DOI: 10.1590/1413-81232022275.10402021

Effects of physical activity on heart rate variability in children and adolescents: a systematic review and meta-analysis

Efeitos da atividade física na variabilidade da frequência cardíaca em crianças e adolescentes: uma revisão sistemática e meta-análise

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Abstract *The aim of the study was to investigate the effects of physical activity (PA) on heart rate variability (HRV) in children and adolescents. We conducted a research of Web of Science, PubMed, ScienceDirect, Springer-Link and EBSCO-host. The revised Newcastle-Ottawa Scale was used in an investigative analysis to assess bias risk. A total of 21 studies were included. Overall, medium-sized associations were found between PA and low frequency and high frequency in children and adolescents. High PA level had significantly higher standard deviation of RR intervals and root of the mean of the sum of the squares of differences between adjacent RR intervals in children and adolescents. The effects of PA on HRV were consistent in children and adolescents. Our systematic review and meta-analysis revealed medium-sized between PA and HRV in children and adolescents. Promoting children's and adolescents' participation in moderate-to-vigorous physical activity (MVPA) will increase parasympathetic nerve activity and decreased sympathetic nerve activity. Our findings support motivating children and adolescents to engage in more MVPA in their daily lives to improve autonomic nervous system function and promote cardiovascular safety.*

Key words *Physical activity, Heart rate variability, Autonomic nervous system, Children, Adolescents*

Resumo *O objetivo do estudo foi investigar os efeitos da atividade física (AF) na variabilidade da frequência cardíaca (VFC) em crianças e adolescentes. Realizamos uma pesquisa nas bases Web of Science, PubMed, ScienceDirect, Springer-Link e EBSCO-host. A Escala Newcastle-Ottawa revisada foi utilizada para avaliar o risco de enviesamento. Um total de 21 estudos foi incluído. De forma geral, foram encontradas associações de médio porte entre AF e baixa frequência e alta frequência em crianças e adolescentes. O alto nível de AF teve um desvio padrão significativamente maior dos intervalos e raiz da média da soma dos quadrados de diferenças entre os intervalos RR adjacentes em crianças e adolescentes. Os efeitos de AF sobre VFC foram consistentes em crianças e adolescentes. Nossa revisão sistemática e meta-análise revelou que AF e VFC em crianças e adolescentes são de médio porte. Promover a participação de crianças e adolescentes em atividade física de moderada à vigorosa (AFMV) aumentará a atividade nervosa parassimpática e diminuirá a atividade nervosa simpática. Nossas descobertas apoiam a motivação de crianças e adolescentes a se envolverem mais na AFMV em suas vidas diárias para melhorar o funcionamento do sistema nervoso autônomo e promover a segurança cardiovascular.*

Palavras-chave *Atividade física, Variabilidade do batimento cardíaco, Sistema nervoso autônomo, Crianças, Adolescentes*

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Introduction

Physical activity (PA) levels have been declining over the last few decades. About 25% of adults not get enough PA in the worldwide[1]. Strong evidence suggests that lower PA levels increases the risk of many adverse health conditions, such as cardiovascular diseases (CVD)[2] and lowers life expectancy[3]. Though CVD usually affects adults, it can begin in childhood[4]. Thus, the prevention of CVD and promotion of PA level should begin with children and adolescents[4,5].

Heart rate variability (HRV) is a non-invasive, repeatable predictorof the cardiac autonomic nervous system function[6] and a major source of cardiovascular health[4]. Farah et al.[7] discovered no substantial association between children's PA and HRV using self-reported PA levels. However, the recall questionnaires should be with caution when used in children or adolescents[8]. Buchheit et al.[9] used an accelerometer to critically assess PA level, and found no significant correlation between the PA and HRV. Interestingly, in a previous study with larger sample size (3,395 adolescents)[10], PA levels were significantly correlated with HRV and there were significant differences between PA levels. Furthermore, one systematic review[11] found a positive relationship between moderate-to-vigorous physical activity (MVPA) and HRV in children and adolescents (ages 5 to 18). Therefore, the relationship between PA levels and HRV is unclear due to the high heterogeneity of the previous studies.

Examining this relationship will assist in understanding how PA affects HRV in children and adolescents. Furthermore, HRV is regarded as a reliable factor that could demonstrate that PA reduces the risk of CVD[12]. Thus, the purpose of our studywas to conduct a systematic review and meta-analysis of the effects of PA for HRV in children and adolescents.

Methods

The review was conducted following the requirements of the international meta-analysis writing guidelines (the PRISMA statement for reporting systematic reviews and meta-analyses of studies)[13].

Identification of studies

A systematic search was conducted using Web of Science, PubMed, Science Direct, Springer-Link, EBSCO-host databases. Search terms included "ANS", "HRV", "PA", "child", "adolescent", all combined with "AND" (Figure 1). The retrospective approach was used for expanded retrieval to optimize the total literature. The retrieval period for data collection was between 2000/01-2019/10 (Figure 1). Only papers written in peer-reviewed journals were considered. Reviews, conference sessions, and abstracts were not taken into account. Removed duplicates, studies were initially assessed by screening titles and abstracts.

