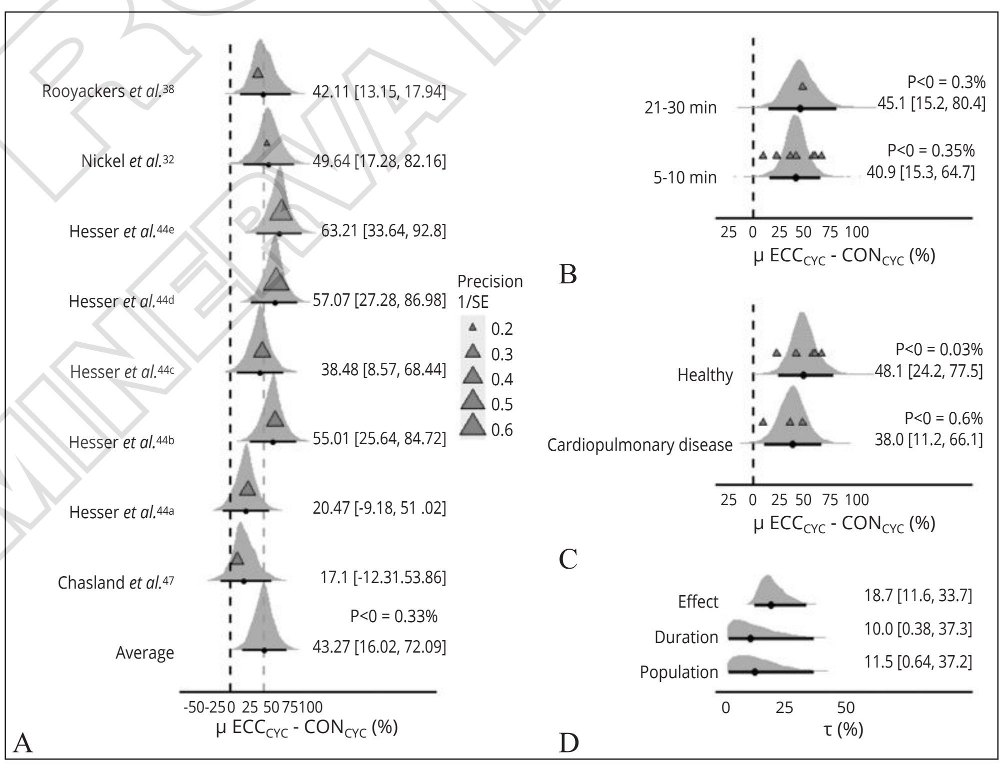

Figure 4.— Forest plot of effect sizes (% mean difference) between pulmonary ventilation during concentric and eccentric cycling sessions performed at the same power output of all effects and the population estimated average effect (A), group-level of exercise duration (B), group-level of subjects' population (C), and heterogeneity between all effects and between group-level effects (D). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and, in the panel *a*, their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[32, 38, 44, 45]

between $\dot{V}O_2$ at CON_{CYC} and ECC_{CYC} increased 2.44% [-2.66%, 7.54%]; for every extra 10% $\dot{V}O_{2max}$ in the intensity of the sessions (*i.e.*, % $\dot{V}O_{2max}$), the difference between CON_{CYC} and ECC_{CYC} increased by 0.94% [-2.32%, 4.11%]; and for every extra 10-min in session duration, the difference between CON_{CYC} and ECC_{CYC} decreased by -0.33% ([-5.75%, 5.27%]). The residual unexplained heterogeneity between effect sizes was $\tau_{Residual}$ =13.7% [9.77%, 20.6%].

Pulmonary ventilation

Four selected studies assessed $\dot{V}E$ during ECC_{CYC} and CON_{CYC} performed at the same PO (N. participants =40) (Figure 4).[32, 38, 44, 45] The meta-analyzed mean effect showed $\dot{V}E$ was 43.27% [16.02%; 72.09%] higher during CON_{CYC} compared to ECC_{CYC} sessions (Figure 4A). The posterior distribution presented minimal probability (P<0=0.33%) of $\dot{V}E$ to be higher during ECC_{CYC} compared to CON_{CYC} performed at the same PO. The posterior distributions of group-level effects of exercise duration were similar (Figure 4B). The posterior distributions of group-level effects of subject's population (Figure 4C) indicated greater difference in $\dot{V}E$ between cycling modes in the studies recruiting healthy individuals (48.1% [24.2%, 77.5%]; P<0=0.03%) compared to those recruiting cardiopulmonary patients (38% [11%, 66.1%]; P<0=0.6%). Considerable heterogeneity was observed between all effects (τ_{Effect} =18.7% [11.6%, 33.7%]) and between group-level effects ($\tau_{Duration}$ =10% [0.38%, 37.3%]; $\tau_{Population}$ =11.5% [0.64%, 37.2%]) (Figure 4D).

Heart rate

A total of 14 studies assessed HR (N. participants =161) (Figure 5).[16, 27, 28, 30-36, 44-47] The estimate of the mean effect size indicated that the HR was 28.16% [23.13%, 33.27%] higher (τ = 12.2 [9.23%, 16.9%]) during CON_{CYC} than ECC_{CYC} sessions performed at the same PO (Figure 5A). The posterior distribution of the mean effect indicated a probability of 0% of HR being higher during ECC_{CYC} compared to CON_{CYC}.

Meta-regression revealed that the difference between HR during CON_{CYC} and ECC_{CYC} was higher in participants with higher $\dot{V}O_{2max}$ and sessions with longer duration (Figure 6). Furthermore, the difference in HR between CON_{CYC} and ECC_{CYC} decreased as the intensity of the sessions increased. Meta-regression-derived modifying effects (Figure 6B) showed that for every extra 10 mL/kg/min in the subjects' $\dot{V}O_{2max}$, the difference in HR between

