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Effect of Physical Exercise on Heart Rate Variability in Persons with Down Syndrome

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ABSTRACT

Melo GLR, Soares BR, Neves RP, Olher RR, Souza LHR, Ferreira CES, Assumpção CO, Rosa TS, Boato EM, Moraes MR. Effect of Physical Exercise on Heart Rate Variability in Persons with Down Syndrome. **JEPonline** 2019;22(1):63-74. The purpose of this study was to analyze the effect of physical exercise on the parameters of heart rate variability (HRV) in people with Down syndrome (DS). A systematic review was carried out until December 2018, which included the following databases: (a) PubMed; (b) SCOPUS; and (c) Web of Science. A combination of keywords relating to HRV and exercise was included during the research process. Initially, 570 articles were found, of which 7 were included in the sample. The 7 studies included in the present review tested 20 interventions and involved 245 participants. Interventions included aerobic training (n = 14), resistance training (n = 2), and concurrent training (n = 4). The results indicated that both aerobic and strength training and combined exercise can improve the parasympathetic modulation even with attenuated response of heart rate and blood pressure during and after physical exercise. Therefore, it is suggested that people with DS should practice some type of exercise to enhance their sympatho-vagal balance and to improve their health status.

Key Words: Autonomic Dysfunction, Down Syndrome, Exercise

INTRODUCTION

The Down syndrome (DS) is characterized by a chromosomal anomaly where by a person has three copies of chromosome 21 instead of two (22). Thus, individuals with DS have their own genetic and phenotypic characteristics (3) that include intellectual disability, congenital heart disease, ligament laxity, and muscular hypotonia (22). Each one can have a direct influence on their life expectancy (7) and to a lesser extent can indirectly influence physical activity practice (25).

Due to the increase in life expectancy in people with DS, understanding the autonomic cardiac responses is of paramount importance in the clinical setting to prevent the onset of secondary diseases (7). Hence, the use of regular exercise as a non-pharmacological tool to improve the sympatho-vagal balance and increase vagal modulation in people with DS is an important means to improving their health (13).

In some individuals with DS, preliminary data indicate that they may have low physical fitness (18), chronotropic incompetence (16), a significant reduction in blood pressure (BP), heart rate (7), and autonomic cardiac function (1). Cabral et al. (6) observed that increased physical activity is an efficient mechanism to raise heart rate variability (HRV) indices in different age groups of people with DS. HRV is an indication of overall health as well as general fitness (28). As HRV increases, it reflects the increase in homeostatic behavior (14).

With the advent of digital technology, there has been an exponential growth in the use of HRV as a device for the evaluation of autonomic modulation under normal and pathological conditions (17). The data obtained from the HRV indexes are of great clinical relevance in verifying the physiological variables, since the HRV reduction can predict diseases or future complications in patients who already have disease (17). As a result, HRV has shown to be a valuable tool for the analysis of cardiac autonomic function in individuals under pathological conditions and in physical training situations (12).

Considering that physical exercise may offer improvements in the sympatho-vagal recovery, it is now necessary to know what type of physical exercise, intensity, and volume and, in addition, if there is a difference in the acute or chronic exercise for the HRV parameters. Thus, to contribute to the literature, the purpose of this study was to determine the effect of physical exercise on the parameters of HRV in people with DS through a systematic analysis of controlled clinical trials.

METHODS

Search Strategy

We conducted a systematic review of the literature up to December 2018 that included the following databases: (a) PubMed; (b) SCOPUS; and (c) Web of Science. We included articles that exhibited the terms: "Down Syndrome", "heart rate variability", "autonomic dysfunction", and "autonomic nervous system". We also manually searched the reference lists of the articles.

Inclusion and Exclusion Criteria

Studies included in the review were checked for the following criteria: (a) whether the study was a randomized or a non-randomized clinical/controlled trial that investigated heart rate variability in individuals with Down syndrome; (b) whether the study assessed humans; (c) whether one or more exercise programs were performed; and (c) whether the keyword combination referred to exercise training. Articles were excluded if: (a) we could not obtain the full-text article; (b) exercise was not performed; (c) there was no control group as part of the study; and (d) the articles that were not written in English, Spanish, or Portuguese.