Inclusion and exclusion criteria

The inclusion criteria for relevant studies in the review were: (1) in non-intervention studies, the association between PA and HRV was studied, or the differences in HRV between PA groups were compared; (2) the participants were children and/or adolescents (3-18 years). Obese and overweight children/adolescents were also includes, but studies on other conditions (congenital heart disease, hypertension, metabolic syndrome, etc.) were excluded; (3) to evaluate the ANS function, the linear and non-linear for HRV analysed[6]. Linear indicators include time and frequency domain indicators. The time domain indicators are limited to standard deviation of RR intervals (SDNN) and square root of the mean of the sum of the squares of differences between adjacent RR intervals (RMSSD). The frequency domain indicators are limited to low frequency (LF), high frequency (HF) and LF/HF. Thenon-linear indicators are limited to the detrended fluctuation analysis (DFA1) and Poincaré plot (SD1). PA: objective assessment and subjective appraisal of PA studies using accelerometers, pedometers, global positioning system equipment, questionnaire surveys, and interviews. Total physical activity (TPA), vigorous physical activity (VPA), MVPA, light physical activity (LPA), and sedentary time (ST) for PA levels.

The exclusion criteria consisted of: (1) intervention studies, meta-analysis; (2) self-controlled trials; (3) repeated publication, insufficient quality literature; (4) unclear description of experimental data.

Selection of studies and data extraction

Titles, abstracts and full texts were screened by CH, and XJ, with disagreements discussed between these two authors. The authors compared their screening results, and if the inclusion results were contradictory, they conferred the decision

a)

#1 "Heart Rate Variability" [Mesh]
#2 "Spectral Analysis" [Text Word]
#3 Frequency [Text Word]
#4 "Time-domain" [Text Word]
#5 "Frequency-domain" [Text Word]
#6 OR/1-5
#7 "Autonomic Nervous System" [Mesh]
#8 "Automic Modulation" [Text Word]
#9 OR/7-9
#10 6 AND 9
#11 "Physical Activity" [Mesh]
#12 "Exp Exercise" [Text Word]
#13 "Activity Level" [Text Word]
#14 "Physical Education" [Text Word]
#15 "Exp Sports" [Text Word]
#16 Sport [text Word]
#17 Bieyel [Text Word]
#18 Swim [Text Word]
#19 Walk [Text Word]
#20 Run [Text Word]
#21 Jog [Text Word]
#22 OR/11-21
#23 Child* [Mesh]
#24 Teen* [Mesh]
#25 Pupil [Text Word]
#26 Adolescen [Text Word]
#27 Puberty [Text Word]
#28 Kid [Text Word]
#29 OR/23-28
#30 10 AND 22 AND 29

b)

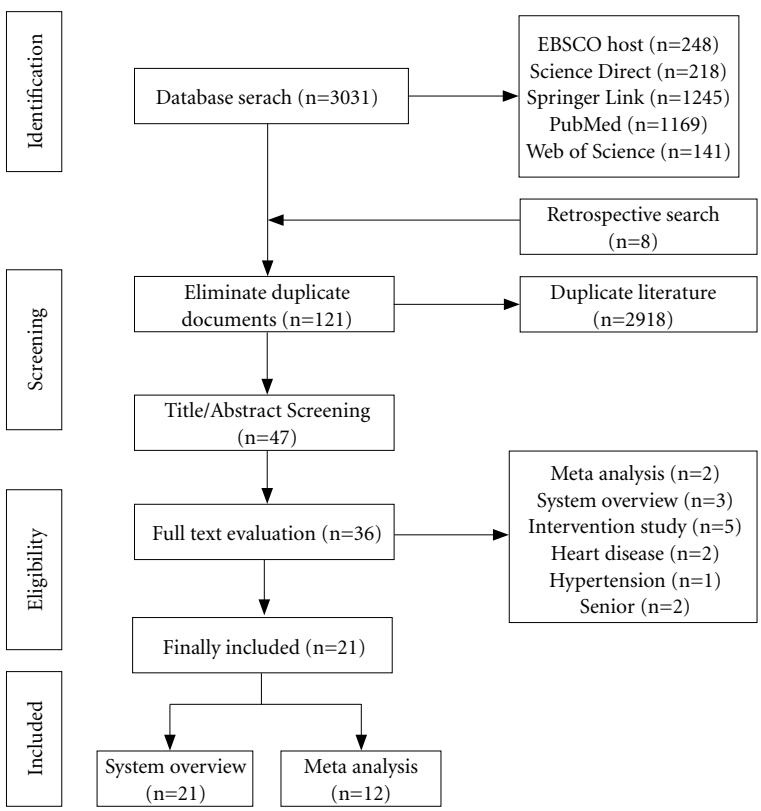

Figure 1. Retrieval strategy diagram and literature selection flow chart.

Source: Authors.

with the third author (XF). If there was a problem such as missing data in the included literature, they contacted the first and/or corresponding authors through e-mail. If the literature was still not available, remove it.

The information in the literature includes author, purpose, design, sample characteristics, recruitment procedures, participant exclusion and inclusion criteria, measurement of results, description of confounding factors and processing methods, and statistical methods and results (content) of leading indicators, used in this analysis. The literature is in Table 1.

Study quality and risk of bias assessment

Two authors (CH and XJ) independently assessed risk of bias using the Newcastle-Ottawa Scale (NOS) document quality evaluation scale (revised edition) assessing risk of bias[14,15]. It consists of seven assessment contents divided into four categories: selection bias, design bias, statistical bias, and result bias. In the NOS scale, seven criteria were rated as either "high" (score = 3) or "low" (score = 0) for each included study, and the highest score is 21 points (see the Chart 1).

Statistical analysis

The original or standardized regression coefficient *(β)* or the coefficient of determination (R^2) and standard error (*SE*) were extracted. The correlation coefficient (*r*) and standard deviation (*SD*) are extracted and summarized for correlation analysis. Used random-effects meta-analysis to derive a pooled estimate of the association between PA and HRV (SDNN, RMSSD, LF, HF). Applied Fisher's *z* transformation to correlation coefficients to calculate the relevant statistics (variance, standard error, confidence intervals) before converting to the correlation to report the summary effect size (*ES*). Using an inverse variance weighting procedure for independent effect sizes to improve overall precision[16]. Independent sample (*k*) as the unit of analysis. Pearson's *r* was the effect size metric selected to report results. Effect sizes used to Cohen's criteria for small (> 0.20), moderate (> 0.40), and large (> 0.80) aid the interpretation of results. Rosenthal's classic fail-safe N was used to examine publication bias. Analyses is carried out using comprehensive meta-analysis (version-2)[17].