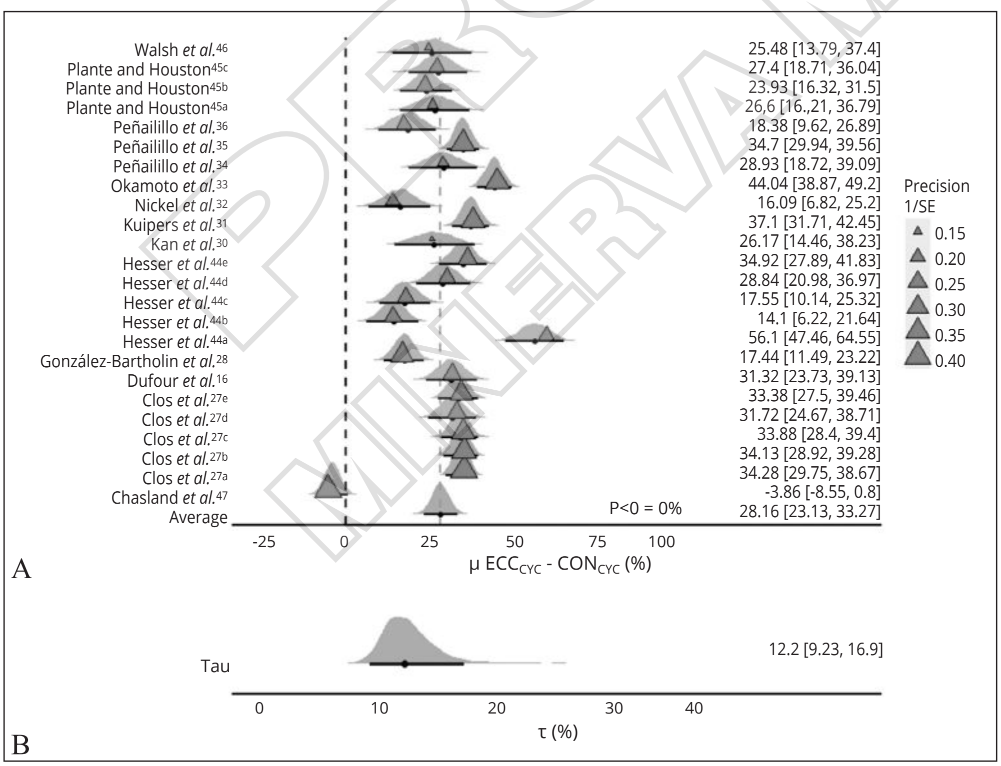

Figure 5.—Forest plot of effect sizes (% mean difference) between heart rate during concentric and eccentric cycling sessions performed at the same power output of all effects and the population estimated average effect (A) and heterogeneity between all effects (B). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[16, 27, 28, 30-36, 44-47]

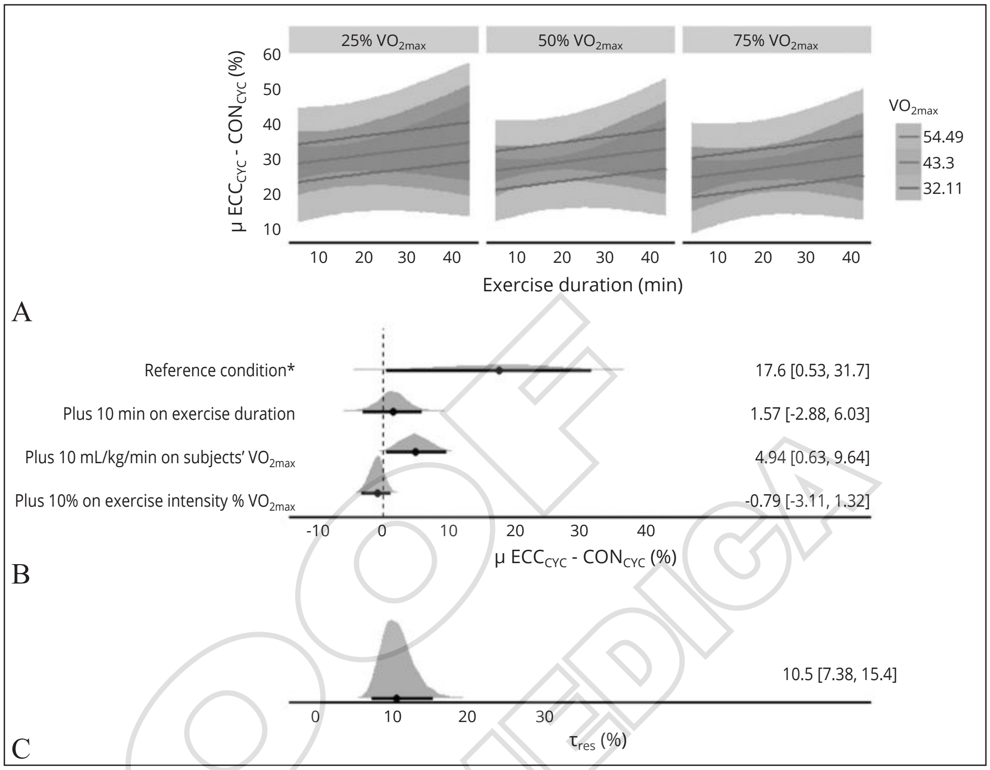

Figure 6.—Meta-regression posterior means and credible intervals of conditional effects on % mean difference between heart rate during concentric and eccentric cycling sessions performed at the same power output with exercise intensity and duration, and subjects' maximal oxygen uptake as covariates (A), reference condition and modifying effects (B), and residual heterogeneity between effect sizes (C). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively.
CON_{CYC}: concentric cycling; ECC_{CYC}: eccentric cycling; $\dot{V}O_{2max}$: maximal oxygen uptake; τ_{res}: residual heterogeneity.
*Reference condition: exercise duration =5 min; subjects $\dot{V}O_{2max}$ =18.8 mL/kg/min; and exercise intensity =17.3% $\dot{V}O_{2max}$.

the modalities increased 4.94% [0.63%, 9.64%]; for every extra 10% $\dot{V}O_{2max}$ in the intensity of the sessions (*i.e.*, % $\dot{V}O_{2max}$), the difference between CON_{CYC} and ECC_{CYC} decreased -0.79% [-3.11%, 1.32%]; and for every extra 10-min in session duration, the difference between cycling modes increased by 1.57% [-2.88%, 6.03%]. The residual heterogeneity between the effects was $\tau_{Residual}$ =10.5% [7.38%, 15.4%] (Figure 6C).

Blood lactate concentration

Three selected studies assessed BLa in both cycling modalities (N. participants =27) (Supplementary Digital Material 2: Supplementary Figure 8). The meta-analyzed mean effect size indicated that BLa was 77.03% [68.28%; 85.64%] higher during CON_{CYC} than ECC_{CYC} sessions performed at the same PO. The probability of BLa being greater during ECC_{CYC} than CON_{CYC} was 0%. The group-level effects of exercise duration indicated similar differences in BLa between cycling modalities for sessions lasting between 5-10 min (77.3% [66.9%, 88.7%]; P<0=0%) and sessions lasting between 21-30 min (76.6% [66.8%, 86.5%]; P<0=0%). The group-level effects of exercise intensity showed similar differences in BLa between cycling modes when sessions were performed at intensities above 95% $\dot{V}O_{2max}$ (77.3% [67.1%, 88.5%]; P<0=0%) and close to 80% $\dot{V}O_{2max}$ (76.7% [66.8%, 86.5%]; P<0=0%). The heterogeneity between all effects (τ_{Effect} =2.59% [0.13%, 12%]) was similar to the heterogeneity observed between group-level effects ($\tau_{Duration}$ =2.87% [0.16%, 11.9%]; $\tau_{Intensity}$ =2.81% [0.14%, 12.1%]).