Identification of Eligible Studies

Acceptable studies were cross-sectional or longitudinal experimental interventions performed on human subjects that analyzed the effects of physical training on the cardiovascular parameters that primarily addressed heart rate variability and did not administer any drugs.

Data Extraction

We extracted all relevant data from the studies that met the eligibility criteria: (a) characteristics of the sample; (b) methodological design; (c) exercise modality; (d) training protocol (volume/intensity); (e) method of measure of cardiovascular parameter (HRV); and (f) the results after physical training.

RESULTS

Search Results

The search of PubMed, SCOPUS, and Web of Science provided a total of 570 citations. After examining the exclusion criteria, 432 articles were excluded. Thus, 138 articles were selected, but after adjusting for duplicates, 34 articles remained. Furthermore, 22 were excluded because they did not meet the inclusion criteria. We examined the full text of the remaining 12 citations in more detail. After further analysis, 5 studies were excluded because they did not provide sufficient data. A total of 7 studies met all the criteria, and were included in the systematic review (Figure 1).

Study Characteristics

All studies selected for this review were controlled trials published in English (n = 7). The duration of the interventions ranged from 1 to 26 wks with 2 to 4 exercise sessions per week. A total of 7 trials had supervised sessions. The 7 studies included in the present review tested 20 interventions that involved 245 participants. The studies included aerobic training (n = 14), resistance training (n = 2), and concurrent training (n = 4) (Table 1).

A more explicit description of each exercise intervention is available in Table 2. The studies used a total of 7 HRV markers, including three of the time domains and four frequency domains (Table 2). HRV was measured by ECG converted into an R-R interval tachogram in three studies and Polar Monitor with continuous R-R intervals (resolution of 1 ms) in three studies, except for one from Goulopoulou et al. (15) who used both methods.