Depending on whether the units are consistent, selected the standardized mean differences (*SMD*) or mean difference (*MD*) for processing. Calculate the *ES* and 95% confidence interval (*CI*) of the outcome indicator. The small number of studies included (n = 4), Utilized Random Effects Models and Bayesian-classical analysis[16]. Analyses is carried out using Stata 16.0 software. The significance level was set at 0.05.

Results

Search results

The initial search yielded a total of 3031studies (EBSCO host = 248, Science Direct = 21, Springer Link = 1,245, PubMed = 1,169, Web of Science = 141). The reviewers excluded 2918 redundant documents in Endnote, removed 47 irrelevant documents after reading the title and abstract, 36 studies after reading the full text, and finally included 21 studies (Figure 1).

Basic characterization and bias risk assessment

There was 11 studies in total over 100 participants[9,18-26], seven studies sample size in 100-1,000 participants[11,20,27-31], and four studies in total over 1,000 participants[7,10,32,33].

Demographics: 21 studies, a total number of 8,740 participants (7,149 males, 1,471 females). Just one study 120 participants without identifying sex[19]. Ten studies reported sample source areas, with eight urban samples[7,9,19-21,29,31-33], and one sample each for rural[18] and mixed areas (urban plus rural)[27]. From the age, one study was a child participant (3-6 y)[11], 12 studies were old children participants (6.1-13 y)[9,19-22,24,26,28,29,31,33,34], seven studies were adolescent participants (13.1-18 y)[7,10,18,24,27,30,32], one study was across ages (10-18 y)[25]. Subject BF%: five studies were obese participants[7,20,21,33,34] and the other studies were of average weight.

The average bias score is less than 11.7 points (4-19 points). The primary cause of bias was subject recruiting and three studies reported random sampling[3,9,29]. Furthermore, eight studies did not control for confounding factors[20,22,25,26,30,33,34], 15 studies were biased in evaluating PA or physical exercise, or did not provide sufficient information, or used subjective assessment[7,9,18-23,25,26,30,32-34]. Seven studies did not descripted HRV testing procedures in detail[21-24,26,30,33]. Table 2 and Table 3 outline the heterogeneity and homogeneity of different metrics based on meta-analysis performance. Because of the insufficient number of experiments used in the meta-analysis, the sensitivity analysis was not performed. The risk of bias is in Table 4.

Table 1. Basic characteristics of included studies.

Researcher/region	Subject characteristics			Mixed factors	PA test tools, types and judgment standards						HRV test method/indicator			Main results
	Health status	Sample size	Age/BF%		Tool	1	2	3	4	5	Judgment criteria / CPM	Time Domain	Frequency domain	Non-linear	
Blom et al., 2009 Stockholm, Sweden	Health	47G,24B	16.5 y	Heart rate; blood sugar	Subjective memories	√	×	×	×	×	1: Physical exercise and sweating	SDNN	LF; HF	No	First: 1 & SDNN: r = 0.28* 1 & LF: r = 0.35* 1 & HF: r= 0.26* Twice: r = 0.37* r = 0.29* r = 0.30*
Buchheit et al., 2007 Eastern France	Health	42G,25B	11.5±0.8 y/18±3.3%	Sex; age; BF%	Accelerom-eter	×	√	√	×	×	3 > 4METs 2 > 6METs	RMSSD	LF; HF (0.15-0.5 Hz); HF/ (LF+HF)	No	3 & HF: β? 2 & HF: β?
Cayres et al., 2015 Sao Paulo, Brazil	1) Health 2) Exerci-seinactive	N =12	1) 12±1 y/31.5±13.6% 2) 11±1 y /28.9±19.4%	Sex; age; race; PHV; maturation; BF%	Pedometer	√	×	×	×	×		RMSSD		No	1 & RMSSD: r = 0.22* 1 & RMSSD: $\boldsymbol{\beta}$ = 0.042*
S. R. Chen et al., 2008 Taiwan	1) Type 1 diabetes 2) Health	1) 48G,45B 2) 50G,57B	1) 10.3±1.6 y 2) 10.4±1.6 y	No	PAQ-C ques-tionnaire	√	×	×	×	×		No	LF; HF; LF/HF	No	1 & LF: R^2= 0.48** 1 & HF: R^2= 0.44** 1 & LF/HF: R^2= 0.12**
S. R. Chen et al., 2012 Taiwan	1) Over-weight 2) Health	1) 44B,40G 2) 44B,43G	1) 10.8±1.6 y 2) 10.6±1.5 y	No	PAQ-C questionnaire	√	×	×	×	×		No	LF; HF	No	1 & LF: r = 0.62* 1 & HF: r = 0.49*
Farah et al., 2014 Pernambuco, Brazil	Health	1152B	16.6±1.2 y	Age; HRV test period	Subjective memories	√	×	×	×	×	1: > 5 h/w	RMSSD; SDNN	LF; HF; LF/HF	No	1 & SDNN: B = 1.14* 1 & RMSSD: B = 1.54* 1 & LF: B = -0.56* 1 & HF: B = 0.56* 1 & LF/HF: B = -0.03