Rating of perceived exertion

Seven selected studies assessed RPE (N. participants =74) (Figure 7).[17, 27, 28, 32, 34, 36, 47] The meta-analyzed mean effect indicated that RPE was 32.24% [11.42%, 53.41%] higher during CON_{CYC} compared to ECC_{CYC} sessions performed at the same PO (P<0=0.3%) (Figure 7A). The group-level effects of exercise duration (Figure 7B) indicated that the studies with sessions lasting between 11-20 min reported greater difference in RPE between cycling modes (38.1% [15.1%, 65%]; P<0=0.15%) compared to those using sessions lasting between 5-10 min (31.7% [10.4%, 53.2%]; P<0=0.43%) and between 21-30 min (26.5% [7.3%, 45.8%]; P<0=0.55%). The group-level effects of subjects' population (Figure 7C) indicated similar effects between studies with healthy individuals (33.1% [17.8%, 50.2%]; P<0=0.03%) and those with cardiopulmonary disease pa-

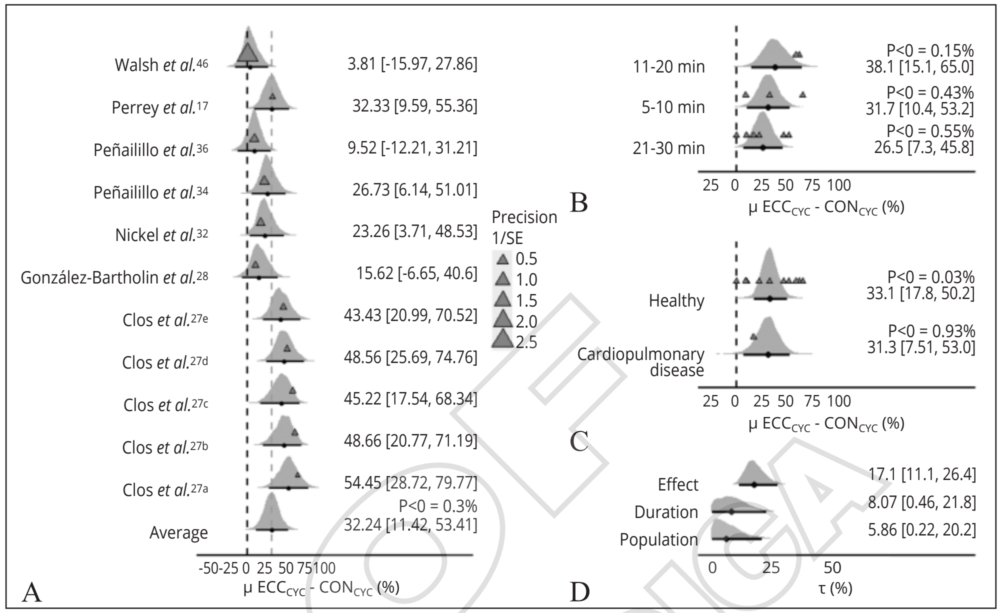

Figure 7.—Forest plot of effect sizes (% mean difference) between perceived exertion during concentric and eccentric cycling sessions performed at the same power output of all effects and the population estimated average effect (A), group-level of exercise duration (B), group-level of subjects' population (C), and heterogeneity between all effects and between group-level effects (D). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and, in the panel *a*, their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[17, 27, 28, 32, 34, 36, 47]

tients (31.3% [7.51%, 53%]; P<0=0.93%). Considerable heterogeneity was observed between all effects (τ_{Effect} =17.1% [11.1%, 26.4%]) and between group-level effects ($\tau_{Duration}$ =8.07% [0.46%, 21.8%]; $\tau_{Population}$ =5.86% [0.22%, 20.2%]) (Figure 7D).

Meta-analyses of the differences between CON_{CYC} and ECC_{CYC} performed at the same $\dot{V}O_2$

Power output

A total of seven selected studies reported the PO sustained during CON_{CYC} and ECC_{CYC} sessions performed at the same energy expenditure (*i.e.*, $\dot{V}O_2$) (N. participants =70) (Figure 8).[16-20, 37] The meta-analyzed mean effect size showed that the PO generated during ECC_{CYC} sessions was 170.33% [133.26%, 222.21%] greater than that generated during CON_{CYC} sessions when both modalities were performed at the same absolute $\dot{V}O_2$ (Figure 8A). The posterior distribution of the mean effect indicated a probability of 100% of PO being higher during ECC_{CYC} compared to CON_{CYC}. There was considerable heterogeneity between all effects (τ_{Effect} = 93.60% [63.70%, 144%]) (Figure 8B).

Heart rate

Seven selected studies evaluated the HR response to ECC_{CYC} and CON_{CYC} performed at the same $\dot{V}O_2$ (N. participants =79) (Figure 9).[16, 18-20, 29, 33, 37] The estimate mean effect showed that HR during ECC_{CYC} sessions was 8.74% [4.46%, 13.32%] higher than HR during CON_{CYC} sessions performed at the same $\dot{V}O_2$ (P<0=99.98%) (Figure 9A). The group-level effects of exercise duration (Figure 9B) showed that the studies with sessions lasting 31-45 min presented greater differences in HR between cycling modes (μ=-10.6% [CrI 95%: -16.2%, -5.72%]; P<0=100%) than those using sessions lasting 5-10 min (μ=-6.59% [-12.2%, -1.06%]; P<0=99.2%), 11-20 min (μ=-9.01% [-14.4%, -4%]; P<0=99.9%), and 21-30 min (μ=-7.6% [-12.7%, -2.4%]; P<0=99.63%). Heterogeneity was low between all effects (τ_{Effect} =3.73% [0.48%, 7.91%]) and between group-level effects ($\tau_{Duration}$ =2.71% [0.17%, 8.22%]) (Figure 9C).

Stroke volume

Three studies included in this review assessed SV during ECC_{CYC} and CON_{CYC} performed at the same $\dot{V}O_2$ (N. participants =33) (Supplementary Digital Material 3: Supplementary Figure 9). The estimated mean effect size indicated that SV was 7.26% [3.68%, 10.82%] (P<0=0%) lower during ECC_{CYC} compared to CON_{CYC} sessions in this condition. Estimate of group-level effects showed similar differences in SV between cycling modes for studies with sessions lasting between 11-20 min (μ=7.27% [3.39%, 11.6%]; P<0=0.1%), 21-30 min (μ=7.94% [2.99%, 13%]; P<0=0.3%) and 31-45 min (μ=7.77% [3.31%, 12.2%]; P<0=0.13%), all indicating lower SV during ECC_{CYC} compared to CON_{CYC}. For the studies using sessions lasting 5-10 min, the estimate effect was slightly smaller (μ=4.92% [-1.72%, 9.49%];