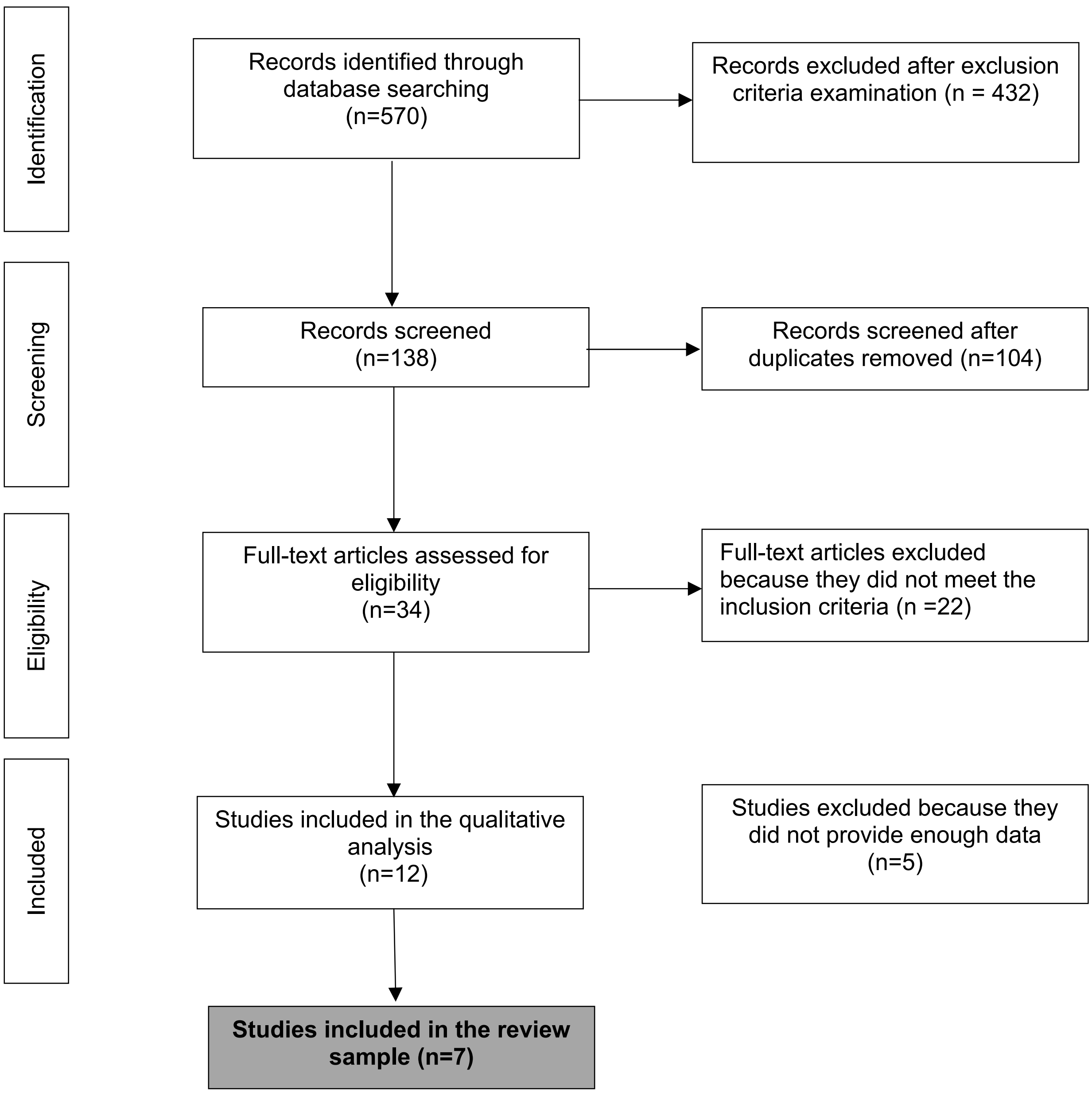

Figure 1. Flow Diagram for the Strategy of Searching for the Studies.

Table 1. Studies that Evaluated the Effects of Physical Exercise on Heart Rate Variability of Individuals with Down Syndrome

Study	EXPERIMENTAL DESIGN		EXERCISE TRAINING PROTOCOL	
	Sample Size (n); Sex (M/F)	Sample Description; Fitness Level; Mean Age (yrs)	Total Duration (wk); Frequency (day); Supervision(Y/N)	Intervention (s)
Baynard et al. (2004)	n=31 DS: 16 (10/6) CT: 15 (8/7)	Young adults untrained and moderately active 20.2	1 2 Y	Aerobic (treadmill) with stages of 4 min. Initial velocity (0.89 to 1.56 m·sec^{-1}) at 0% slope. The velocity was maintained in a manner increasing by 2.5% every 4 min to 7.5%. Thereafter, speed increased by 0.22 m·sec^{-1} every minute until exhaustion.
Figueroa et al. (2005)	n=27 DS: 13 (8/5) CT: 14 (6/8)	Young adults untrained 27.1	1 2 Y	Handgrip, 3 set 30% of MVC for 5 sec with 2-min interval.
Goulopoulou et al. (2006)	n=74 DS: 50 CT: 24	Young adults untrained and moderately active 25.	2 3 Y	Aerobic (treadmill) Stage 1 of the treadmill protocol, comfortable speed for 3 min, followed by fast speed of 2 min (speed range of 5 to 1.5 mi·hr^{-1}). The slope increased by 2.5% every 2 min to 12.5%. The speed increased 1 mi·hr^{-1} every minute until exhaustion.
Giagkoudaki et al. (2010)	n=20 DS: 10 (4/6) CT: 10 (5/5)	Young adults untrained 23.75	26 3 Y	Aerobics (walking, running, dancing and simple men's basketball exercises and rhythmic gymnastics with balls and tapes for women) 60 min at 60% and progressed to 80% reserve HR.
Mendonca et al. (2011)	n=25 DS: 13 (9/4) CT: 12 (8/4)	Adults, sedentary or less active 34.85	2 3 Y	Aerobic (treadmill) Stage 1 of the treadmill protocol, comfortable speed for 3 min, followed by fast speed of 2 min (speed range of 5 to 1.5 mi·hr^{-1}). The slope increased by 2.5% every 2 min to 12.5%. The speed increased 1 mi·hr^{-1} every minute until exhaustion.
Mendonca et al. (2013)	n=41 DS1: 11 (6/5) DS2: 15 (8/7) CT: 15 (5/10)	Young adults sedentary or less active 37.6	12 3 Y	Aerobic (treadmill) was performed 3 d·wk^{-1} for 30 min at 65 to 85% of (VO_2 peak). Resistance training (9 exercises); 2 sets each in a circuit of at 12-reps.
Bunsawat and Baynard (2016)	n= 27 HG DS: 10 (6/4) CT: 8 (2/6) CE DS: 9 (9/0) CT: 9 (3/6)	Young adults untrained HG: 27 CE: 28.5	2 2 Y	Handgrip, 3 set 30% of MVC for 5 sec with 2-min interval. Aerobic (cycle-ergometer) sessions included two 6-min stages with 0 W during stage 1 and 50% of body weight (kg) in watts during stage 2.

