Effects of Physical Training on Heart Rate Variability in Children and Adolescents with Chronic Diseases: A Systematic Review and Meta-analysis

Authors

Agustín Jesús Estévez-González[1], Margarita Pérez-Ruiz[1], Fernando Cobo-Vicente[1], Márcio Vinícius Fagundes Donadio[2], Eneko Larumbe-Zabala[1]

Affiliations

1 Faculty of Sport Sciences, Universidad Europea de Madrid Campus de Villaviciosa de Odón, Madrid, Spain

2 Laboratory of Pediatric Physical Activity, Infant Center, PUCRS, Porto Alegre, Brazil. Visiting Professor (2019-2020), Universidad Europea de Madrid, Madrid, Spain.

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Georg Thieme Verlag, Rüdigerstraße 14

70469 Stuttgart, Germany

Correspondence

Márcio Vinícius Fagundes Donadio

Laboratory of Pediatric Physical Activity, Infant Center, PUCRS

Av. Ipiranga, 6690

90619–900 Porto Alegre

Brazil

Tel.: + 555133205000, Fax : + 555133205000

mdonadio@pucrs.br

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ABSTRACT

This study analyzed the effects of physical training programs on heart rate variability, as a measure of sympathovagal balance, in children and adolescents with chronic diseases. Relevant articles were systematically searched in Pubmed, Science Direct, Web of Science, Scopus, Google Scholar and Embase scientific databases. We performed a meta-analysis using an inverse variance heterogeneity model. Effect size calculation was based on the standardized mean differences between pre- and post-intervention assessments, assuring at least a single-group repeated-measures model for each extracted group. Ten studies (252 participants) were included, seven in obese subjects, two in type-1 diabetes, and one in cerebral palsy. When time-domain variables were analyzed, exercise was found to moderately increase RMSSD (SMD = 0.478; 95 %CI: 0.227 to 0.729; $p < 0.001$), SDNN (SMD = 0.367; 95 %CI: 0.139 to 0.595; $p = 0.002$) and pNN50 (SMD = 0.817; 95 %CI: 0.139 to 0.595; $p = 0.002$). As for frequency-domain variables, exercise presented a moderate increasing effect on HF (SMD = 0.512; 95 %CI: 0.240 to 0.783; $p < 0.001$), a negligible effect for LF (SMD = 0.077; 95 %CI: −0.259 to 0.412; $p < 0.001$) and a non-significant reduction for LF/HF (SMD = −0.519; 95 %CI: -1.162 to 0.124; $p = 0.114$). In conclusion, physical training programs are able to modulate heart rate variability in children and adolescents with chronic diseases, affecting mainly the time-domain variables.

Introduction

Functional misbalance of the autonomic nervous system (ANS) is associated with chronic diseases as a consequence of the underlying neurodegenerative influence of ANS neurons [1], which may be influenced by both physiological and psychological factors [2]. The sympathovagal balance has been reported in the literature as one of the main elements of the ANS and its dysfunctions are considered as an early predictor of clinical changes [3]. Thus a simple and non-invasive method to analyze the ANS function is to evaluate the sympathetic-parasympathetic balance, which can be measured through heart rate variability (HRV) [4]. While heart rate (HR) is the number of heartbeats per minute, HRV is the fluctuation in the time intervals between adjacent heartbeats [5], which is associated with the neurocardiac function and generated by the brain-heart interactions and dynamic nonlinear modulation of the ANS. This variability provides individuals with the flexibility to rapidly cope with internal or external environmental changes [6], reflecting the regulation of sympathovagal balance, blood pressure, gas exchange and cardiac function. Thus, HRV has long been used in stratification of the risk of sudden cardiac death, diabetic autonomic neuropathy and several chronic diseases [3].