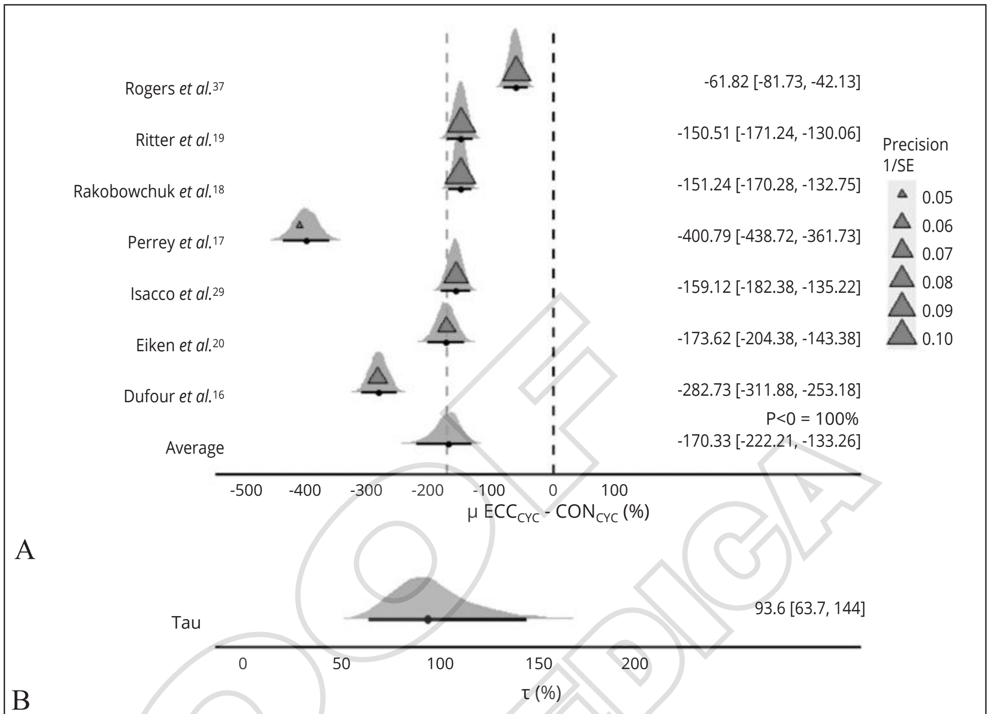

Figure 8.— Forest plot of effect sizes (% mean difference) between power output generated during concentric and eccentric cycling sessions performed at the oxygen uptake of all effects and the population estimated average effect (A) and heterogeneity between effects (B). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[16-20, 37]

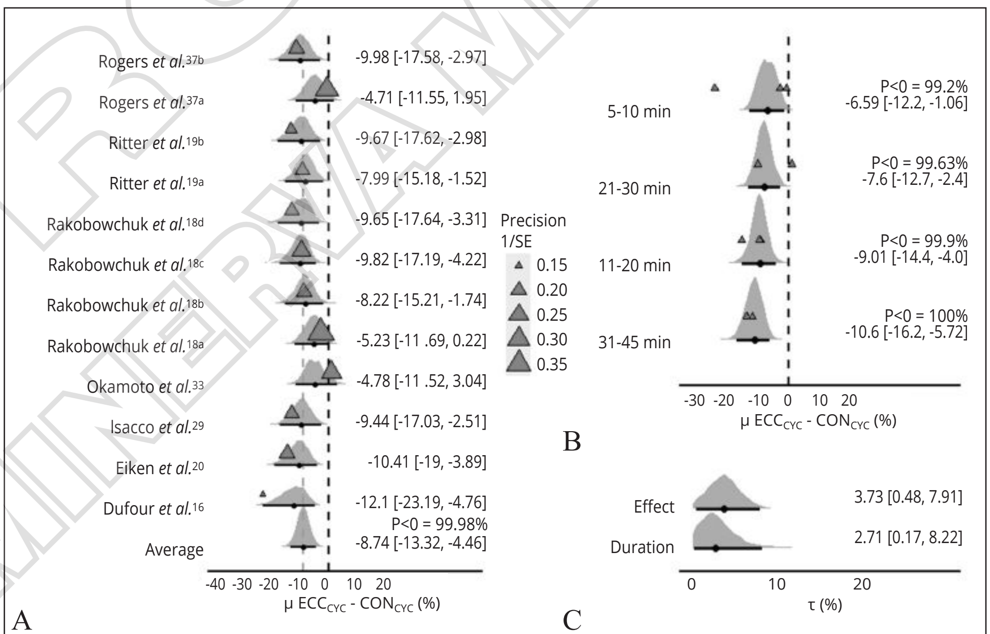

Figure 9.— Forest plot of effect sizes (% mean difference) between heart rate during concentric and eccentric cycling sessions performed at the same oxygen uptake of all effects and the population estimated average effect (A), group-level of exercise duration (B), and heterogeneity between all effects and between group-level effects (C). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and, in the panel *a*, their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[16, 18-20, 29, 33, 37]

P<0=5.93%) than the other group-level effects. Heterogeneity was low between all effects (τ_{Effect} =2.87% [0.13%, 7.97%]) and between group-level effects ($\tau_{Duration}$ =2.44% [0.17%, 7.53%]).

Cardiac output

Only 3 selected studies assessed Q (N. participants =33) (Supplementary Digital Material 4: Supplementary Figure

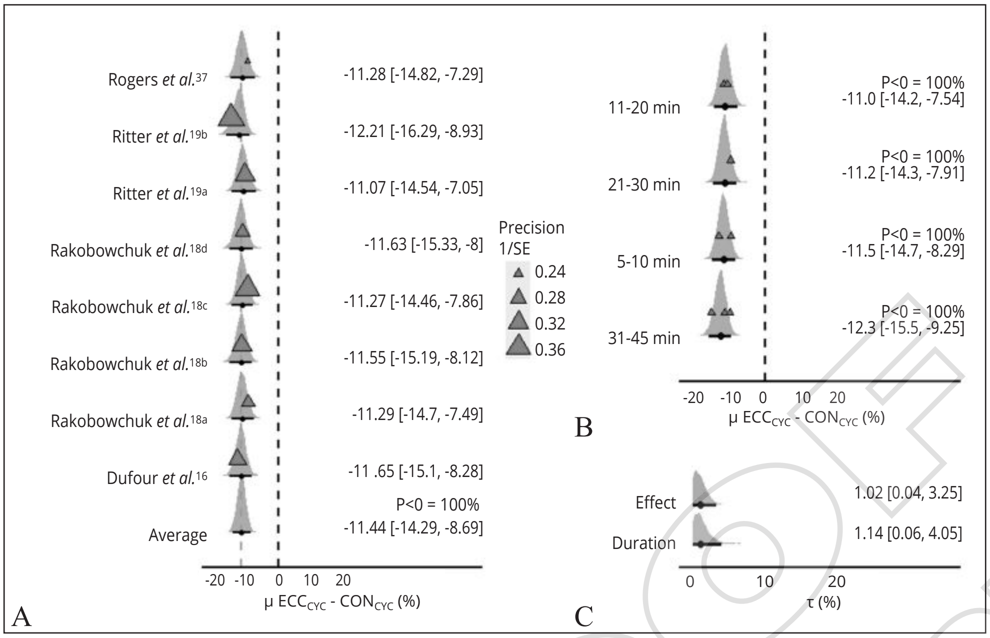

Figure 10.—Forest plot of effect sizes (% mean difference) between mean arterial blood pressure during concentric and eccentric cycling sessions performed at the same oxygen uptake of all effects and the population estimated average effect (A), group-level of exercise duration (B), and heterogeneity between all effects and between group-level effects (C). The densities represent model estimates (*i.e.*, the posterior distribution). Black dots and whiskers are the posterior effect size median and 95% credible interval, respectively. The triangles are the studies' observed mean effect sizes, and, in the panel *a*, their sizes represent the precision of the effect, presented as the inverse of the standard error (1/SE), *i.e.*, the larger the size of the triangle the smaller the standard error.[16, 18, 19, 37]

10). The estimated mean effect size indicated that Q during ECC_{CYC} sessions was 2.23% [-2.61%, 7.84%] (P<0=84.65%) higher than CON_{CYC} sessions performed at the same $\dot{V}O_2$. The group-level effects of exercise duration showed that the studies with sessions lasting 5-10 min presented greater difference in Q between cycling modes (μ=-3.56% [CrI 95%: -13.7%, 3.21%]; P<0= 87.1%) than those using sessions lasting 21-30 min (μ=-1.93% [-10.2%, 7.24%]; P<0=71.7%), 11-20 min (μ=-2.14% [-9.49%, 5.5%]; P<0=74.55%), and 31-45 min (μ=-2.58% [-9.98%, 4.83%]; P<0=79.22%). There was considerable heterogeneity between all effects (τ_{Effect} =7.81% [2.67%, 15%]) and low heterogeneity between group-level effects ($\tau_{Duration}$ =2.72% [0.16%, 10.7%]).