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Researcher/region	Subject characteristics			Mixed factors	PA test tools, types and judgment standards						HRV test method/indicator			Main results	
	Health status	Sample size	Age/BF%		Tool	1	2	3	4	5	Judgment criteria / CPM	Time Domain	Frequency domain	Non-linear	
Fiuza-Luces et al., 2018 Pernambuco, Brazil	1) Abdominal obesity 2) Non-abdominal obesity	1) N = 149 2) N = 933	1) 17±1 y 2) 17±1 y	Age; HRV test period; BMI; blood pressure	Subjective memories	√	×	×	×	×	1: > 5 h/w	No	LF; HF; LF/HF	No	Abdominal obesity **1 & RMSSD: *B* = 1.51**** 1& LF/HF: *B* = -0.022	Non-abdominal obesity *B* = 1.39 *B* = -0.025
Gutin et al., 2000 United States, Georgia	Obesity	53G,26B	9.5±1 y	Sex; age; BF%; blood pressure; Race; Heart rate	Subjective memories	×	√	√	×	×	2: > 3.2 h/w 3: < 3.2 h/w	RMSSD	No	No	2 & RMSSD: *r* = -0.03 3 & RMSSD: *r* = 0.03	
Gutin et al., 2005 United States, Georgia	Health	1) 171G 2) 133B	1) White: 16.2±1.1 y/29.3±7.5%; Negro: 16.3±1.3 y/30±7.9% 2) White: 16.4±1.3 y/18.6±8%; Negro: 16.0±1.1 y/17.9±11.6%	sex; age; blood pressure; Race; Heart rate; Tanner stage; BF%	Accelerometer	×	√	√	×	×	3: 3-6 METs 2: 6-9 METs	RMSSD	LF (0.05-0.15 Hz); HF; LF/HF	No	**3 & RMSSD: *β* = 0.18*** 3 & HF: *β* = ? **3 & LF/HF: *β* = -0.0018***	
Herzig et al., 2017	Health	162B,147G	3.9±0.7 y	Heart rate; age	Accelerometer	√	×	√	×	×	1: ? 3: ?	RMSSD; SDNN	LF; HF	α1	Heart rate**:1 & SDNN: *β* = -0.63**** **1 & RMSSD: *β* = -0.69**** **1 & α1: *β* = 0.49**** **3 & SDNN: *β* = -0.63**** **3 & RMSSD: *β* = -0.7**** **3 & α1: *β* = 0.49****	

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Table 1. Basic characteristics of included studies.

Researcher/region	Subject characteristics			Mixed factors	PA test tools, types and judgment standards						HRV test method/indicator			Main results	
	Health status	Sample size	Age/BF%		Tool	1	2	3	4	5	Judgment criteria / CPM	Time Domain	Frequency domain	Non-linear	
Iwasa et al., 2005	Health	12G,17B	7.5±1.4 y	No	Pedometer	×	√	×	×	×	Rest: 0-0.5 kCal Walking: 1-3 kCal Quick walk: 4-6 kCal Vigorous exercise: 7-9 kCal	No	LF; HF; LF/HF	No	**2 & HF: r = -0.66** 2 & LF/HF: r = ?	
Krishnan et al., 2009	Health	101G,107B	G: 9.0±0.3 y/ 22% B: 9.0±0.3 y/ 27%	Boys and girls analysed in separate models; Heart rate	Single-axis accelerom-eter	×	√	√	√	×	4 < 1000 cpm 3 < 2500 cpm 2 > 2500 cpm	RMSSD; SDNN	LF; HF	No	**1& SDNN: r = 0.356**** **1 & RMSSD:r =0.364****	
Michels et al., 2013 Northern Belgium	Health	N = 460	G: 8.0±0.3 y /18.4±3% B: 8.1±0.4 y/15.7±2%	Boys and girls analysed in separate models; Age; Heart rate; BF%; Time-point	Single-axis accelerom-eter	×	√	√	√	×	3 > 2296 cpm 2 > 4012 cpm	RMSSD; SDNN	LF; HF; LF/HF	No	**B:** 3 & SDNN: β = 0.13 3 & RMS-SD: $\boldsymbol{\beta}$ = **0.17*** 3 & LF: β = 0.12 **3 & HF: $\boldsymbol{\beta}$ = 0.16*** 3 & LF/HF: β = -0.06	**G** β = 0.11 β = 0.10 β = 0.14 β = 0.06 β = -0.12

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Researcher/region	Subject characteristics			Mixed factors	PA test tools, types and judgment standards						HRV test method/indicator			Main results	
	Health status	Sample size	Age/BF%		Tool	1	2	3	4	5	Judgment criteria / CPM	Time Domain	Frequency domain	Non-linear	
Nagai & Moritani, 2004	1) Health and obese children 2) Normal exercise 3) Not exercise normally 4) Exercise overweight 5) Overweight without exercise	1) 576B,504G 2) 23B,1G/ 3) 23B,1G/ 4) 8B,16G/ 5) 8B,16G	1) ? 2) 9.6±1.3 y 3) 9.5±1.4 y 4) 9.4±1.8 y 5) 9.3±1.7 y	No	Sports practice	×	×	×	×	×	Exercise group: > 3 h/w	No	LF; (0.03-0.15 Hz); HF (0.15-0.5 Hz)	No	Exercise VS. no exercise health **LF*; HF**** obesity LF; **HF****	
Radtke et al., 2013a	1) Health 2) High exercise volume 3) Inactive	1) 29G,20B 2) 14G,9B 3) 26G,11B	11±1.0 y	No	Subjective memories	×	×	×	×	×	3: > 3 h/w	No	LF; HF	α1	B 3 & LF: R^2= 0.59 (P?) 3 & HF: R^2= 0.64 (P?) 3 & α1: R^2= 0.64 (P?)	**G** R^2= 0.06(P?) R^2= 0.06(P?) R^2= 0.06(P?)
Radtke et al., 2013b	Health	28G 24B	14.5±0.7 y 14.5±0.7 y	Sex; age;Tanner stage; Sum of skinfolds	Accelerometer	×	√	√	×	×	3 > 3000 cpm 2 > 5200 cpm	RMSSD	No	No	**3 & RMSSD: β = 0.448*** 2 & RMSSD: β = 0.011	
Sharma et al., 2015	1) Health 2) Non-athletes 3) Athletes	1) 250B,189G 2) 205B,155G 3) 45B,34G	13.5±0.6 y	No	Sports practice	×	×	×	×	×	Sports group: National athletes	RMSSD	LF; HF	No	**Exercise VS. no exercise** **G: SDNN**; RMSSD**; LF**; HF**** **B: SDNN**; RMSSD**; LF**; HF****	