In recent years, HRV frequency and time-domain indices have also gained interest in sports science. The sympathovagal activity, measured through HRV, has been used for several purposes, including training status monitoring of top athletes [7] in order to control the working load during training periods [8]. Researchers from other areas such as nutrition have also studied the influence of ergogenic supplements and their association with changes in the ANS [9]. Therefore, in order to analyze HRV, different protocol durations have been established [10, 11], including "long-term" (24 hours) and "short-term" (approximately 5 min). Long-term recordings are used as a tool to gather information related to the prognostic and risk of cardiovascular illnesses, while short-term protocols report immediate effects. Electrocardiographic short-term records (5–15 min) performed under a controlled situation (lying down position without moving or speaking) may provide information about changes on physiological, pharmacological or pathological functions of the ANS. On the other hand, 24 h recordings may assess responses of the ANS to daily life activities, disorders and therapeutic interventions [12]. Although the measured values are not interchangeable, both long and short-term protocols assess HRV information through data on parametric variables, and are usually categorized in two main domains: time-domain and frequency-domain. In the time-domain analysis, the intervals between adjacent normal R waves (NN intervals) are measured over the recording period and a variety of statistical variables can be calculated directly from the intervals or derived from the differences between intervals [12]. On the other hand, frequency-domain is the estimate distribution of absolute or relative power values into different frequency bands [13].

Previous studies have reported lower HRV in children and adolescents with chronic diseases [14, 15], indicating an impaired balance of the ANS [16]. In fact, the clinical importance of exercise has long been recognized, as well as its influence on the regulation of the sympathovagal balance, increasing parasympathetic activity and decreasing sympathetic activity [17]. Although the beneficial effects of physical training on HRV in healthy adults are well documented in the literature [7], data regarding both acute and long-term effects are not to be directly applied to children. However, specific evidence for pediatric population has also shown that exercise in healthy children may positively modulate the ANS [18].

Although populations with chronic disease may not present clinical symptoms or abnormalities, subclinical alterations still may be present [3]. Several studies indicate that metabolic diseases, such as diabetes or obesity, are also characterized by cardiac autonomic dysfunction [19, 20], usually with reduced HRV, leading to poorer cardiovascular health outcomes [21]. Considering that the ANS regulates both cardiovascular and respiratory physical activities, exercise programs have focused on aerobic training, not only to reduce comorbidities in children but also aiming to improve HRV [22], as evidence has shown that physical activity and diet interventions may regulate HRV [23]. Therefore, HRV parameters may be used to evaluate health status in risk populations.

Thus we hypothesized that physical training may modulate the ANS activity in children and adolescents with chronic diseases. Consequently, the present study aimed to perform a systematic review and quantitative synthesis of all available studies that reported the effects of physical training programs on HRV, as a measure of sympathovagal balance, in children and adolescents with chronic diseases.

Materials and Methods

Protocol and registration

This systematic review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines [24]. The study protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO) under the registry number CRD42020175377.

Search strategy

The search was conducted in June 2020 on Pubmed, Science Direct, Web of Science, Scopus, Google Scholar and Embase scientific databases. Tentatively, a combination of the following terms were used to search records: (((heart rate variability OR vagal tone OR autonomic nervous system OR cardiac autonomic regulation OR cardiovascular autonomic function OR cardiac autonomic nervous system) AND (child OR children OR adolescents)) AND (exercise OR training OR physical activity)) AND (diabetes OR diabetic OR asthma OR obesity OR obese OR cerebral palsy OR cystic fibrosis). A record of search terms and strategies was saved for further publication in order to assure reproducibility (see **Supplementary Material**, ▶**Table 1S**). No filters were used. Additionally, a manual search was performed on the bibliographic references of the selected articles to search for additional publications that were pertinent to the study purpose.

Inclusion and exclusion criteria

The review aimed to find studies evaluating physical activity programs in children and adolescents, including aerobic, endurance, resistance, sports, and other recreational physical activity programs. The main inclusion criteria were the following: (i) presence of a physical training protocol; (ii) participants aged between 6 and 17 years; (iii) clinical diagnosis of a chronic disease; (iv) measurement of either short or long-term of HRV outcomes; (v) presence of at least an English-written abstract. On the other hand, the following exclusion criteria were used: (i) sample of healthy or athlete individuals; (ii) studies performed on adults; (iii) studies presenting only reference values for HRV; (iv) not fully peer-reviewed publications, such as abstracts from conferences or similar.

