JIDR Journal of Intellectual Disability Research
Published on behalf of mencap and in association with IASSID

Journal of Intellectual Disability Research doi: 10.1111/jir.12894

Training responsiveness of cardiorespiratory fitness and arterial stiffness following moderate-intensity continuous training and high-intensity interval training in adults with intellectual and developmental disabilities

X. Melo,[1,2] R. Pinto,[1,3] V. Angarten,[1] M. Coimbra,[4] D. Correia,[4] M. Roque,[4] J. Reis,[1] V. Santos,[1] B. Fernhall[5] & H. Santa-Clara[1]

1 *Faculdade de Motricidade Humana, Universidade de Lisboa, Centro Interdisciplinar de Estudo da Performance Humana (CIPER), Lisbon, Portugal*

2 *Ginásio Clube Português, Research & Development Department, GCP Lab, Lisbon, Portugal*

3 *Exercise and Cardiovascular Rehabilitation Laboratory, Centro Cardiovascular da Universidade de Lisboa (CCUL), Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*

4 *CERCIOEIRAS - Cooperativa de Educação e Reabilitação dos Cidadãos com Incapacidade, CRL, Barcarena, Portugal*

5 *College of Applied Health Sciences, The University of Illinois at Chicago, Integrative Physiology Laboratory, Chicago, IL, USA*

Abstract

Background Cardiorespiratory fitness (CRF) prompts antiatherogenic adaptations in vascular function and structure. However, there is an extraordinary interindividual variability in response to a standard dose of exercise, wherein a substantial number of adults with intellectual and developmental disabilities (IDD) do not improve CRF. We (1) evaluated the effects of 12-month of moderate-intensity continuous training (MICT) on CRF and arterial stiffness and (2) tested whether an additional 3-month of high-intensity interval training (HIIT) would add to improvements in CRF responsiveness and arterial stiffness.

Methods Fifteen adults with mild-to-moderate IDD (male adults = 9, 30.1 ± 7.5 years old) met 3 days per week for 30 min MICT for 12 months, after which the incidence of CRF responsiveness was calculated (≥5.0% change in absolute peak VO_2). Thereafter, responders and non-responders started HIIT for 3 months with identical daily training load/frequency. Peak VO_2, local and regional indices of arterial stiffness were assessed prior to and after each period.

Results Sixty per cent of the participants were non-responders following MICT, but the incidence dropped to 20% following HIIT ($P = 0.03$). Absolute peak VO_2 values reached significant difference from pre-intervention (+0.38 ± 0.08 L min^{-1}, $P = 0.001$) only when HIIT was added. Lower limb pulse wave velocity (PWV) decreased following MICT (−0.8 ± 1.1 m s^{-1}, $P = 0.049$), whereas central PWV only decreased following HIIT (−0.8 ± 0.9 m s^{-1}, $P = 0.013$).

Conclusions Cardiorespiratory fitness responsiveness and reductions in PWV to a 12-month MICT period in adults with IDD improved following a period of HIIT programme inducing higher metabolic stress.

Correspondence: Dr. Xavier Melo, Ginásio Clube Português, Research & Development Department, GCP Lab, Praça Ginásio Clube Português 1, 1250-111 Lisbon, Portugal. (e-mail: xaviermelo@campus.ul.pt)

Keywords exercise training, individual, intellectual disability, peak oxygen uptake, pulse wave velocity, responders