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Table 1. Basic characteristics of included studies

Researcher/region	Subject characteristics			Mixed factors	PA test tools, types and judgment standards						HRV test method/indicator			Main results
	Health status	Sample size	Age/BF%		Tool	1	2	3	4	5	Judgment criteria / CPM	Time Domain	Frequency domain	Non-linear	
Subramanian et al., 2019	1) Health 2) Non-athletes 3) Athletes	1) ? 2) 30B 3) 30B	10-19 y	No	Sports practice	×	×	×	×	×	Sports group: National athletes	RMSSD; SDNN	LF; HF; LF/HF		**Exercise VS. no exercise SDNN*; RMSSD*; LF*; HF*; LF/HF***
Tornberg et al., 2019/ Finland		3395B	18±1 y	Blood pressure; coffee; smoking	Subjective memories	×	×	×	×	×	Low = < 0.5 h/w Medium = 0.5–2 h/w High = 2–4 h/w Top => 4 h/w	RMSSD; SDNN	LF; HF	No	**1 & RMSSD: β = 0.09*** **1 & LF: β = 0.14*** **1 & HF: β = 0.11*** **(top; high; medium) VS low SDNN**; RMSSD**; LF**; HF****; LF/HF
Veijalainen et al., 2019 Finland		185B 192G	7.7±0.4 y 7.6±0.4 y	PHV; BF%; CRS	Accelerometer	√	√	√	√	√	5: ≤ 1.50 METs 4: 1.51-4.00 METs 3: 4.01-7.00 METs 2: > 7.00 METs	RMSSD; SDNN	LF; HF	No	1 & SDNN: β = 0.22 **1 & RMSSD: β = 0.26*** 1 & LF: β = 0.15 1 & HF: β = 0.23 1 & LF/HF: β = 0.20
Vinet et al., 2005	Health	20B		No	Sports practice	×	×	×	×	×	Sports group: > 6 h/w	RMSSD	LF; HF		**Exercise VS. no exercise** SDNN; RMSSD; LF; HF; LF/HF

Note: *, P < 0.05; **, P < 0.01. B = boys; G = girls; ? = information could not be retrieved; BF% = body fat percentage; CRS = cardiometabolic risk score; CPM = counts per minute; ECG = electrocardiogram; HF = high-frequency; HRV = heart rate variability; LF = low frequency; METs = metabolic Equivalent of energy; PA = physical activity; PAQC = Physical Activity Questionnaire for Children; PHV= peak height velocity; RMSSD = square root of the mean of the sum of the squares of differences between adjacent RR intervals; SDNN = standard deviation of RR intervals; 1 = total physical activity, TPA; 2 = vigorous physical activity, VPA; 3 = moderate-to-vigorous physical activity, MVPA; 4 = light physical activity, LPA; 5 = sedentary time, ST.

Source: Authors.

Chart 1. Literature quality evaluation scale.

Bias category	Score	Comment content	Evaluation criteria (0 to 3 points)
Selection bias	3 points	selection	This domain contained one subdomain regarding the source of the population. Low risk of bias was considered when random sampling was used and a high risk of bias was considered when a convenience sample was used without explanation of the recruitment procedures undertaken.
Design bias	3 points	sample size	Low risk of bias was considered when the study provided an appropriate power analysis for sample size calculation, and when the study controlled for important confounders using appropriate statistical methods.
	3 points	confounders	
Statistical bias	3 points	statistical approach	Low risk of bias was considered when an appropriate statistical approach was used, and the authors properly described how missing cases were handled. Studies not mentioning missing cases were considered to have a low risk of bias.
	3 points	missing data	
Result bias	3 points	PA test	Low risk of bias was considered when the exposures were objectively measured and sufficient details provided to enable the measurement to be replicated by the reader. In addition, the appropriate subdomain for the measurement of HRV was duplicated. In this case, a low risk of bias was considered when studies presented sufficient details of the procedures taken before and during the measurement of HRV according to published guidelines [11].
	3 points	HRV test	

Source: Authors.

Table 2. Sample characteristics subgroup analysis for the association between PA (all variables) and HRV (subsample is the maturation of analysis).

Sample characteristics		Effect size statistics†					Heterogeneity statistics			Publication bias classic
		k	r	SE	s^2	95% CI	Z	Q	I^2	fail-safe N
SDNN	Child	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	350	0.34	0.01	0.00	(0.25, 0.43)	6.62	0.44	0.00	28
RMSSD	Child	486	0.22	0.03	0.03	(0.13,0.30)	4.75	12.54	76.07	12
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HF	Child	400	0.52	0.32	0.26	(0.45, 0.59)	11.41	58.24	96.57	49
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	542	0.46	0.14	0.17	(0.39, 0.53)	11.54	66.75	94.01	87
LF	Child	341	0.66	0.01	0.00	(0.60, 0.71)	15.12	1.37	27.05	N/A
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	513	0.58	0.06	0.06	(0.52, 0.63)	14.92	22.43	86.63	183

Note: †Fisher's Z was used to calculate effect size statistics, *k* number of effect sizes, *r* effect size, SE standard error, s^2 variance, 95% CI 95% confidence interval, Z the test of the null hypothesis, Q total Q-value used to determine heterogeneity, I^2 the percentage of total variation across studies that is due to heterogeneity rather than chance, fail-safe N: the potential for publication bias to have influenced the results of a meta-analysis. Fail-safe N is the number of additional studies that would be needed to increase the P-value for the meta-analysis to above 0.05. The Same as below.