Study selection

Titles and abstracts of the studies were independently assessed for eligibility by two investigators according to inclusion and exclusion criteria. Researchers were blinded to each other's decisions. In case of discrepancy on the study selection, a third investigator assessed the study and the disagreement was resolved by consensus. Spreadsheets and reference managing software were used for selection.

Data extraction

Data of included records were obtained independently by two investigators. In case of disagreement, a third investigator performed a review and discrepancies were resolved by consensus. Pre- and post-exercise mean (M) and standard deviation (SD) parameters of each outcome variable were extracted and recorded using a spread-

▶ **Table 1** Main characteristics of the included studies.

Study	Number of participants	Disease	HRV protocol	HRV tool	Type of intervention	Diet	Program Length	Relevant findings
Mazurak et al. 2016 [16]	Total (n = 60); Female (n = 32)	Obesity	20 minutes	ECG	Weight Loss program	Yes	26 days	Time-domain (↑Mean R-R, ↑SDNN, ↑RMSSD) Frequency-domain (↔ LF, ↔ LF/HF, ↔ HF).
Farah et al. 2014 [22]	Total (n = 9); Female (n = 5)	Obesity	7 minutes	HR Band	HIT (VT1); 3 days/week	No	6 months	Time-domain (↑Mean R-R, ↑PNN50,) Frequency-domain (↔ LF, ↓ HF)
Huang et al. 2019 [14]	Total (n = 21)	Obesity	NR	SphygmoCor	Aerobic training (70–90 % V02max) and Strength training (40 –50 % RM) with diet; 6 days/week	Yes	6 weeks	Time-domain (↑SDNN, ↑RMSSD, ↑PNN50) Frequency-domain (↔ LF, ↓ LF/HF, ↔HF)
Prado et al. 2010 [43]	Total (n = 18)	Obesity	3 minutes	ECG	Aerobic training (VT2) with diet; 3 days/week	Yes	4 months	Frequency-domain (↓LF, ↑HF, ↓ LF/HF)
Chen et al. 2016 [44]	Total (n = 25); Female (n = 9)	Obesity	5 minutes	ECG	Aerobic training (60–70 % HR max); 4 days / week	No	3 months	Frequency-domain (↑LF, ↑HF)
Cohen-Holzer et al. 2017 [45]	Total (n = 24); Female (n = 8)	Cerebral palsy	NR	HR Band	Aerobic training + Constraint; 5 days / week	No	2 weeks	Time-domain (↑SDNN, ↑RMSSD)
Farinatti et al. 2016 [26]	Total (n = 24); Female (n = 17)	Obesity	15 minutes	NR	Resistance training (50–85 % 10RM); 3 days/week	No	12 weeks	Time-domain (↑Mean R-R, ↑SDNN, ↑RMSSD) Frequency-domain (↓LF/HF, ↑HF).
Lucini et al. 2013 [46]	Total (n = 39); Female (n = 17)	Type-1 diabetes	10 minutes	ECG	Aerobic training	No	15–16 months	Time-domain (↑Mean R-R) Frequency-domain (↓LF, ↑HF, ↓ LF/HF).
Gutin et al. 1997 [47]	Total (n = 17); Female (n = 11)	Obesity	256 R-R intervals	ECG	Aerobic training (HR > 150); 5 days/week	No	4 months	Time-domain (↑RMSSD) Frequency-domain (↓LF, ↓HF, ↓ LF/HF).
Shin et al. 2014 [48]	Total (n = 15)	Type-1 diabetes	NR	ECG	Aerobic training (60 % VO2max); 3 days week	No	12 weeks	Frequency-domain (↑LF)

NR: not reported; ECG: electrocardiogram; HR: heart rate; VT: ventilatory threshold; RM: Maximum repetition; SDNN: Standard deviation of N-N intervals; RMSSD: Root Mean Square of standard deviation of N-N intervals; LF: Low-frequency band; HF: High-frequency band; ↑: increase; ↓: decrease; ↔: no change.