Introduction

The leading causes of cardiovascular disease (CVD) death, that is, coronary heart disease (43.2%), stroke (16.9%) and hypertension (9.8%), are all arterial diseases (Benjamin *et al.* 2019). Arterial stiffness, a composite measure of both arterial structure and function, is associated with early manifestation CVD (Kim and Kim 2019), as well as kidney disease (O'Rourke and Safar 2005) and impaired cognitive function (Pase *et al.* 2016). Arterial stiffness is also associated with both CVD and total mortality (Laurent *et al.* 2001; Redheuil *et al.* 2014). The exact cause of arterial stiffening is incompletely understood, but structural and functional changes in the arterial wall that make it more stiff (Lyle and Raaz 2017) include alterations in the extracellular matrix and in vascular smooth muscle (Crosas-Molist *et al.* 2015), vascular calcification (Rattazzi *et al.* 2012) and oxidative stress (Zhou *et al.* 2012). The gold standard measure of arterial stiffness is aortic pulse wave velocity (PWV), which measures the velocity of the pressure wave generated by ventricular contraction as blood travels through the aorta. A stiffer aorta transmits the pressure wave at a faster velocity resulting in a higher PWV (Chirinos *et al.* 2019). While a high PWV is associated with increased risk (Laurent *et al.* 2001; Redheuil *et al.* 2014), a decrease in PWV reduces the risk of both total and CVD mortality (Guerin *et al.* 2001; Orlova *et al.* 2010). Thus, reducing arterial stiffness is a desirable therapeutic goal.

People with intellectual and developmental disabilities (IDD) exhibit similar levels of CVD as the general population (Erickson *et al.* 2016; Schroeder *et al.* 2020). However, CVD is often underdiagnosed in IDD (Draheim 2006), even though this population exhibit elevated levels of CVD risk factors. For example, people with IDD have low levels of cardiorespiratory fitness (CRF), high prevalence of obesity (Baynard *et al.* 2008) and hypertension (Sarı *et al.* 2016). Both obesity and hypertension are associated with increased arterial stiffness (Blacher *et al.* 1999; Zebekakis *et al.* 2005), whereas higher CRF is associated with lower arterial stiffness in individuals without disabilities (Gando *et al.* 2010). Consequently, people with IDD may also exhibit higher levels of arterial stiffness, but this has not been thoroughly investigated.

Moderate-intensity continuous exercise training (MICT) and high-intensity interval exercise training (HIIT) can increase CRF (Hottenrott *et al.* 2012) and reduce the risk of many adverse health outcomes, independent of age, sex, ethnicity or the presence of comorbidities (Pelliccia *et al.* 2021). Habitual exercisers have a 20–30% reduction in cardiovascular and all-cause mortality compared with sedentary individuals, in a dose-dependent manner (Lear *et al.* 2017). HIIT may elicit adaptations in CRF indices of similar (Gibala *et al.* 2006) or greater magnitude (Helgerud *et al.* 2007), despite a substantially reduced time commitment to exercise. Regular exercise also prevents vascular stiffening and can reverse ageing-induced vascular stiffening (Tanaka 2019). There is also an inverse association between exercise intensity and arterial stiffness (Ashor *et al.* 2014; Huang *et al.* 2016), suggesting that HIIT could be a more effective modality than MICT, although this is not an universal finding (Way *et al.* 2019). Still, the modulatory influence of regular exercise on selective changes in arterial stiffness in persons with IDD has not yet been addressed.

Studies on MICT (Fernhall 1993; Millar *et al.* 1993; Varela *et al.* 2001; Seron *et al.* 2015) and HIIT (Boer *et al.* 2014; Boer and Moss 2016) in people with IDD show positive effects on CRF and muscle endurance, coupled with significant reductions in blood pressure. However, several studies only focused on people with Down syndrome and not IDD in general. Syndrome-specific issues, such as congenital heart disease (Freeman *et al.* 1998), hypotonia and ligament laxity, impair generalisation of these results to people with IDD in general (Weterings *et al.* 2020). In addition, the findings from these investigations demonstrate an extraordinary interindividual variability in response to a standard dose of exercise (Varela *et al.* 2001; Rimmer *et al.* 2004; Elmahgoub *et al.* 2009; Calders *et al.* 2011; Mendonca *et al.* 2011; Oviedo *et al.* 2014); a substantial number of adults with

IDD did not improve CRF beyond the day-to-day variability in response to regular exercise (Varela *et al.* 2001; Elmahgoub *et al.* 2009; Calders *et al.* 2011). However, recent research showed that high-intensity exercise eliminated exercise training non-responders in individuals without disabilities (Ross *et al.* 2015), suggesting that HIIT may effectively increase CRF in IDD as well. This may have important clinical implications as CRF is independently associated with survival in adults with IDD (Oppewal and Hilgenkamp 2019). Whether the individual CRF response to a given exercise dose is a permanent feature or may be improved by altering the exercise dose in this population is unknown. Therefore, the purpose of this study was twofold: (1) to evaluate the effects of 12 months of MICT on CRF and indices of arterial stiffness and (2) to test whether an additional 3-month exercise training period utilising HIIT would add to improvements in CRF responsiveness and indices of arterial stiffness.