Mean arterial blood pressure

Four selected studies assessed MAP (N. participants =44) (Figure 10).[16, 18, 19, 37] The meta-analyzed mean effect indicated that MAP was 11.44% [8.69%, 14.29%] (P<0=100%) higher during ECC_{CYC} compared to CON_{CYC} sessions performed at the same $\dot{V}O_2$ (Figure 10A). Group-level effects of session duration were similar among levels (Figure 10B). Heterogeneity was low between all effects (τ_{Effect} =1.02% [0.04%, 3.25%]) and between group-levels ($\tau_{Duration}$ =1.14% [0.06%, 4.05%]) (Figure 10C).

Norepinephrine concentration

Three selected studies assessed norepinephrine blood concentration (N. participants =32) (Supplementary Digital Material 5: Supplementary Figure 11). The meta-analyzed mean effect indicated that norepinephrine was 10.18% [0.86%, 19.76%] (P<0=98.5%) higher during ECC_{CYC} compared to CON_{CYC} sessions performed at the same $\dot{V}O_2$. The group-level effects of exercise duration indicated that the studies with sessions lasting 31-45 min presented greater difference in norepinephrine concentration between cycling modes (μ=-11.4% [CrI 95%: -22.7%, -1.37%]; P<0=98.65%) than those using sessions lasting 11-20 min (μ=-9.56% [-21.2%, 3.4%]; P<0=93.35%) and 5-10 min (μ=-9.78% [CrI 95%: -20.5%, 1.85%]; P<0 = 95.43%). Heterogeneity was low between all effects (τ_{Effect} =2.99% [0.13%, 9.5%]) and between group-levels ($\tau_{Duration}$ =3.05% [0.15%, 10.1%]).

Discussion

The main aim of this systematic review and meta-analysis was to provide accurate estimates of the differences in acute physiological responses to ECC_{CYC} and CON_{CYC} sessions. The results of the present study showed that cardiorespiratory, metabolic, and perceptual responses were lower during ECC_{CYC} compared to CON_{CYC} sessions performed at the same PO. However, when both cycling modes were performed at the same $\dot{V}O_2$, the PO during ECC_{CYC} sessions was considerably higher than during CON_{CYC} sessions, while ECC_{CYC} induced greater cardiovascular responses than CON_{CYC}.

An inherent characteristic of eccentric exercise is the low metabolic cost of production (or "absorption") of mechanical work.[3, 49] The results of the present review support this notion, indicating that the $\dot{V}O_2$ and BLa values were, respectively, 54% [95% CrI 48%, 60%] and 77% [95% CrI 68%, 86%] higher during CON_{CYC} compared to ECC_{CYC} sessions. Furthermore, the posterior distribution of the meta-analyzed mean effect indicated a probability of 0% of the $\dot{V}O_2$ and BLa values being higher during the ECC_{CYC} compared to CON_{CYC}. Therefore, it is safe to infer that ECC_{CYC} sessions generate less metabolic stress than CON_{CYC} sessions performed at the same PO.

An argument frequently used to justify the prescription of ECC_{CYC} for frail individuals and those with chronic diseases is the lower cardiorespiratory burden triggered by ECC_{CYC} compared to CON_{CYC} sessions performed at the same workload.[10, 11] The meta-analysis of the studies investigating physiological responses to both cycling modes performed at the same PO, showed a probability of 0.33% and 0% of $\dot{V}E$ and HR, respectively, being higher during ECC_{CYC} compared to CON_{CYC} sessions. Therefore, these results indicated that ECC_{CYC} is unlikely to induce a greater cardiorespiratory burden than CON_{CYC} performed at the same PO. Moreover, the estimated mean effect showed that $\dot{V}E$ during CON_{CYC} was about 43% [95% CrI 16%, 72%] higher than during ECC_{CYC}, and HR was 28% [95% CrI 23%, 33%] higher during CON_{CYC} compared to ECC_{CYC}. These findings support the notion that the lower metabolic cost of eccentric muscle work triggers reduced cardiorespiratory responses during ECC_{CYC} compared to CON_{CYC} performed at the same PO.

From the meta-regressions and group-level analyzes, it was possible to identify the characteristics of the participants and exercise protocols that influenced the differences between acute responses to ECC_{CYC} and CON_{CYC}. The results indicated that the intensity of sessions could influence the magnitude of the differences in $\dot{V}O_2$ and HR in response to ECC_{CYC} and CON_{CYC} performed at the same workload. The meta-regressions showed that the difference in $\dot{V}O_2$ between modalities was greater when the sessions were performed at higher intensities (*i.e.*, PO corresponding to $\%\dot{V}O_{2max}$), while the difference in HR between ECC_{CYC} and CON_{CYC} was smaller at higher intensities. The contribution of non-contractile structural elements of the muscle fiber during eccentric force production may explain, in part, the lesser dependence of increased oxygen supply to sustain increases in eccentric muscle workload,[50] since these structures passively contribute to the production of PO, without the need for ATP hydrolysis and, consequently, the increase in $\dot{V}O_2$. Results from incremental tests support this idea, demonstrating a lower proportion of increases in $\dot{V}O_2$ per increment in workload during ECC_{CYC} compared to CON_{CYC}.[7, 13]

Accordingly, the smaller difference between HR in ECC_{CYC} and CON_{CYC} observed in sessions performed at greater intensities may be related to the greater proportion of increases in HR per increment in $\dot{V}O_2$ during incremental sessions of ECC_{CYC} compared to CON_{CYC}.[13] Moreover, recent evidence indicates that maximal heart rate (HR_{max}) reached during incremental tests of CON_{CYC} and ECC_{CYC} are similar, despite the attainment of different $\dot{V}O_{2max}$.[13, 14] As previously mentioned, for the same PO, CON_{CYC} induced greater HR responses than ECC_{CYC} and, thus, the former was performed at a higher % of HR_{max}. Hence, considering that the main cardiovascular adjustments occurring at near-maximal intensities are related to an inotropic effect,[51] it is plausible to infer that the increases in HR with increments in exercise intensity would be lesser for the CON_{CYC} compared to ECC_{CYC}, due to the different HR reserve available during each cycling condition.

The duration of the exercise session also appears to influence the difference in HR observed between cycling modes performed at the same PO. Considering the results from meta-regression (Figure 6), it was possible to identify that the difference between HR during ECC_{CYC} and CON_{CYC} becomes greater as the duration of the sessions progresses. When compared to ECC_{CYC} performed at the same workload, the greater cardiovascular demand of CON_{CYC} is associated with its greater metabolic demand.[16] Moreover, the existence of different intensity domains within the concentric exercise intensity continuum, which can be essentially distinguished by the occurrence or not of a steady state of metabolite accumulation,[52] has been vastly reported while no study addressed the existence of such intensity domains during ECC_{CYC}.[15] Hence, it is possible that there is a difference between CON_{CYC} and ECC_{CYC} regarding to the exercise intensity continuum, with the former presenting non-steady state physiological responses to a fixed workload that does not elicit such responses in the latter.