sheet. If raw data were not included in the text, the investigators searched for any additional effect size or graphical information that could be used for effect size calculation. In the absence of any available data, an attempt to contact the correspondence author was made. Time, frequency and non-linear domains of HRV measurements were sought within the study outcomes. Based on these categories, the HRV variable extraction included: (i) mean HR, the standard deviation of normal R-R (N-N) interval - SDNN (ms), the root mean square of successive R-R interval differences - RMSSD (ms), and the percentage of successive R-R intervals that differ by more than 50 ms - PNN50 (%) for the time-domain; (ii) low frequency - LF (ms^2; log and n.u), high frequency - HF (ms^2; log and n.u), and LF/HF ratio for the frequency-domain; and (iii) SD1, SD2 and SD1/SD2 for non-linear measurements. Furthermore, sample size, HRV recording protocol and device used, type of intervention and exercise, and dietary intervention were extracted from the records. When median, range (minimum and maximum), and standard error (SE) were provided, we estimated mean and standard deviation values using the methods described in Hozo et al. [25]. For one study [26] that presented relevant data in figures, we first saved the graphs as high-quality digital images and then used image-processing software to measure the distances of all markers from the y-axis origin in pixels and transformed the values into the original scale.

Risk of bias assessment

A revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the following characteristics: (i) bias arising from the randomization process; (ii) bias due to deviations from intended interventions; (iii) bias due to missing outcome data; (iv) bias in the measurement of the outcomes; (v) bias in the selection of the reported results. Two investigators performed separate assessments of risk-of-bias (Cohen's Kappa was 0.94, showing almost perfect agreement). In case of disagreement, a third investigator assessed the study and the disagreement was resolved by consensus.

The quality of included records was reported as the overall risk of bias, which was categorized as: (i) low risk of bias, (ii) some concerns for risk of bias, or (iii) high risk of bias. Considering that not all studies were randomized controlled trials, the following adjustment was performed to the score computation: (i) if at least two out of five domains were assessed as high risk, the overall risk of bias score was considered high risk; (ii) if at least two out of five domains presented some concerns, the overall risk of bias score was considered some concerns; (iii) if at least one domain was assessed as high risk and another one presented some concerns, the overall risk of bias score was considered high risk; (iv) the rest of combinations were considered as low overall risk of bias.

Effect size calculation

As a result of the variety of study designs used in the included research areas, we found that some studies in this review did not include a control group. Therefore, the effect size calculation was based on the standardized mean differences (SMD) between pre- and post-intervention assessments on the same participants, assuring at least a single-group repeated-measures model for each extracted group. Using the equations recommended in Borenstein et al. [27], we computed Hedges' *g* and SE of *g* from the sample size, M and SD data at baseline and post-treatment for each group. Hedges' *g* effect size is a variation of Cohen's *d* that corrects for biases associated with small sample sizes [28] and might be interpreted in the same way as Cohen's *d*: 0.2, small; 0.5, medium; 0.8, large [29]. For frequency-domain measurements (i. e. HF, LF), effect sizes were calculated using the available data regardless of the unit (e. g. absolute power in ms^2 vs. relative power in normal units), since we aimed to address the magnitude of the effects in the domain irrespective of the specific scales of measurement.

Statistical analysis

Data synthesis was performed when at least four studies per outcome were found, provided enough statistical power was achieved. Due to the variety of designs and interventions, some variability of true effects between studies was expected, suggesting the need for a random effects (RE) meta-analysis model. However, due to the generalized presence of heterogeneity among studies, in order to overcome the underestimation of the statistical error and spuriously overconfident estimates with the RE model, we adopted the inverse variance heterogeneity (IVhet) model [30]. The statistical analyses were performed using *admetan* [31] package in Stata 15.1 (StataCorp, College Station, TX, USA). For each outcome, summary SMD and 95 % CI was calculated from Hedges' g and SE, and Q-values and I^2 were used to assess heterogeneity between studies. For outcomes including at least nine studies, the effect of combining diet (or calorie restriction) with exercise was compared with exercise alone as a moderator using Q statistic.