Methodology

Participants

Eighteen adults (male adults = 12) from an education and rehabilitation cooperative for people with IDD (CERCIOEIRAS, Portugal), with mild-to-moderate IDD (interquartile: 40–55) were invited to participate in the present study. During the early months of the study, 2 participants dropped out because they changed their workplace and 1 started manifesting behavioural disorders towards other people, which left the study with 15 participants (male adults = 9, 30.1 ± 7.5 years old). We were unable to classify the cause of aetiology in 11 adults with IDD, the remaining were diagnosed with Down syndrome (n = 2), aphasia (n = 1) and autism (n = 1). Most frequent activities in this centre involved light to moderate physical work and workshops fulfilling 6–7 h day^{-1}. Exclusion criteria included any form of CVD, significant respiratory disorder, metabolic disease, atlanto-axial instability, severe or profound intellectual disability, smoking, and/or use of heart rate (HR) and blood pressure altering or non-steroidal anti-inflammatory medications, inability to comply with guidelines for participation in exercise testing and training (Riebe *et al.* 2018). All participants and parents and/or legal guardians signed an informed consent to participate in the present study. After signing the informed consent, a health screening questionnaire was completed by each participant and/or guardian. The protocol was approved by the Ethics Committee of the Faculty of Human Kinetics – University of Lisbon (03/2017) and conducted in accordance with the Declaration of Helsinki.

Experimental design

Participants met 3 days a week for a supervised (1:2) 30 min moderate-intensity continuous aerobic exercise (50–59% HR reserve according to the Karvonen formula) for 12 months (Riebe *et al.* 2018), consisting of treadmill walking, indoor rowing or cycling at the Occupational Day Centre. To unequivocally overcome suggestions that CRF non-response might ultimately be the result of inadequate exercise stimuli, the incidence of CRF responsiveness was calculated and less than 7 days after the end of the 12-month exercise training period, both responders and non-responders started a second exercise programme for 3 months, with an identical daily training load and frequency, but performed at a different intensity profile, to test whether the incidence of CRF responsiveness would increase (Mann *et al.* 2014). HIIT was elected because it has been shown to further improve CRF compared with moderate continuous exercise (Helgerud *et al.* 2007), despite a substantially reduced time commitment. During this period, participants warmed up for 10 min at 50% HR reserve before walking 4 × 2 min intervals at 75% to 85% of HR reserve. Each interval was separated by 2 min active pauses where participants walked at 50% HR reserve. Average duration of the session was 29 min. All participants wore a HR chest strap (Polar Electro, Kempele, Finland) to continuously monitor exercise intensity and had their blood pressure measured before and immediately after each exercise session. The treadmill speed, incline or resistance of the available ergometers was adjusted continuously to ensure that every training session was carried out at the assigned HR throughout the training period. The Training Impulse (Banister 1991) was used to characterise and balance daily exercise sessions over the two training periods through an integration of time, intensity and volume. This method uses the mean exercise HR zones during each exercise bout and the accumulated time spent on

each zone (minutes × exercise intensity zone) (Foster *et al.* 2001). Sessions were deemed complete when at least 90% of the prescribed exercises were successfully performed. Participants were instructed to maintain their usual diets throughout the study.

Experimental measures

Participants were asked to fast from solids for at least 3 h, refrain from alcohol for 24 h, caffeine for 8 h and vigorous exercise for 48 h prior to the data collection (Van Bortel *et al.* 2012). All evaluations were performed in the morning on 2 days of testing. On the first day of testing, participants rested quietly for at least 15 min in the supine position prior to data collection in the following order: (1) brachial arterial pressure, (2) carotid intima-media thickness (cIMT), (3) stiffness indices by carotid vascular ultrasonography, (4) regional arterial stiffness by applanation tonometry, (5) incremental test to exhaustion and (6) recovery cardiovascular measurements. On the second day of testing, (7) total-body scans were performed by dual-energy x-ray absorptiometry no longer than 7 days apart from Day 1 of testing, and (8) were asked to wear an accelerometer on the right hip, near the iliac crest for seven consecutive days.