Source: Authors.

Table 3. Sample characteristics subgroup analysis for the high and low PA levels and HRV(subsample is the unit of analysis).

Sample characteristics N_1		Effect size statistics†					Heterogeneity statistics		
		N_1	N_2	MD	95% CI	P	Z	I^2	P
SDNN	Child	1452	2007	22.83	(7.89, 37.77)	0.00	3.00	97.47	0.00
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	1482	2037	22.45	(9.37, 35.5)	0.00	3.36	96.01	0.00
RMSSD	Child	90	369	28.35	(15.26, 41.44)	0.00	4.25	55.07	0.11
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	120	399	28.08	(17.50, 38.66)	0.00	5.20	24.82	0.22
HF	Child	90	369	**569.61**	(-154, 1293.24)	0.12	1.54	80.84	0.02
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	120	399	**602.78**	(0.47, 1205.08)	0.05	1.96	64.42	0.03
LF	Child	90	369	309.69	(95.44, 523.94)	0.00	2.83	0.00	0.39
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	120	399	309.96	(96.24, 523.68)	0.00	2.84	0.00	0.59
LF/HF	Child	1373	1647	**0.33**	(-0.31, 0.97)	0.31	1.02	92.90	0.00
	Adolescent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Child and adolescent	1403	1677	**0.31**	(-0.18, 0.80)	0.22	1.23	84.58	0.00

Note: N_1 – number of top PA levels; N_2 – number of low PA levels; MD – mean difference.

Source: Authors.

The relationship between PA and HRV

PA were associated with significant cardiac autonomic control in children and adolescent. Twelve studies[7,9-11,19,23,24,27,29,31,32,34] used regression analysis (nine items β, three items R^2), and six studies[18-22,28] used correlation analysis (r). Three studies[18,19,28] reported SDNN forcardiac autonomic function, the meta-analysis showed amedium-sized association (r = 0.34; 95%CI = 0.25, 0.43). Six studies[18-22,28,34] reported parasymptomatic nerve activity such as RMSSD and HF. PA and RMSSD (r = 0.22; 95%CI = 0.13, 0.30.) were small-sized association, HF (r = 0.52; 95%CI = 0.45, 0.59) were medium-sized association in children. Two studies[18,20] reported LF for sympathetic nerve regulation indicators. The meta-analysis showed a medium-sized association (r = 0.66; 95%CI = 0.60, 0.71).

High PA level significantly increases cardiac autonomic nervous control in children and adolescent. Five studies[10,25,26,30,33] have reported significant differences between the high and low PA levels. Three studies[10,25,30] reported cardiac autonomic function, subgroup analysis showed that children's high PA group SDNN (MD = 22.83; 95%CI = 7.89, 37.77) increased significantly. Three studies[25,26,30] reports parasympathetic nerve activity such as RMSSD and HF. A subgroup analysis showed that children's high PA group RMSSD (MD = 28.35; 95%CI = 15.26, 41.44), but non-significant increases in HF (MD = 569.61; 95%CI = -154, 1,293.24). Four studies[7,25,30,33] reported LF for sympathetic nerve regulation, showed that children's high PA group LF (MD = 309.69; 95%CI = 95.44, 523.94) increased significantly. Three studies[10,25,26] reported LF/HF for reflects the sympathetic-vagal balance. A subgroup analysis showed that LF/HF was non-significant differences in children (MD = 0.33; 95%CI = -0.31, 0.97).

Among the 21 studies included, 16 studies used regression or correlation analysis, and 12 studies reported a significant correlation between PA and HRV (P < 0.05). VPA (one study)[22]; MVPA (four studies)[11,24,27,29]; TPA (nine studies)[7,10,11,18-20,28,31,32,34]. For cardiac ANS's function, MVPA (one study)[11]; TPA (four studies)[7,11,18,28]. For cardiac parasympathetic nerve activity, MVPA (four studies)[11,23,27,29]; TPA (ten studies)[7,10,11,18-20,28,31,32,34]. For cardiac sympathetic nerve activity, TPA (five studies)[10,18,20,32,34]. For cardiac sympathetic-vagal tension balance, MVPA (one study)[27]; TPA (one study)[34] have significant correlation.

Table 4. Bias risk evaluation results.