Publication bias was assessed using funnel plots of effect size against SE of the effect size. We also examined the regression of the intervention effect estimates on their standard errors, weighting by the reciprocal of the variance of the intervention effect estimate (Egger's test). Significance level was set at 0.05 for all tests.

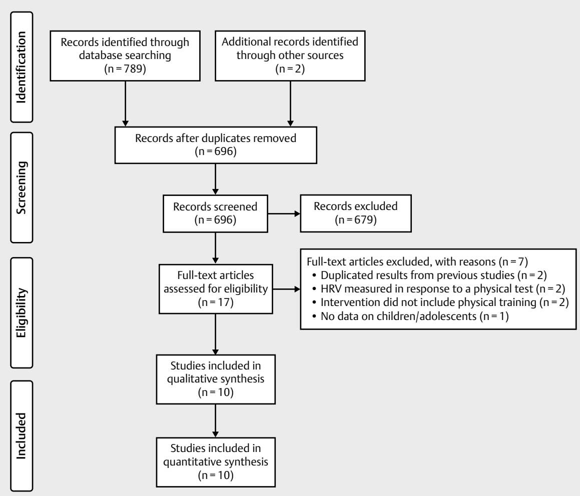
Results

Study selection

The total number of records found was 791. However, after removing duplicates, 696 studies were selected for title and abstract screening. Once inclusion/exclusion criteria were applied, 17 records remained to be assessed for eligibility, from which 7 studies were rejected. Reasons for rejection included: i) Presenting data from previously published studies; ii) HRV measurement in response to a physical test; and iii) presence of an intervention program that was not based on a physical training protocol. Thus a total of 10 studies were included for both qualitative and quantitative syntheses. The total number of participants was 252 (99 female). Although 7 studies used a comparison group, three reports did not include a control group or equivalent. ▶ **Fig. 1** presents the complete flow diagram of the study.

Quality assessment

The risk of bias analysis revealed that four studies (40 %) presented low risk, two studies (20 %) were classified as presenting some concerns, and four studies (40 %) presented high risk of bias. The complete risk of bias assessment of the included studies is presented in ▶ **Fig. 1S**, and the overall quality is shown in ▶ **Fig. 2S**. Neither funnel plots nor Egger's test showed evidence of significant publication



▶ **Fig. 1** Flow diagram of the study.

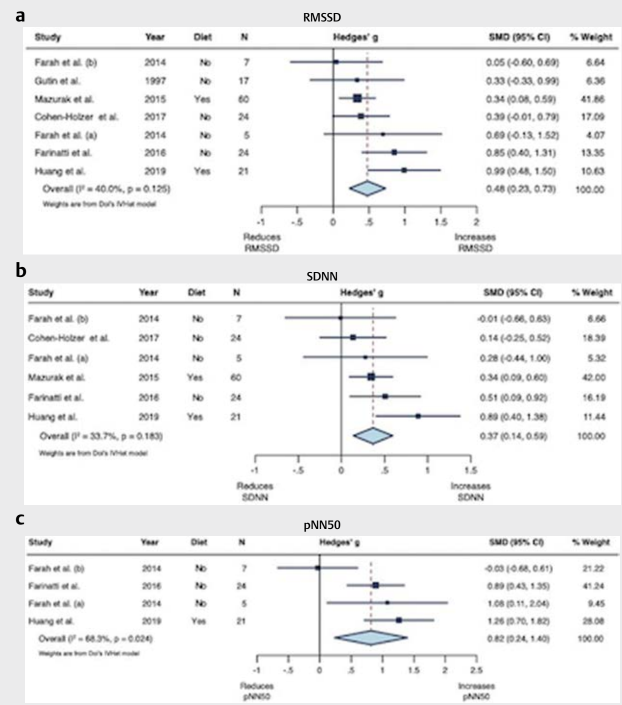
bias for any of the six HRV metrics assessed. Funnel plots, bias coefficients and *p* values are available as **Supplementary Material** (▶ **Fig. 3S**).