The meta-regressions showed that individuals with higher $\dot{V}O_{2max}$ exhibited greater differences in $\dot{V}O_2$ and HR between the ECC_{CYC} and CON_{CYC} when performed at the same workload. These results suggested that the physical fitness status (expressed by the $\dot{V}O_{2max}$) of participants could influence the difference in cardiorespiratory responses between ECC_{CYC} and CON_{CYC}. It is possible that individuals with higher VO_{2max} also have more experience with physical exercise and, consequently, they were more familiarized with eccentric muscle work. Peñailillo *et al.*[34] suggested that BLa and HR during ECC_{CYC} become lower with the effect of repeated sessions. However, the real impact of an individual's training level on acute responses to ECC_{CYC} has not yet been investigated.

The RPE during physical exercise is strongly associated with metabolic and cardiorespiratory disturbances generated in the body.[53] Thus, ECC_{CYC} is suggested as an exercise modality that induces a low psychophysiological burden, since the accumulation of by-products of energy metabolism, and cardiorespiratory responses are lower during eccentric compared to concentric exercises. In fact, a recent literature review indicated that RPE during CON_{CYC} would be on average 37% higher than RPE during ECC_{CYC} performed at the same PO, and approximately twice as high in CON_{CYC} compared to ECC_{CYC} in COPD patients.[6] The results of the present study showed that the RPE values observed during ECC_{CYC} sessions were 32% [95% CrI 11%, 53%] lower than those assessed during CON_{CYC} sessions performed at the same workload. Furthermore, a minimal probability (P<0=0.3%) of RPE to be higher during ECC_{CYC} compared to CON_{CYC} was found, however, the posterior distributions of group-level effects did not indicate differences between healthy individuals and those with cardiopulmonary diseases, as previously reported in the literature.[6] Nevertheless, the results of the present study demonstrated that ECC_{CYC} induced lower psychophysiological burden compared to CON_{CYC} performed at a similar workload and, therefore, ECC_{CYC} is a feasible modality for the treatment of individuals with low adherence and tolerance to physical exertion.

The meta-analyses of the differences between physiological responses to ECC_{CYC} and CON_{CYC} performed at the same energy expenditure (*i.e.*, $\dot{V}O_2$) showed that cardiovascular demand was greater during eccentric exercise sessions. Specifically, Q, HR, and MAP were higher (2% [95% CrI -3%, 8%], 9% [95% CrI 5%, 13%], and 11% [95% CrI 9%, 14%], respectively) and SV was lower (7% [95% CrI 4%, 11%]) during ECC_{CYC} compared to CON_{CYC} sessions. The posterior distributions showed probabilities >84% of ECC_{CYC} inducing higher Q, HR, and MAP responses than CON_{CYC}. Thus, the present review provides consistent evidence of greater cardiovascular strain during ECC_{CYC} sessions compared to CON_{CYC} sessions performed at the same absolute $\dot{V}O_2$. This has direct implications for the clinical practice of health professionals who seek to prescribe physical exercises safely for individuals with cardiovascular limitations using ECC_{CYC}. In this case, the present results indicated that the prescription of ECC_{CYC} based on the $\dot{V}O_2$ of CON_{CYC} sessions should be conducted with caution, considering the high probability of additional cardiovascular overload in such condition.

The results of the present study showed that ECC_{CYC} would be performed at a PO 170% [95% CrI 133%, 222%] greater than that used for CON_{CYC}, to match the same $\dot{V}O_2$ between cycling modalities. Thus, the differences in acute cardiovascular responses to ECC_{CYC} and CON_{CYC} performed at the same $\dot{V}O_2$ can be attributed to different mechanical workloads (*i.e.*, muscle tension) performed during each modality.[16] Although the main mechanisms of cardiovascular control during exercise are related to the body's metabolic demand,[54, 55] the greater muscle tension generated during ECC_{CYC} may have resulted in greater activation of peripheral mechanoreceptors, increasing sympathetic activation and, consequently, Q and HR.[16, 19] Accordingly, our results showed that norepinephrine concentration was 10% [95% CrI 1%, 20%] higher during ECC_{CYC} than CON_{CYC}, with a probability of 98% of this variable being higher during ECC_{CYC}. Thus, the present evidence indicates the presence of increased autonomic nervous system activity during ECC_{CYC} compared to CON_{CYC} performed at the same $\dot{V}O_2$.

Possibly, the greater mechanical stress on muscle tissue generated during ECC_{CYC} sessions partially impairs blood flow in active muscles[56] by increasing peripheral vascular resistance (*i.e.*, afterload) and decreasing SV. Peripheral vascular resistance being higher during ECC_{CYC} sessions could also explain, at least in part, the higher MAP values during ECC_{CYC} compared to CON_{CYC} performed at the same $\dot{V}O_2$. Additionally, Eiken *et al.*[20] showed that the higher HR observed during ECC_{CYC} sessions was associated with greater thermal stress produced by eccentric work. Thus, it is plausible to assume that the greater cardiovascular stress produced during ECC_{CYC} compared to CON_{CYC} performed at the same $\dot{V}O_2$ is related to a greater mechanical load on active muscles and greater thermal stress generated by eccentric muscle work. Finally, other possible mechanisms underpinning increased peripheral vascular resistance and reduced SV may include enhanced renal vasoconstriction induced by exaggerated muscle mechanoreflex activation[57, 58] and/or enhanced sympathoexcitation due to sensitization of muscle mechanoreceptors by metabolic byproducts.[59]

The duration of the sessions seems to influence the difference in HR between the two cycling modalities performed at the same metabolic load. The group-level estimates showed that the difference in HR between ECC_{CYC} and CON_{CYC} was greater for sessions with longer duration.

Group-level analysis of SV effect sizes also indicated a greater difference between cycling modalities for sessions with longer duration. Recent evidence demonstrated that during constant-load ECC_{CYC} and CON_{CYC} sessions, HR presented a steady state during the initial 15 minutes of eccentric exercise and then increased progressively until the end of the session (total duration of 45 min), while HR during the CON_{CYC} remained stable after the initial 5 min of the session.[18, 19] In these studies, SV increased less during ECC_{CYC} than during CON_{CYC}.[18, 19] Thus, it is possible that the effects calculated for HR and SV from studies using sessions with short durations were smaller due to the absence of the cardiac drift observed in longer-lasting ECC_{CYC} sessions and the short time for SV increase during CON_{CYC}. Nevertheless, the results of this study indicated an important effect of session duration on cardiovascular adjustments during ECC_{CYC} and suggest that shorter durations should be used if greater cardiovascular strain is to be avoided.