Body composition

Participants' height measured to the nearest 0.1 cm with a stadiometer (SECA, Hamburg, Germany) and body weight measured to the nearest 0.1 kg on a weight scale (SECA, Hamburg, Germany) were used to calculate body mass index (BMI). Total body mass was estimated by DEXA (Hologic Explorer-W, fan-beam densitometer, software QDR for windows version 12.4, Hologic, USA). Estimations were compared with sex-specific, age-specific and ethnicity-specific DEXA body composition reference values (Kelly *et al.* 2009).

All scans were submitted to additional analysis by region of interest to assess fat content on trunk and abdominal regions. The trunk region included the neck, chest, abdominal and pelvic areas. Its upper perimeter was the inferior edge of the chin, and the lower boundary intersects the middle of the femoral necks without touching the brim of the pelvis. The leg region was defined as the point of separation from the pelvic region at an angle perpendicular to the femoral neck. The android region was defined as the area between the ribs and the pelvis that is totally enclosed by the trunk region. The upper boundary was 20% of the distance between the iliac crest and the neck and the lower boundary was at the top of the pelvis. The gynoid region included the hips and upper thighs and overlaps both the leg and trunk regions.

Cardiorespiratory fitness

Peak oxygen uptake was determined using an incremental test to exhaustion on a motorised treadmill following a full week of familiarisation with the treadmill and silicon face masks. The protocol started with a 3-min warm up at 5 km h^{-1}, followed by 1 km h^{-1} increments every minute until exhaustion (Fernhall *et al.* 1990). The protocol ended with a 3-min active recovery at 5 km h^{-1} plus 2 min of passive recovery in the sitting position. HR was continuously monitored (Polar Electro Oy, Finland). Data were evaluated in 20-s averages, and peak VO_2 was defined as the highest 20-s value attained in the last minute of effort provided two of the following criteria are met: (1) attaining ~90% of predicted maximal HR [IDD: 210–0.56(age) − 15.5(DS) (Fernhall *et al.* 2001)]; (2) plateau in VO_2 with an increase in workload ($<$2.0 mL kg^{-1} min^{-1}); (3) respiratory exchange ratio ≥ 1.1; and/or (4) subjective judgement by the observer that the participant could no longer continue, even after encouragement. Relative values were compared with CRF classifications by age and sex (Pescatello and American College of Sports Medicine 2014). Chronotropic response to exercise was calculated as: HR reserve/(predicted maximal HR − HR at rest) × 100 (Azarbal *et al.* 2004). Chronotropic incompetence was defined as a failure to reach 80% of chronotropic response (Brubaker and Kitzman 2011). HR recovery was calculated as the difference in HR after 1 min of recovery in relation to peak HR. An abnormal HR recovery was defined as a decline in HR inferior to 12 bpm (Cole *et al.* 1999).

Defining cardiorespiratory fitness responder and non-responder

Cardiorespiratory responsiveness (responder) was defined as ≥5.0% change in peak VO_2 (L min^{-1}) from baseline (Pandey *et al.* 2015; Hetherington-Rauth *et al.* 2020). This cut-off point was chosen based on the reported technical error of measurement (TEM) for VO_2 using a Cosmed K4 portable gas analyser (Rome, Italy) (Duffield *et al.* 2004). Any value greater

than the TEM is more likely to be a true biological response to exercise training rather than a result of the typical error variation present in the measurement technique and the day-to-day biological variability present in the individual (Harris and Smith 2009).