Characteristics of included studies

All selected studies included individuals with chronic diseases. 7 out of ten were carried out in obese subjects, two in type-1 diabetes, and one in cerebral palsy. All reports assessed the effects of an exercise program on HRV, although intervention protocols were heterogeneous. Only one study included resistance training, four were based on aerobic training, and two used a combination of both training program types. Moreover, three studies included diet as a complement of the intervention. Nine studies specified the tool used for HRV recording. Six articles measured HRV using ECG, two used a HR Band, one used a SphygmoCor device, and one did not specify the tool employed. No long-term (24 h) protocol was found; five articles used short-term protocols (5 to 20 min), one used an ultra-short-term protocol (< 5 min), and four studies did not describe the time of HRV recording. ▶ **Table 1** shows the main characteristics of the included studies.

Effect of exercise on time-domain metrics

Based on the available 158 participants' data from 7 groups (▶ **Fig. 2a**), exercise was found to moderately increase RMSSD (SMD = 0.478; 95 %CI: 0.227 to 0.729; $p < 0.001$). Heterogeneity between studies was small to moderate but not statistically significant for this measure (Q[6] = 10.0, $p = 0.125$; $I^2 = 40.0\,\%$). Similarly, the SDNN data (n = 141) reported in six groups (▶ **Fig. 2b**) showed a small to moderate positive effect of exercise (SMD = 0.367; 95 %CI: 0.139 to 0.595; $p = 0.002$), where heterogeneity between studies was not statistically significant (Q[5] = 7.54, $p = 0.183$; $I^2 = 33.7\,\%$). Finally, pNN50 data (n = 57) only included four groups showing a significant amount of heterogeneity (Q[3] = 9.47, $p = 0.024$; $I^2 = 68.3\,\%$). Besides the small number of studies included, evidence for large effects of exercise on pNN50 was found (SMD = 0.817; 95 %CI: 0.139 to 0.595; $p = 0.002$), as depicted in ▶ **Fig. 2c**.

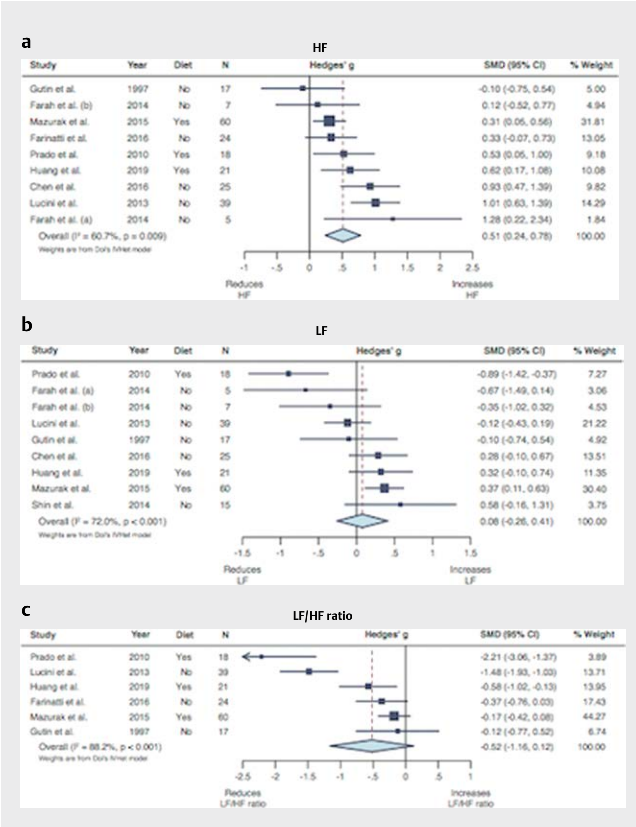


▶ **Fig. 2** Effect of exercise on time-domain heart rate variability (HRV) measurements. (**a**) RMSSD: Root Mean Square of standard deviation of N-N intervals; (**b**) SDNN: Standard deviation of N-N intervals; and (**c**) PNN50: the percentage of successive R-R intervals that differ by more than 50 ms.