Inclusion study	Selection bias	Design bias		Statistical bias		Result bias		Total score
	Subject source	Sample size	Confounding factors	Statistical methods	Missing data	HRV test	PA test	
Blom et al., 2009	0	1	1	2	1	3	1	9
Buchheit et al., 2007	3	1	3	3	1	2	1	14
Cayres et al., 2015	1	1	3	3	3	3	0	14
Chen et al., 2008	1	2	0	2	2	2	1	10
Chen et al., 2012	0	1	0	2	0	3	1	7
Farah et al., 2014	0	2	2	3	3	3	1	14
Farah et al., 2018	2	2	3	2	1	2	1	13
Gutin et al., 2000	0	1	3	3	3	1	1	12
Gutin et al., 2005	0	3	3	3	3	3	2	17
Herzig et al., 2017	3	2	2	2	2	3	3	17
Iwasa et al., 2005	0	0	0	1	3	1	1	6
Krishnan et al., 2009	2	2	0	2	1	2	2	11
Michels et al., 2013	3	2	3	3	3	3	2	19
Nagai & Moritani, 2004	0	0	0	2	3	1	0	6
Radtke et al., 2013a	0	1	3	3	1	1	0	9
Radtke et al., 2013b	0	0	3	3	2	1	3	12
Sharma et al., 2015	0	2	0	1	0	1	0	4
Subramanian et al., 2019	1	2	0	2	3	3	1	12
Tornberg et al., 2019	2	3	2	3	2	2	2	16
Veijalainen et al., 2019	2	2	3	3	2	3	3	18
Vinet et al., 2005	0	0	0	2	3	1	0	6

Source: Authors.

Confounding factors and test tools

Confounding factors

Confounding factors was reported in 12 studies, including: (a) age (ten studies)[7,9,11,19,21,24,29,32]; (b) heart rate (six studies)[11,18,27-30]; (c) sex (five studies)[9,19,21,24,27]; (d) BF%/BMI/skinfold thickness (four studies)[7,9,21,23]; (e) PHV/maturity degree/tanner stage (four studies)[9,24,27,31]; (f) blood pressure (four studies)[7,21,27,31]; (g) race (three studies)[19,21,27]; (h) HRV test time (three studies)[7,29,32]; (i) blood glucose (one study)[18].

Test tool

Heart rate variability – our included studies that tested HRV using Polar Wearlink 3[29], Polar 810s[9], Polar RS800CS[7,10,19,32] and ECG[11,20,22-25,27,28,31,33]. Rather than testing HRV during sleep at night[11,22,23,26], researchers can select from a larger variety of studies during the day[9,10,19,20,25,29,33]. The test durations are 2 minutes[18], 5 minutes[7,9-11,20,23,25,28,29,31,32], 6 minutes[26], 5 hours[22], 24 hours[24], and some studies have chosen 256 R-R interval (RRi)[21,27] and 1,000 RRi[19] as HRV analysis samples.

Physical activity – inclusion studies use objective or subjective tests to evaluate PA. Scales[23] and questionnaires[10,18,20,21,32,33] are the most common subjective evaluation tools. The objective evaluation tools mainly use accelerometers (single-axis[24,27,29]and three-axis[6,9,28,31]) or pedometers[19,22]. Nonetheless, the cut-off values for PA intensity in each sample are not consistent (Table 1).

Discussion

The findings of our review show that: (a) PA and HRV were significantly positive correlated, PA can effectively improve cardiac autonomic function; (b) VPA and MVPA can improve HRV, while LPA and ST may have no effect on improving HRV; (c) The differences in the physiological characteristics of the participants (age, sex) and the testing tools (PA, HRV) may affect the results.

The relationship between PA and HRV

Our results show that there is a positive relationship between PA and HRV in children and adolescents. Our findings are consistent with previous studies which investigated different age groups, including young adults[35] and seniors[36]. There are three main ways to increase the ANS function: increased parasympathetic nerve activity, decreased sympathetic nerve activity and the role of the vagus nerve on sympathetic-parasympathetic. Our study shows a significantly positive correlated between PA and vagus nerve and parasympathetic nerve activity RMSSD (r = 0.22; 95%CI = 0.13, 0.30), HF (r = 0.46; 95%CI = 0.39, 0.53). Meanwhile, RMSSD was significantly higher in participants with high PA than the low PA levels (MD = 28.08; 95%CI = 17.50, 38.66). However, no statistical differences were found in HF (MD = 602.78; 95%CI = 0.47, 1,205.08). This is most likely due to the natural log transformation distribution distorting the short-term linear HRV metrics[10,33]. According to the effects of the sympathetic nerve activity, PA was significantly positive correlated with the LF (r = 0.58; 95%CI = 0.52, 0.64). The LF decreased significantly as compared to the population with low PA levels (MD = 309.96; 95%C I = 96.24, 523.68). This means the positive relationship between children's and adolescents' PA and HRV.

According to the current findings, MVPA has a significant effect on improving HRV and the impact of VPA on HRV is weak. Four of the 21 studies investigated the relationship between VPA and parasympathetic nerves[9,22,24,27]. Only one study[22] found a negative correlation between VPA and the HF (r = -0.66, $P < 0.05$) using a pedometer to distinguish PA levels. However, this study did not control for confounding factors and the pedometer test's validity for children and adolescents is low[8]. In addition, while combining MPA and VPA (MVPA), there is a significantly positive relationship between MVPA and HRV. Gutin et al.[21] and Radtke et al.[23] used subjective questionnaire distinguish PA level, and it was discovered that MVPA was unrelated to HRV. However, the recall questionnaires should be with caution when used in children or adolescents[8]. Four studies[11,24,27,29] used accelerometers to distinguish PA leveland discovered a strongpositive association between MVPA and HRV. The current findings show that MVPA could be a significant factor for increasing HRV and improving ANS function.

Confounding factors and test tools

Our research aims to investigate the effect of PA levels on HRV in 3-18 years. The interpretation of the results is hampered by sample size, statistical methods, regional, outcome assessments and confounding factors. There is a positive relationship between PA level and HRV for participants aged 3-18 years remains controversial.