Intima-media thickness by carotid vascular ultrasonography

Carotid intima-media thickness was defined as the distance between the leading edge of the lumen–intima interface to the leading edge of the media–adventitia interface of the far wall of the right carotid artery using an ultrasound scanner equipped with a linear 13-MHz probe (MyLab One, Esaote, Italy) and implemented with a previously validated radiofrequency-based tracking of arterial wall that allows a real-time determination of common carotid far-wall thickness (QIMT®) with high spatial and temporal resolution (Hoeks *et al.* 1997). cIMT was automatically measured within a segment of the carotid artery about 1 cm before the flow divider, where the operator placed the region of interest (Touboul *et al.* 2007). Values obtained were compared with estimated age-specific and sex-specific percentiles of cIMT in populations with different cardiovascular risk profiles (Engelen *et al.* 2013).

Local arterial stiffness indices by carotid vascular ultrasonography

Carotid artery stiffness measurement was conducted with the participants in the supine position following a 15-min rest period. We used an ultrasound scanner equipped with a linear 13-MHz probe (MyLab One, Esaote, Italy) with Quality Arterial Stiffness technology, based on radio frequency signal in a common carotid artery segment ~1 cm before the bifurcation. The carotid pressure waveform was calibrated to diastolic brachial (DBP) and mean arterial pressure [MAP = DBP + 1/3 (SBP − DBP)] by iteratively changing the wall rigidity coefficient (Laurent *et al.* 2006). This allows the calculation of carotid stiffness indices: PWV, distensibility coefficient, compliance coefficient and stiffness index β.

Regional arterial stiffness indices and carotid blood pressure by applanation tonometry

Pulse wave velocity was measured by applanation tonometry immediately after ultrasound imaging. A single operator located the carotid, femoral, radial and distal posterior tibial arteries and marked the point for capturing the corresponding pressure curves with two specific pressure sensitive transducers. The distance between the carotid and femoral, radial and distal posterial tibial arteries was measured directly and entered the Complior Analyse software (ALAM Medical, Paris, France). Brachial blood pressure was measured and entered the software, and then signal acquisition was launched. Values obtained from the carotid to femoral artery, carotid to radial artery and carotid to distal posterior tibial artery were taken as indices of central/aortic, upper and lower limb arterial stiffness, respectively. The quality of the PWV records was immediately evaluated by a second observer with considerable experience in this methodology. Whenever a continuous decrease before the sharp systolic upstroke was not clearly seen or tolerance was above 5 ms, a second measure was taken (Van Bortel *et al.* 2012). Aortic PWV values were compared with established age-specific and blood-pressure-specific reference values for PWV in a European population (Reference Values for Arterial Stiffness' Collaboration, 2010). Representing a model of impedance mismatch, we considered the stiffness of the aortic arterial segment relative to the stiffness of the brachial arterial segment (Schultz *et al.* 2015; Fortier *et al.* 2017).

Carotid systolic blood pressure (SBP) from the Complior Analyser was obtained from carotid traces acquired during the PWV assessment. The waveforms were averaged, and the mean values were extracted from 15 s window of acquisition. The carotid waveforms were calibrated to brachial MAP, measured immediately before the acquisition. Pulse pressure was calculated as SBP-DBP.

Objective measured physical activity

Physical activity patterns were assessed by accelerometry (ActiGraph, GT1M, Fort Walton Beach, FL) at pre-intervention, following MICT and HIIT. All participants were asked to wear the accelerometer on the right hip, near the iliac crest for seven consecutive days, and were instructed to remove the devices for water-based activities and sleeping. The devices were activated on the morning of the first day and data were recorded in 15-s epochs and reintegrated into 60-s epochs to allow comparison with other studies. Periods of at least 60 consecutive minutes of

zero activity intensity counts were considered as non-wear time. A valid day was defined as having ≥600 min of monitor wear, and the study included the results from participants with at least three valid days (including one weekend day).

The amount of activity assessed by accelerometery was expressed in minutes per day spent in different intensities. The cut-off counts per minute (cpm) used to define the intensity of physical activity and, therefore, to quantify the mean time at each different intensity were the following: low-intensity physical activity: 100–2019 cpm; and moderate-to-vigorous physical activity: ≥2020 cpm (Troiano *et al.* 2008). The device activation and data download were performed using the ActiLife Lifestyle software (v.3.2; Fort Walton Beach, FL). The MAHUffe v.1.9.0.3 was used for processing (available from www.mrc-epid.cam.ac.uk) from the original downloaded files (in DAT format). Compliance with physical activity recommendations was assessed according to the World Health Organisation (150 min week^{-1} of moderate-to-vigorous physical activity, defined as ≥21.4 min day^{-1}) (World Health Organization 2010).