No statistically significant differences were found when studies were compared based on the use of additional diet or calorie restriction treatment. Exercise and diet (E + D) vs. exercise-only (EO) SMD [95 %CI] estimates were: RMSSD, (E + D) 0.468 [−0.237 to 1.173] vs. (EO) 0.489 [0.212 to 0.766], $p = 0.903$; SDNN, (E + D) 0.46 [−0.113 to 1.033] vs. (EO) 0.26 [0.016 to 0.504], $p = 0.240$; pNN50, (E + D) 0.701 [1.823 to 28.08] vs. (EO) −0.069 [1.355 to 71.92], $p = 0.066$.

Effect of exercise on frequency-domain metrics

Regarding frequency-domain measures, nine groups (n = 216) included HF data, another nine (n = 207) included LF data, and six studies (n = 179) presented LF/HF ratio. Programmed exercise was shown to have a moderate increasing effect on HF (SMD = 0.512; 95 %CI: 0.240 to 0.783; $p < 0.001$), although significant heterogeneity (Q[8] = 20.33, $p = 0.009$; $I^2 = 60.7\,\%$) between studies was also found (▶ **Fig. 3a**). However, mixed results were found for LF (▶ **Fig. 3b**), resulting in a negligible summary effect of exercise on this measure (SMD = 0.077; 95 %CI: −0.259 to 0.412; $p < 0.001$), which also presented large heterogeneity between studies (Q[8] = 28.53, $p < 0.001$; $I^2 = 72\,\%$). Finally, LF/HF ratio data (▶ **Fig. 3c**) also presented very large heterogeneity (Q[5] = 42.29, $p < 0.001$; $I^2 = 88.2\,\%$) and the overall reduction due to programmed exercise was not statistically significant (SMD = −0.519; 95 %CI: −1.162 to 0.124; $p = 0.114$).



▶ **Fig. 3** Effect of exercise on frequency-domain heart rate variability (HRV) measurements. (**a**) HF: high-frequency band; (**b**) LF: low-frequency band; and (**c**) LF/HF: ratio between LF and HF.

No statistically significant differences were found when E + D and EO studies were compared. SMD [95 %CI] estimates were: HF, (E + D) 0.207 [0.609 to 51.07] vs. (EO) 0.198 [1.042 to 48.93], $p = 0.148$; LF, (E + D) -0.617 [0.955 to 49.02] vs. (EO) –0.32 [0.295 to 50.98], $p = 0.213$; LF/HF ratio, (E + D) –1.47 [0.686 to 62.11] vs. (EO) –1.591 [0.138 to 37.89], $p = 0.057$.

Discussion

The present study reviewed 10 articles included in the systematic review, as well as performed statistical analysis for the main HRV variables, demonstrating that the use of exercise programs for children diagnosed with obesity, cerebral palsy and type-1 diabetes were effective in modulating the sympathovagal balance. Although the evidence is still limited, this study reveals that exercise tends to positively modulate sympathovagal balance measured through HRV for both frequency and time domains in children diagnosed with chronic diseases (obesity, cerebral palsy and type-1 diabetes). Furthermore, the effects of exercise on all time-domain parameters (i. e. SDNN, RMMSSD and PNN50 %) showed that exercise might moderately increase HRV, although for frequency-domain the evidence is less clear, as a moderate effect was seen for HF, but very heterogeneous results for LF and LF/HF ratio were found.

ANS evaluation, measured through HRV, is usually categorized in time and frequency domains [13]. Time-domain indices of HRV quantify the amount of variability in measurements of the interbeat interval, which is the time period between successive heartbeats. The results of the present review and meta-analysis have shown that exercise-training programs were able to positively influence all time-domain variables evaluated (i. e. SDNN, RMMSSD and PNN50 %). Similar findings were found by Mandigout et al. (2002) for healthy children, where 13 weeks of aerobic training induced changes in HRV by increasing SDNN, RMSSD and PNN50 %. In contrast to time-domain findings, heterogeneous results for frequency-domain values were found in the present review with meta-analysis, especially LF and LF/HF ratio. However, a moderate effect was seen for HF. Positive effects of exercise-training on HF were also seen in healthy children [32, 33], adolescents [34] and young obese adults [35], although there is also evidence of no significant effects in prepubescent children [32, 33]. It is possible that type of exercise, health condition and the level of ANS alteration may play a role in the effects of exercise on frequency-domain response [32–34]. Taken together, the results indicate that an exercise-training program is able to modulate the autonomic dysfunction of children with chronic diseases.