Limitations of the study

Some limitations must be considered when interpreting the results of the present study. The number of studies that evaluated $\dot{V}E$ and BLa during ECC_{CYC} and CON_{CYC} sessions performed at the same PO was small (*i.e.*, 4 and 3, respectively), as well as the number of selected studies evaluating Q, SV, MAP, and norepinephrine concentration during sessions performed at the same $\dot{V}O_2$ (*i.e.*, 3, 3, 4, and 3, respectively). Thus, the accuracy of the estimates of combined effects (*i.e.*, population average effect) may have been affected in these variables.[60] Additionally, few studies have investigated the acute responses to ECC_{CYC} and CON_{CYC} in frail individuals and patients with cardiopulmonary diseases. Finally, the main sources of bias in the present study are related to the lack of blinding of participants and evaluators, and the absence of concealed allocation in the studies.

Conclusions

In conclusion, the present results indicate that ECC_{CYC} sessions can induce less cardiorespiratory and psychophysiological stress compared to CON_{CYC} sessions performed at the same external workload (*i.e.*, PO), and greater cardiovascular strain compared to CON_{CYC} sessions performed at the same $\dot{V}O_2$. Therefore, the prescription of ECC_{CYC} sessions matching workloads used for CON_{CYC} sessions can be considered safe and feasible in contexts of rehabilitation and treatment of individuals with poor exercise tolerance. Furthermore, the prescription of ECC_{CYC} matching the $\dot{V}O_2$ produced during CON_{CYC} sessions should be conducted with caution, especially in clinical settings, since there is a high probability of additional cardiovascular strain in such condition.

Perspective

Previous evidence has demonstrated the safety, feasibility, and benefits of the utilization of eccentric exercises for rehabilitation of patients with poor exercise tolerance as well as training of healthy individuals.[6, 8, 10, 11] The reduced cardiorespiratory and perceptual responses observed during eccentric compared to concentric exercises are the main argument for the utilization of ECC_{CYC} as alternative to CON_{CYC} for exercise treatment of clinical patients. On this matter, the present study is the first systematic review with meta-analysis providing reliable estimates of the differences between metabolic, cardiorespiratory, and perceptual responses to ECC_{CYC} and CON_{CYC} sessions. Hence, the present results contribute to a better understanding of the acute physiological responses to ECC_{CYC} and provide support for sports scientists and health professionals aiming to prescribe this modality.

References

1. Elmer SJ, Madigan ML, LaStayo PC, Martin JC. Joint-specific power absorption during eccentric cycling. Clin Biomech (Bristol, Avon) 2010;25:154–8.
2. Green DJ, Thomas K, Ross EZ, Green SC, Pringle JS, Howatson G. Torque, power and muscle activation of eccentric and concentric isokinetic cycling. J Electromyogr Kinesiol 2018;40:56–63.
3. Abbott BC, Bigland B, Ritchie JM. The physiological cost of negative work. J Physiol 1952;117:380–90.
4. Fenn WO. The relation between the work performed and the energy liberated in muscular contraction. J Physiol 1924;58:373–95.
5. Peñailillo L, Blazevich A, Nosaka K. Energy expenditure and substrate oxidation during and after eccentric cycling. Eur J Appl Physiol 2014;114:805–14.
6. Clos P, Laroche D, Stapley PJ, Lepers R. Neuromuscular and Perceptual Responses to Sub-Maximal Eccentric Cycling. Front Physiol 2019;10:354.
7. Dufour SP, Lampert E, Doutreleau S, Lonsdorfer-Wolf E, Billat VL, Piquard F, *et al.* Eccentric cycle exercise: training application of specific circulatory adjustments. Med Sci Sports Exerc 2004;36:1900–6.
8. Ellis R, Shields N, Lim K, Dodd KJ. Eccentric exercise in adults with cardiorespiratory disease: a systematic review. Clin Rehabil 2015;29:1178–97.
9. Lechauve JB, Perrault H, Aguilaniu B, Isner-Horobeti ME, Martin V, Coudeyre E, *et al.* Breathing patterns during eccentric exercise. Respir Physiol Neurobiol 2014;202:53–8.
10. LaStayo P, Marcus R, Dibble L, Frajacomo F, Lindstedt S. Eccentric exercise in rehabilitation: safety, feasibility, and application. J Appl Physiol 2014;116:1426–34.

11. Hoppeler H. Moderate Load Eccentric Exercise; A Distinct Novel Training Modality. Front Physiol 2016;7:483.

12. Spruit MA, Augustin IM, Vanfleteren LE, Janssen DJ, Gaffron S, Pennings HJ, *et al.*; CIRO+ Rehabilitation Network. Differential response to pulmonary rehabilitation in COPD: multidimensional profiling. Eur Respir J 2015;46:1625–35.

13. Lipski M, Abbiss CR, Nosaka K. Cardio-pulmonary responses to incremental eccentric and concentric cycling tests to task failure. Eur J Appl Physiol 2018;118:947–57.

14. Nahmias O, Ritter O, Sagawa Y, Roux P, Degano B, Soumagne T. Ventilatory adaptation during eccentric cycling in patients with severe COPD: potential implications for exercise training. Respir Physiol Neurobiol 2021;292:103706.

15. Barreto RV, de Lima LC, Denadai BS. Moving forward with backward pedaling: a review on eccentric cycling. Eur J Appl Physiol 2021;121:381–407.

16. Dufour SP, Doutreleau S, Lonsdorfer-Wolf E, Lampert E, Hirth C, Piquard F, *et al.* Deciphering the metabolic and mechanical contributions to the exercise-induced circulatory response: insights from eccentric cycling. Am J Physiol Regul Integr Comp Physiol 2007;292:R1641–8.

17. Perrey S, Betik A, Candau R, Rouillon JD, Hughson RL. Comparison of oxygen uptake kinetics during concentric and eccentric cycle exercise. J Appl Physiol 2001;91:2135–42.

18. Rakobowchuk M, Isacco L, Ritter O, Represas AG, Bouhaddi M, Degano B, *et al.* Muscle oxygenation responses to low-intensity steady rate concentric and eccentric cycling. Int J Sports Med 2018;39:173–80.

19. Ritter O, Isacco L, Rakobowchuk M, Tordi N, Laroche D, Bouhaddi M, *et al.* Cardiorespiratory and autonomic nervous system responses to prolonged eccentric cycling. Int J Sports Med 2019;40:453–61.

20. Eiken T, Harrison AJ, Burdon CA, Groeller H, Peoples GE. Elevated body temperature contributes to the increased heart rate response during eccentric compared to concentric cycling when matched for oxygen consumption. Temperature 2020;8:30–8.

21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.

22. Lastayo PC, Reich TE, Urquhart M, Hoppeler H, Lindstedt SL. Chronic eccentric exercise: improvements in muscle strength can occur with little demand for oxygen. Am J Physiol 1999;276:R611–5.

23. Steiner R, Meyer K, Lippuner K, Schmid JP, Saner H, Hoppeler H. Eccentric endurance training in subjects with coronary artery disease: a novel exercise paradigm in cardiac rehabilitation? Eur J Appl Physiol 2004;91:572–8.

24. MacMillan NJ, Kapchinsky S, Konokhova Y, Gouspillou G, de Sousa Sena R, Jagoe RT, *et al.* Eccentric ergometer training promotes locomotor muscle strength but not mitochondrial adaptation in patients with severe chronic obstructive pulmonary disease. Front Physiol 2017;8:114.

25. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016;5:210.

26. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther 2003;83:713–21.

27. Clos P, Mater A, Laroche D, Lepers R. Concentric versus eccentric cycling at equal power output or effort perception: neuromuscular alterations and muscle pain. Scand J Med Sci Sports 2022;32:45–59.

28. González-Bartholin R, Mackay K, Valladares D, Zbinden-Foncea H, Nosaka K, Peñailillo L. Changes in oxidative stress, inflammation and muscle damage markers following eccentric versus concentric cycling in older adults. Eur J Appl Physiol 2019;119:2301–12.

29. Isacco L, Ritter O, Tordi N, Laroche D, Degano B, Bouhaddi M, *et al.* Similar substrate oxidation rates in concentric and eccentric cycling matched for aerobic power output. Appl Physiol Nutr Metab 2016;41:1204–7.

30. Kan B, Speelman C, Nosaka K. Cognitive demand of eccentric versus concentric cycling and its effects on post-exercise attention and vigilance. Eur J Appl Physiol 2019;119:1599–610.

31. Kuipers H, Keizer HA, Verstappen FT, Costill DL. Influence of a prostaglandin-inhibiting drug on muscle soreness after eccentric work. Int J Sports Med 1985;6:336–9.

32. Nickel R, Troncoso F, Flores O, Gonzalez-Bartholin R, Mackay K, Diaz O, *et al.* Physiological response to eccentric and concentric cycling in patients with chronic obstructive pulmonary disease. Appl Physiol Nutr Metab 2020;45:1232–7.

33. Okamoto T, Kobayashi R, Hashimoto Y, Nosaka K. Changes in arterial stiffness after eccentric versus concentric cycling. Appl Physiol Nutr Metab 2019;44:533–8.

34. Peñailillo L, Blazevich A, Numazawa H, Nosaka K. Metabolic and muscle damage profiles of concentric versus repeated eccentric cycling. Med Sci Sports Exerc 2013;45:1773–81.

35. Peñailillo L, Blazevich AJ, Nosaka K. Factors contributing to lower metabolic demand of eccentric compared with concentric cycling. J Appl Physiol 2017;123:884–93.

36. Peñailillo L, Mackay K, Abbiss CR. Rating of perceived exertion during concentric and eccentric cycling: are we measuring effort or exertion? Int J Sports Physiol Perform 2018;13:517–23.

37. Rogers B, Gronwald T, Mourot L. Analysis of fractal correlation properties of heart rate variability during an initial session of eccentric cycling. Int J Environ Res Public Health 2021;18:10426.

38. Rooyackers JM, Dekhuijzen PN, van Herwaarden CL, Folgering HT. Potassium and ventilation during positive and negative work in patients with chronic obstructive pulmonary disease. Clin Physiol 1997;17:475–85.

39. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, *et al.* Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane; 2022 [Internet]. Available from: www.training.cochrane.org/handbook [cited 2023, Jun 16].

40. Bürkner PC. brms: an R package for Bayesian multilevel models using Stan. J Stat Softw 2017;80:1–28.

41. Gelman A, Lee D, Guo J. Stan. J Educ Behav Stat 2015;40:530–43.

42. Gelman A, Rubin DB. Inference from iterative simulation using multiple sequences. Stat Sci 1992;7:457–72.

43. Bürkner PC. Handle Missing Values with brms. In: The Comprehensive R Archive Network; 2022 [Internet]. Available from: https://cran.rproject.org/web/packages/brms/vignettes/brms_missings.html [cited 2023, Jun 16].

44. Chasland LC, Green DJ, Maiorana AJ, Nosaka K, Haynes A, Dembo LG, *et al.* Eccentric Cycling: A Promising Modality for Patients with Chronic Heart Failure. Med Sci Sports Exerc 2017;49:646–51.

45. Hesser CM, Linnarsson D, Bjurstedt H. Cardiorespiratory and metabolic responses to positive, negative and minimum-load dynamic leg exercise. Respir Physiol 1977;30:51–67.

46. Plante PD, Houston ME. Effects of concentric and eccentric exercise on protein catabolism in man. Int J Sports Med 1984;5:174–8.

47. Walsh JA, Stapley PJ, Shemmell JB, Lepers R, McAndrew DJ. Global corticospinal excitability as assessed in a non-exercised upper limb muscle compared between concentric and eccentric modes of leg cycling. Sci Rep 2019;9:19212.

48. Cashin AG, McAuley JH. Clinimetrics: Physiotherapy Evidence Database (PEDro) Scale. J Physiother 2020;66:59.

49. Douglas J, Pearson S, Ross A, McGuigan M. Eccentric Exercise: Physiological Characteristics and Acute Responses. Sports Med 2017;47:663–75.

50. Lindstedt SL, LaStayo PC, Reich TE. When active muscles lengthen: properties and consequences of eccentric contractions. News Physiol Sci 2001;16:256–61.

51. Stöhr EJ, González-Alonso J, Shave R. Left ventricular mechanical limitations to stroke volume in healthy humans during incremental exercise. Am J Physiol Heart Circ Physiol 2011;301:H478–87.

52. Burnley M, Jones AM. Power-duration relationship: Physiology, fatigue, and the limits of human performance. Eur J Sport Sci 2018;18:1–12.

53. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377–81.

54. Rowell LB. Ideas about control of skeletal and cardiac muscle blood flow (1876-2003): cycles of revision and new vision. J Appl Physiol 2004;97:384–92.

55. Seals DR, Victor RG, Mark AL. Plasma norepinephrine and muscle sympathetic discharge during rhythmic exercise in humans. J Appl Physiol 1988;65:940–4.

56. Sadamoto T, Bonde-Petersen F, Suzuki Y. Skeletal muscle tension, flow, pressure, and EMG during sustained isometric contractions in humans. Eur J Appl Physiol Occup Physiol 1983;51:395–408.

57. Middlekauff HR, Nitzsche EU, Hoh CK, Hamilton MA, Fonarow GC, Hage A, *et al.* Exaggerated muscle mechanoreflex control of reflex renal vasoconstriction in heart failure. J Appl Physiol 2001;90:1714–9.

58. Momen A, Bower D, Boehmer J, Kunselman AR, Leuenberger UA, Sinoway LI. Renal blood flow in heart failure patients during exercise. Am J Physiol Heart Circ Physiol 2004;287:H2834–9.

59. Sinoway LI, Hill JM, Pickar JG, Kaufman MP. Effects of contraction and lactic acid on the discharge of group III muscle afferents in cats. J Neurophysiol 1993;69:1053–9.

60. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. Introduction to Meta-Analysis. West Sussex: Wiley; 2009.

Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding
This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

Authors' contributions
Renan V. Barreto had the idea for the article; Renan V. Barreto and Leonardo C. Lima performed the literature search; Fernando K. Borszcz conducted the data analyses. All authors drafted and critically revised the work. All authors read and approved the final version of the manuscript.

History
Article first published online: __________________. - Manuscript accepted: June 8, 2023. - Manuscript revised: May 23, 2023. – Manuscript received: February 16, 2023.

Supplementary data
For supplementary materials, please see the HTML version of this article at www.minervamedica.it