Statistical analysis

Variables were examined for normality, skewness and kurtosis by performing the Shapiro–Wilk test of normality, visual inspection of normal quantile and histogram plots, and kurtosis and skewness summary statistics. Variables with a skewed distribution were log transformed for parametric statistical analyses. Changes over time were assessed by one-way repeated measures analysis of variance. Possible interactions with sex and age were tested a priori. Proportions were compared using χ^2 test. Statistical significance level was set at $P < 0.05$ for all tests. The statistical analyses were computed and analysed using the SPSS Statistics 26.0 (SPSS Inc., Chicago, IL, USA).

Results

Characterisation of the exercise training programmes

The 15 participants who took part in this study attended 132 (79.9 ± 10.0%) of the 165 training sessions offered (Table 1). At pre-intervention, 14 (93%) of the participants were physically active and those levels tracked similarly following MICT and HIIT ($P > 0.05$). Average HR and percent HR reserve during HIIT sessions was significantly higher than in MICT sessions, although average Training Impulse and duration of the session did not differ between exercise regimes.

Body composition

Indices of body composition following MICT and HIIT are summarised in Table 2. At pre-intervention, 12 (80%) of the participants were overweight (40%) or obese (40%) according to BMI, and this prevalence tracked well until the end of the study period ($P = 0.657$). Still, only four (27%) of the participants deviated from sex-specific, age-specific and ethnicity-specific DEXA body fat and lean body mass 'healthy targets', and by the end of the exercise intervention this prevalence was reduced to 2 (13%) and 3 (20%), respectively, although it did not reach statistical significance ($P > 0.05$). No significant time effects were observed in whole body or regional indices of body composition except for lean body mass that decreased following MICT intervention ($P = 0.026$). Significant interaction effects with sex were observed, suggesting that whole body fat (+1.4 ± 1.0 kg, $P = 0.008$) and trunk fat (+1.1 ± 0.7 kg, $P = 0.02$) increased in male adults throughout the study period.

Cardiovascular indices

Cardiovascular indices derived from the incremental protocol to exhaustion following MICT and HIIT are summarised in Table 3. At pre-intervention, 12 (80%) of the participants were classified as unfit. This prevalence was reduced to 11 (73%) following MICT, and to 10 (66%) following HIIT, but without reaching statistical significance ($P > 0.05$). At pre-intervention, abnormal HR Recovery and chronotropic incompetence was observed in two (15%) and four (27%) of the participants, respectively, and tracked similarly throughout the study period ($P > 0.05$). No significant interactions were observed with age and sex. Significant main effects of time were observed in absolute ($P < 0.001$, = 0.460) and relative peak VO_2 ($P < 0.001$, = 0.456 to = 0.484). Absolute values of peak VO_2 did not increase significantly following MICT (+0.12 ± 0.04 L min^{-1}, $P = 0.447$). Following the HIIT regime, mean values reached significant differences from pre-intervention values

Table 1 Characterisation of the moderate-intensity continuous training and high-intensity interval training

		Pre-intervention	MICT	HIIT	*P*
	Months	**0**	**12**	**15**	
MVPA	min	270.2 (150.5)	278.8 (158.7)	276.2 (146.6)	0.970
HR	bpm	—	134.7 (6.2)	141.7 (6.6)	<0.001
HR reserve	%	—	63.0 (4.1)	69.8 (1.2)	<0.001
TRIMP	—	—	47.3 (9.2)	42.3 (16.3)	0.165
Duration (session)	min	—	28.7 (2.3)	28.8 (2.5)	0.707
Adherence	%	—	79.9 (10.0)	79.6 (12.0)	0.851

Data are mean (SD). *P* is *P* value.