DS = Down Syndrome, **CT** = Group Control, **Y** = Yes, **N** = No, **HG** = Handgrip, **CE** = Cycle-ergometer, **HR** = Heart Rate, **MVC** = Maximal Voluntary Contraction

Table 2. Markers and Measures of Heart Rate Variability used at Rest, During, and in Recovery from Physical Exercise.

ESTUDO	*MARCADORES E MEDIDAS*	*RESULTADOS*		
		REST	DURING EXERCISE	RECOVERY
Baynard et al. (2004)	Polar Monitor Continuous R-R intervals (1ms resolution) analyzed Heart Signal software. RMSSD (ms²); pNN50 (%) SDNN (ms²); HF (ms²); LF (ms²); LF/HF (ratio) HR (bpm)	DS:RMSSD (4421.5±833.1) CT:RMSSD (1498.8±862.4) DS: pNN50 (32.8±5.8) CT:pNN50 (14.9±6.0) DS: SDNN (66.1±5.3) CT: SDNN (48.5±5.5) DS:HF (1418.1±268.6) CT: HF (579.9±278.0) DS: LF (1264.1±226.2) CT: LF (884.8±234.2) DS: LF/HF (1.18±0.42) CT: LF/HF (2.28±0.44) DS: HR (71±3.4) CT: HR (78±2.6)	**SUBMAXIMAL 1** DS: RMSSD (380.9±207.2) CT: RMSSD (883.1±214.4) DS: pNN50 (2.7±1.3) CT: pNN50 (2.0±1.3) DS: SDNN (23.1±3.2) CT: SDNN (31.1±3.3) DS: HF (115.1±68.7) CT: HF (308.9±71.1) DS: LF (203.5±72.3) CT: LF (370.1±274.8) DS: LF/HF (2.88±0.61) CT: LF/HF (2.63±0.63) **SUBMAXIMAL 2** DS: RMSSD (395.8±173.1) CT: RMSSD (343.6±179.2) DS: pNN50 (1.4±0.6) CT: pNN50 (0.79±0.6) DS: SDNN (21.5±3.4) CT: SDNN (19.4±3.5) DS: HF (122.1±58.1) CT: HF (102.8±60.1) DS: LF (135.9±49.2) CT: LF (140.8±50.9) DS: LF/HF (2.61±0.95) CT: LF/HF (3.09±0.98) SD: HR (161±5.3) CT: HR (179±4.6)	
Figueroa et al. (2005)	ECG converted to interval tachogram R-R; HF (In ms²); LF (In ms²); LF/HF (In ratio) HR (bpm)	DS: HF (5.4±0.2) CT: HF (5.6±0.4) DS: LF (6.3±0.2) CT: LF (7.2±0.1) DS:LF/HF (1.18±0.0) CT:LF/HF (1.36±0.08) DS: HR (76±3) CT: HR (78±3)	DS: HF (5.1±0.2) CT: HF (4.6±0.4) DS: LF (6.2±0.2) CT: LF (6.2±0.2) DS:LF/HF (1.23±0.06) CT:LF/HF (1.44±0.10) DS: HR (80±3) CT: HR (90±3)	DS: HF (5.4±0.3) CT: HF (6.3±0.3) DS: LF (6.5±0.2) CT:LF (7.1±0.2) DS: LF/HF (1.24±0.07) CT: LF/HF (1.17±0.05) DS: HR (78±3) CT: HR (77±2)
Goulopoulou et al. (2006)	Polar Monitor Continuous R-R intervals (1 ms resolution) analyzed Heart Signal software. RMSSD (ms); SDNN(ms); HF (In ms²); LF (In ms²); LF/HF (In ratio) HR (bpm)	DS: RMSSD (7.65±0.15) CT: RMSSD (7.72±0.22) DS: SDNN (4.12±0.5) CT: SDNN (4.37±0.09) DS: HF (6.57±0.16) CT: HF (6.65±0.24) DS: LF (6.93±0.12) CT: LF (7.26±0.14) DS: LF/HF (0.35±0.11) CT: LF/HF (0.60±0.17) DS: HR (70±1.5) CT: HR (66±1.7)		