Confounding factors

The standard deviationof participants' age is very small (< 2) in the included study,except for Subramanian's study[25]. It means that the age range of included study is not large. Although half of the studies reported confusion about the age factor, only one[11] study controlled for age variables and discovered a significant link between 3-6 year old children's PA and HRV (β = -0.7, $P < 0.01$). There was also a link in the studies between the ages 6.1-13 y (β = 0.17, $P < 0.05$)[29] and 13.1-18 years (β = 0.18, $P < 0.05$)[27]. However, the difference inregression coefficient suggested that the influence of age in the results may be slight. Although biological maturity increases with age in children and adolescents. There was no research investigated the effect of biological maturity on the relationship between PA and HRV. It is difficult to conduct subgroup analyses based on maturity. Our findings show that reporting HRV in childhood alone is similar to combining childhood and adolescence, as describe in Table 2 and Table 3. Therefore, we speculated that maturity may have a minor impact on the relationship between PA and HRV.

The effect of body weight status on the observed relationship is weak. Two studies[20,33] found a significant positive correlation between PA and HRV in overweight children, although one of study has a higher risk of bias. In comparison, the lower risk of bias study with Farah et al.[7] also found a significant correlation. However, no significant correlation was found in a study of the risk of the same bias[21]. Therefore, we hypothesize that obesity will disrupt the normal maturation

of cardiac autonomic function, while the weight shift induced by PA will encourage cardiac autonomic function improvement[37].

Concerning the effect of sex on relationships, two studies[28,29]discovered a significant positive correlationin boys. Boys and girls aged 8-9 years were surveyed in studies, suggesting that the correlation between PA and HRV differs by sex[28,29]. Furthermore, boys have more MVPA than girls, which may explain the reproductive consequences of sex differences[29].

Test tools

HRV – the first guideline for HRV measurement standards, physiological interpretation, and clinical use was published in 1996[6]. Our review included studies that were all published after 2000, adopting the HRV method and the measurement method obtained is generally well reported. The majority of studies provide linear HRV metrics indicators, which are described in Table 1. Only two studies have[11,23] reported on the currently popular non-linear indicator. Furthermore, using different devices (wearlink31, 810s, Rs810cs) to record HRV or different algorithms for analysis when comparing results will introduce possible deviations.When compared to ECG[38], these Polar recorders have been recorded to be reliable and useful tools, particularly in such application scenarios. They can use Polar to collect and edit HRV data if appropriate[38]. Furthermore, the method of deciding HRV presents some challenges. The majority of the research used daytime test times and five-minute durations, but Herzig et al. used deep sleep to prevent environmental interference[11]. However, some tests for 2 minutes[18], 6 minutes[26], 5 hours[22] and 24 hours[24]. There were some studies using 256 RRi[21,27], 1000 RRi[19] and short-term HRV. Although short-term HRV results are easy to measure, they can be difficult to interpret[39], resulting in mistakes.

PA – self-reporting accounts for nearly half of the study's data, which has a number of advantages, convenience, efficiency, burden, and low cost[40]. The questionnaire, on the other hand, is inaccurate, particularly when evaluating the PA of young children[40,41]. While activity monitors, such as accelerometers, are an alternative or complementary tool for assessing PA[40], but there is currently no agreement on which specifications should be used to collect and process data[41]. Published research, on the other hand, defined the criteria for collecting and processing accelerometer data in order to determine PA[42]. Among them are wearing position, sampling frequency, filter, epoch length, non-wearing time, significant day (week) time, sedentary behaviour, and cut-off value. Despite the fact that many studies failed to reveal significant methodological problems, seven studies[9,22,24,27-29,31] include the accelerometer cut-off values (Table 1). Therefore, we recommend that researchers report detailed methodologies to improve the quality and reproductivity of future research.

Limitations

One limitation of our systematic review and meta-analysis is that it is cross-sectional in design. Therefore, cause and effect relations cannot be deduced. Furthermore, confounding factors such as gender, age, and BF% may interfere with the effect of PA on HRV. In addition, due to the relatively small number of studies on this issue, adolescents cannot be analysed separately when grouped by age. However, we present the results of the analysis for the children group and use the separated ages (children and adolescents) as the benchmark. The results show that there was no difference in analysis between combined (children) and separated ages (children and adolescents).It was also in the studies between the ages of 6.1-13 years ($\beta = 0.17$)[29] and 13.1-18 years ($\beta = 0.18$)[27]. However, the difference inregression coefficient suggested that the influence of age on the results may be slight. Therefore, we speculate that the effects of PA on HRV were consistent in children and adolescents' further studies are needed to determine whether age affects the relationship between PA and HRV.

Conclusion

The findings of our study revealed that there was a medium-sized association between PA and HRV in children and adolescents. Promoting children's and adolescents' participation in moderate-to-vigorous physical activity (MVPA) will increase parasympathetic nerve activity and decreased sympathetic nerve activity. The confounding factors and the testing tools will influence the relationship between PA and HRV. Our findings support motivating children and adolescents to engage in more MVPA in their daily lives to improve autonomic function and promote cardiovascular safety. In the future, there is still needed for high-quality cross-sectional studies in children and adolescents, more stringent control factors, more unified testing tool, greater doses of PA and more diverse cardiovascular health outcomes.

Collaborations

H Chen: conceptualization, methodology, analyses, writing-original and edited drafts. J XU: methodology, analyses, writing-original and edited drafts. H Xie: writing-original draft, editing. Y Huang and X Shen: supervision, editing. F Xu: conceptualization, writing-review and editing, funding acquisition.

Acknowledgment

This work was supported by grants from the Humanities and Social Sciences Project of the Ministry of Education of China (No. 19YJC890050), Hangzhou Philosophy and Social Science Key Research Base (No. 2021JD19) and Zhejiang Provincial Natural Science Foundation Project (No. LY18C110002).

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Article submitted 10/12/2020
Approved 27/07/2021
Final version submitted 29/07/2021

Chief editors: Romeu Gomes, Antônio Augusto Moura da Silva