HIIT, high-intensity interval training; HR, heart rate; MICT, moderate-intensity continuous training; MVPA, moderate-vigorous physical activity; TRIMP, training impulse.

(+0.38 ± 0.08 L min^{-1}, $P = 0.001$) and MICT (+0.26 ± 0.03 L min^{-1}, $P = 0.023$) (Fig. 1). The results remained significant when peak VO_2 was indexed to body weight (+4.7 ± 3.6 mL kg^{-1} min^{-1}, $P = 0.001$), lean body mass (+8.9 ± 6.7 mL kg^{-1} min^{-1}, $P = 0.001$) or converted to METs (+1.5 ± 0.9, $P < 0.001$). Accordingly, nine (60%) of the participants were non-responders by the end of the MICT period, while the incidence of non-responders decreased to three (20%) by the end of the HIIT period ($P = 0.03$). No significant effects of time were observed in cardiovascular indices during recovery. Peak respiratory exchange ratio values following MICT (−0.16 ± 0.11, $P < 0.001$) and HIIT (−0.16 ± 0.09, $P < 0.001$) were significantly lower than those attained during peak effort at pre-intervention testing. Still, values were on average ≥ 1.1, and together with the attainment of an average percent HR max ≥ 93%, certifies that a maximal effort was reached in all cardiopulmonary incremental tests to exhaustion performed.

Vascular stiffness and structure

Indices of carotid structure, stiffness and hemodynamics at rest following MICT and HIIT are summarised in Table 4. Elevated blood pressures were recorded in five (33.3%) of the participants at

Table 2 Body composition indices of the participants following moderate-intensity continuous training and high-intensity interval training

		Pre-intervention	MICT	HIIT	*P*/*η*
	Months	**0**	**12**	**15**	
Whole body					
Body mass index	kg m^{-2}	30.4 (7.6)	30.0 (7.3)	30.0 (7.7)	0.161/0.131
Body fat	kg	28.5 (12.7)	28.8 (11.7)	28.7 (12.1)	0.885/0.009
Body fat	%	35.40 (9.2)	36.63 (8.0)	35.86 (7.9)	0.126/0.161
Lean body mass	kg	50.0 (10.6)	48.5 (10.6)*	49.5 (10.8)	0.008/0.312
Regional					
Trunk fat	kg	13.99 (6.3)	14.20 (5.6)	14.30 (5.7)	0.673/0.022
Android fat	kg	2.5 (1.2)	2.5 (1.1)	2.6 (1.2)	0.486/0.046
Gynoid fat	kg	5.0 (2.4)	5.1 (2.1)	5.1 (2.3)	0.897/0.008

*Indicates significant differences from pre-intervention.

Data are mean (SD). *P* and *η* are *P* value and partial eta squared for the effect of time on selected variable, respectively.

HIIT, high-intensity interval training; MICT, moderate-intensity continuous training.

Table 3 Cardiovascular indices following moderate-intensity continuous training and high-intensity interval training

		Pre-intervention	MICT	HIIT	*P*/*η*
	Months	**0**	**12**	**15**	
Rest					
Heart rate	bpm	72.6 (12.6)	75.3 (11.6)	69.4 (12.4)	0.193/0.124
Peak effort					
METS	—	8.2 (2.5)	8.7 (2.2)	9.7 (2.9)*†	<0.001/0.520
Heart rate	bpm	171.1 (9.1)	172.1 (12.9)	169.0 (10.2)	0.570/0.042
RER	—	1.3 (0.1)	1.1 (0.1)*	1.1 (0.1)*	<0.001/0.641
Predicted heart rate	%	93.0 (7.5)	93.7 (7.4)	93.1 (7.2)	0.889/0.008
Recovery					
Oxygen uptake 1′	L min^{-1}	0.7 (0.4)	0.7 (0.4)	0.7 (0.5)	0.841/0.008
Oxygen uptake indexed to body weight 1′	mL kg^{-1} min^{-1}	8.7 (4.7)	8.8 (6.2)	9.3 (6.8)	0.796/0.017
Oxygen uptake indexed to lean body mass 1′	mL kg^{-1} min^{-1}	13.1 (5.6)	13.3 (8.4)	14.0 (9.3)	0.881/0.010
Heart rate 1′	bpm	24.8 (19.3)	16.5 (17.4)	22.7 (15.2)	0.268/0.104

*Indicates significant differences from pre-intervention.