Table 2. Continued

ESTUDO	MARCADORES E MEDIDAS	RESULTADOS		
		REST	DURING EXERCISE	RECOVERY
Giagkoudaki et al. (2010)	24-hr ECG converted to interval tachogram R-R SDNN (ms); SDANN index (ms); SDNN index(ms); rMSSD(ms); pNN50 (ms) HF(ms²); LF (ms²); LF/HF (ratio) HR (bpm)	DS: SDNN (152.8±833.8) CT: SDNN (182.1±27.5) DS: SDANN (134.6±30.8) CT: SDANN (163.9±27.8) DS: SDNN (69.9±12.7) CT: SDNN (84.2±15.4) DS: RMSSD (40.8±12.0) CT: RMSSD (55.6±16.6) DS: pNN50: (17.0±10.1) CT: pNN50: (28.5±12.2) DS: HF (575.5±321.9) CT: HF (896.5±279.0) DS: LF: (1126.6±289.1) CT: LF (1421.4±276.3) DS: LF/HF (2.45) CT: LF/HF (1.71) DS: HR (78.3±7.7) CT: HR (70.5±7.1)		DS: SDNN (152.6±833.7) DS: SDANN (137.5±29.9) DS: SDNN (72.5±12.5) DS: RMSSD (44.7±10.6) DS: pNN50: (24.0±9.0) DS: HF (685.8±96.1) DS: LF (1164.8±289.8) DS: LF/HF (1.72)
Mendonca et al. (2011)	Polar Monitor Continuous R-R intervals (1 ms resolution) analyzed software Kubios HRV Analysis 2.0 HF(In ms²); LF (In ms²); LF/HF (In ratio) HR (bpm)	DS: HF (5.8) CT: HF (5.9) DS: LF (6.8) CT: LF (6.1) DS: LF/HF (1.3) CT: LF/HF (1.0) DS: HR (77) CT: HR (73)	**45% VO_2 max** DS: HF (3.3) CT: HF (2.4) DS: LF (4.2) CT: LF (2.1) DS: LF/HF (4.8) CT: LF/HF (3.3) DS: HR (108) CT: HR (118)	DS: HF (5.5) CT: HF (5.7) DS: LF (6.4) CT: LF (6.1) DS: LF/HF (1.4) CT: LF/HF (1.1) DS: HR (78) CT: HR (75)
Mendonca et al. (2013)	Polar Monitor Continuous R-R intervals (1 ms resolution) analyzed software Kubios HRV Analysis 2.0 HF (In ms²); LF (In ms²); LF/HF (In ratio) HR (bpm)	DS: HF (6.1±0.3) CT: HF (5.5±0.3) DS: LF (6.6±0.2) CT: LF (6.4±0.3) DS: LF/HF (1.08±0.03) CT: LF/HF (1.17±0.04) DS: HR (62.7±3.4) CT: HR (62.6±2.5)		DS: HF (6.5±0.3) CT: HF (5.7±0.4) DS: LF (6.7±0.2) CT: LF (6.3±0.3) DS: LF/HF (1.04±0.03) CT: LF/HF (1.15±0.04) DS: HR (63.4±1.9) CT: HR (61.9±1.7)
Bunsawat and Baynard (2016)	24-hr ECG converted to interval tachogram R-R; rMSSD (ms); HF (ms²); LF (ms²); LF/HF (ratio) HR (bpm)	**HG** DS: RMSSD (53±10) CT: RMSSD (36±11) DS: HF (1461±467) CT: HF (604±522) DS: LF: (1985±568) CT: LF (1378±635) DS: LF/HF (2.65±1.78) CT: LF/HF (9.66±1.99) DS: HR (68±4) CT: HR (80±3) **CE** DS: RMSSD (31±8) CT: RMSSD (41±8) DS: HF (359±124) CT: HF (343±131) DS: LF: (972±284) CT: LF (1679±284) DS: LF/HF (4.76±1.58)		**HG** DS: RMSSD (43±7) CT: RMSSD (24±8) DS: HF (728±185) CT: HF (282±207) DS: LF: (1214±327) CT: LF (693±366) DS: LF/HF (2.98±1.62) CT: LF/HF (6.55±1.81) DS: HR (75±1) CT: HR (86±1) **CE** DS: RMSSD (15±3) CT: RMSSD (11±3) DS: HF (93±29) CT: HF (49±31); DS: LF: (127±46) CT: LF (163±46) DS: LF/HF (2.31±5.27)