The present study shows that exercise programs have induced overall positive results on HRV in children with chronic diseases, although there is still contradictory evidence. A recent systematic review and meta-analysis in healthy children and adolescents have shown no major impacts of physical training on HRV, although only two studies were included [18]. It is possible that both direct and indirect influence of underlying alterations from chronic diseases upon the ANS would create an unbalanced scenario in which exercise may have a positive impact [36]. Moreover, the large heterogeneity of results could be related with either dose or intensity at which exercise is prescribed. The study by Farah et al. (2014) compared the effects of two different exercise programs on HRV and results suggested that high-intensity aerobic exercise could induce greater changes upon the ANS. On the other hand, 7 weeks of high-intensity intermittent exercise did not induce positive effects on the heart rate autonomic function in healthy children [32]. In physically inactive adults, a high-intensity exercise program was superior when compared to a moderate intensity program in improving HRV [37]. When a structured program was compared to an unstructured one, results have shown that structured exercise is more beneficial for improving HRV in adolescents, irrespective of their gender and sports activities [34]. In children with asthma, high-intensity interval training was associated with a short-term shift towards greater sympathetic predominance in response to an exercise challenge [38]. In the present review, length of the exercise programs ranged from 26 days to 16 months, and the most frequent type was the aerobic training. It is possible that different length, intensity, type and duration may influence outcomes related to the effects on the modulation of the ANS in children with chronic diseases.

Although HRV is considered and easy and simple-to-perform measurement, protocols are very heterogeneous in the literature [10, 11, 39]. Our findings reveal that all studies included in the present review have used different protocols. Thus, as there is no consensus regarding an optimal protocol, different variables involving HRV measurements may influence results, including the respiratory pattern [40], the position of the body, and the duration of the recordings [10, 11]. Other factors considered as non-controllable, such as age [6] and gender [41] may also affect the results obtained and must be considered carefully when interpreting HRV findings. Different HRV protocol durations are usually applied according to the purposes of measurement [10, 11]. Usually, long-term (24 hours) recordings are used to evaluate the cardiovascular risk, while short-term (approximately 5–15 min) protocols are commonly applied to report immediate effects, as the effects of interventions [12]. All studies included in the present review that reported the protocol duration have performed short-term measurements, which contribute to decrease bias involved in the comparisons.

During the performance of this systematic review and meta-analysis limitations were found, among which we believe it is important to highlight (i) the low sample size found in most of the studies analyzed, which could be related to the difficulty in recruiting pediatric patients with chronic diseases; (ii) the lack of inclusion, in some studies, of a comparison group or equivalent, as the use of a control group would contribute to a better understanding of the possible effects of a training program on HRV values; (iii) the inclusion of diet as a complement of the exercise training may have also influenced results, although there is not enough evidence on the topic to hypothesize that there is direct consequences on HRV. More research to compare the influence of diet or other moderators is highly needed. Furthermore, future studies including RCT are still necessary in order to elucidate the effects of exercise training on HRV. Standardized and complete description of HRV parameters could contribute to improved interpretation of findings. The heterogeneous results published so far may be related to several factors, including insufficient study size and design, as well as different HRV methods applied. Large-sized and prospectively designed studies are still necessary for clarification.

Conclusions

The results obtained in the present systematic review with meta-analysis indicate that physical training programs are able to modulate HRV in children and adolescents with chronic diseases, affecting mainly the time-domain variables. HRV analysis may be a useful and easy-to-apply clinical tool in order to evaluate altered sympathovagal balance in pediatric chronic diseases.

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Conflict of Interest

The authors have no conflicts of interest to declare, and confirm that this study meets the ethical standards of the journal [42].

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