	CT: LF/HF (8.60±1.68) DS: HR (73±3) CT: HR (77±3)	CT: LF/HF (12.39±5.59) DS: HR (102±3) CT: HR (106±3)

DS = Down Syndrome, **CT** = Group Control, **Y** = Yes, **N** = No, **HG** = Handgrip, **CE** = Cycle-ergometer, **HR** = Heart Rate, **HF** = High-Frequency, **LF** = Low-Frequency, **RMSSD** = Square Root of the Mean Squared Differences of Successive Differences, **SDNN** = Standard Deviation of all R-R Intervals, **SDANN** = Standard Deviation of the Average Interbeat (RR) Interval Calculated Over Short Periods, usually 5 min, **SDNN index** = Mean of the 5-min Standard Deviation of the RR Interval Calculated over 24 hrs, **pNN50** = Proportion Derived by Dividing the Number of Interval Differences of Successive RR Intervals Greater than 50 ms by the Total Number of RR Intervals

DISCUSSION

After a careful analysis of the research articles, it is appropriate to conclude that there is a benefit of physical exercise on the autonomic dysfunction of adults with DS. This is true even though the papers varied in type of exercise, volume, intensity, and in the HRV markers used. As for the type of exercise, aerobic exercise was the most frequent throughout the research protocols (2,5,13,15,18,20). The studies used different types of equipment to train the subjects (e.g., cycle-ergometer or treadmill), varied the stimuli (e.g., graded or continuous), and even employed sports games.

Regarding the effects of aerobic training, Giagkoudaki et al. (13) and Mendonça et al. (20) used 6 wks and 12 wks, respectively, of which they reported an improvement in autonomic function with a decrease in the Low frequency (LF)/High frequency (HF) ratio and an increase of the sympathetic-vagal balance. According to Carvalho et al. (7) this may occur due to a reduction of the sympathetic response or inadequate vagal withdrawal. Nonetheless, it was observed that there was a difference between the DS group and the control group for the frequency domain: LF, HF. and LF/HF. The same did not occur in the time domain indexes, so that the sympathetic branch presents high indices compared to the general modulation in the supine position. During the exercise of handgrip and cold pressure test, individuals with DS had an attenuated increase in HR that suggested an attenuated response to symptoexcitatory (10). In contrast, Mendonça et al. (18) reported an increase in sympathetic modulation, however they also observed parasympathetic reduction during the submaximal treadmill exercise in the DS subjects.

Concurrent training is effective in improving different health-related parameters, as well as being effective in the improvement of cardiopulmonary fitness and muscle strength in adults (27). Mendonça et al. (20) observed that a 12-wk intervention of aerobic exercise and strength training produced similar resting HR and HRV results in adults with and without DS, mainly with regards to cardiovagal modulation. Figueroa et al. (11) found that HR and HRV at rest were similar in both the DS adults and their non-DS pairs. Therefore, these studies show that DS does not present altered autonomic modulation of resting HR. In obese adolescents, Farinatti et al. (8) stated that strength training attenuates autonomic cardiac dysfunction and blood pressure, besides increasing parasympathetic activity and decreasing the sympatho-vagal balance.

Michael and colleagues (21) also reported that HRV responses are associated with intensity, volume, and duration of exercise. They concluded that the preceding exercise intensity has a graded effect on recovery HRV measures, thus reflecting cardiac vagal activity. Also, they observed that during incremental exercise HRV measures tend to decrease according to exercise intensity (21). With regard to the chronic cardiovascular autonomic adaptations in athletes during aerobic and resistance training, the physiological adaptations promote the increase in the parasympathetic component in order to increase the HRV (26).

When it comes to cardiac dysfunction in DS, little is known about the topic. Bunsawat et al. (4) report that individuals with DS have a lower baroreflex sensitivity that results in an altered autonomic function. In addition, Mendonça and Pereira (19) found that adults with DS presented an attenuated recovery of heart rate at 1 min and 2 min after peak exercise, even though they presented a lower chronotropic response after the sympathetic stimulatory task. This occurs as a function of the continuous post-exercise parasympathetic reactivation and at the 2-min recovery the sympathetic withdrawal assumes the activation control (23). However, in people with DS after aerobic exercise, it was observed that there was no increase in the concentration of catecholamines, which is essential for rapid sympathetic activation (9).

In relation to the behavior of sympathetic modulation in people with DS during exercise, there is an increase in the sinoatrial node, which is determined by the intensity of the exercise so that DS requires a greater sympathetic activation to reach 60% of the HR peak (18). Interestingly, Iellamo et al. (16) indicate that cardiac sympatovagal balance can be altered according to the intensity of the exercise that has a relative contribution of the central command and the muscular meta-reflexus. The central command of the muscular metaborreceptors signals that there is a delay of the vagal output flow, in contrast, it stimulates the increase of the HR during the execution of the low intensity exercise (such as the handgrip test) (11).

Another point that stands out is the sedentary lifestyle of people with DS that influences low levels of physical fitness and cardiovascular morbidity (15). Thus, the continuous practice of training programs is an alternative to improve their HRV, since exercise can modify the two arms of the autonomic nervous system in order to improve the sympathetic-vagal balance and to restore the vagal modulation (13).

Goulopoulou et al. (15) stated that the improvement of physical fitness and the reduction of body weight during a training program did not alter the cardiac autonomic control with HRV in people with DS, while the same does not happen with its non-disabled pairs. These results demonstrate that autonomic dysfunction is independent of obesity in individuals with DS. In addition, the individual with DS presented reduced work capacity that was associated with chronotropic incompetence, since when they exercised they exhibited attenuated HR and systolic BP responses (11). Therefore, from this context, it is suggested that individuals with DS present autonomic dysfunction that physical exercise can plays a crucial role in the improvement of the condition.

CONCLUSIONS

The effects of physical training on HRV parameters were analyzed in 7 studies included in the present review that tested 20 interventions of different types of exercise. The exercise protocols observed were quite heterogeneous in intensity, volume, and duration (acute or chronic). However, the results indicated that aerobic and strength training and concurrent training combined exercise can improve parasympathetic modulation, even with attenuated response of heart rate and blood pressure during and after exercise in individuals with DS. However, it was observed that individuals with DS have dysfunction of the ANS. Therefore, it is appropriate to conclude that physical training in an important tool in the improvement of the sympatho-vagal balance in individuals with DS. In addition, HRV is a low-cost, non-invasive technology resource that may be important to assist in the prescription and control of training, whether for DS or non-DS users. We suggest that future studies should evaluate the association between exercise and HRV with adolescents and children with DS.

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