†Indicates significant differences from MICT.

Data are mean (SD). *P* and *η* are *P* value and partial eta squared for the effect of time on selected variable, respectively.

HIIT, high-intensity interval training; LBM, lean body mass; MICT, moderate-intensity continuous training; RER, respiratory exchange ratio.

pre-intervention, decreasing to two (13.3%) following MICT and HIIT, but without reaching statistical significance ($P = 0.206$). Carotid IMT was above the 75th age-specific and sex-specific percentile in six (40%) of the participants throughout the study period. As for central PWV, at pre-intervention, two (13%) of the participants were above +2SD from age-specific and blood-pressure-specific mean reference values, and the incidence kept dropping following MICT (1; 6.7%) and HIIT (0; 0%). No significant interactions were observed with age and sex. Significant main effects of time were observed in lower limb PWV ($P = 0.011$, = 0.364) and central PWV ($P = 0.049$, = 0.207). Lower limb PWV decreased following MICT (-0.8 ± 1.1 m s^{-1}, $P = 0.049$) and the reduction tracked similarly until the end of the study period (-1.1 ± 1.5 m s^{-1}, $P = 0.04$) (Fig. 2). As for central PWV, it was only when the HIIT regime was added that average values reached significant difference from pre-intervention

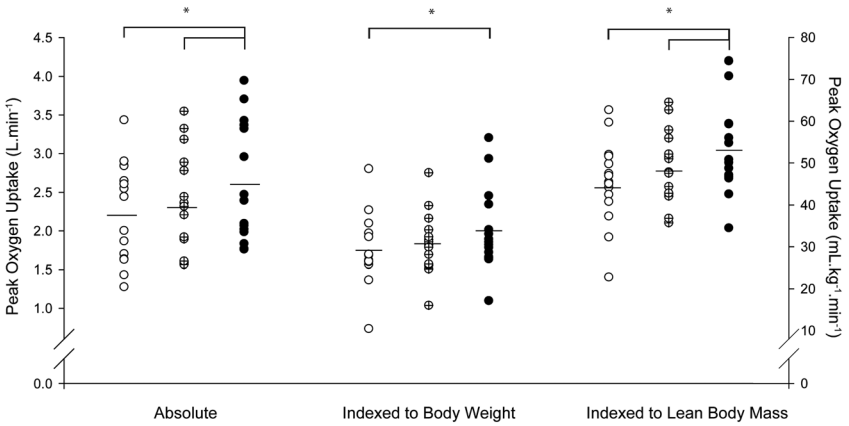

Figure 1. Absolute and relative values of peak oxygen uptake before and after a 12-month supervised moderate-intensity continuous aerobic training, and a subsequent 3-month supervised high-intensity interval training. Data are individual values. Horizontal lines represent mean values at each time point '*' indicates significant differences ($P < 0.05$). '*O*' indicates values at pre-intervention (0 months), '⊕' indicates values following moderate-intensity continuous aerobic training (12 months), and '●' indicates values following high-intensity interval training (15 months).

Table 4 Indices of arterial stiffness, structure and haemodynamics following moderate-intensity continuous training and high-intensity interval training

		Pre-intervention	MICT	HIIT	*P*/*η*
	Months	**0**	**12**	**15**	
Brachial					
SBP	mmHg	123.2 (17.2)	119.8 (12.5)	114.8 (14.3)	0.102/0.317
DBP	mmHg	78.2 (12.2)	76.9 (7.4)	67.7 (8.5)*†	0.005/0.418
PP	mmHg	44.9 (10.3)	42.9 (11.3)	47.1 (12.2)	0.159/0.132
MAP	mmHg	94.50 (13.4)	91.14 (7.7)	83.29 (9.2)*†	0.014/0.355
Carotid					
SBP	mmHg	114.4 (23.2)	114.6 (12.8)	106.1 (16.6)	0.241/0.105
Carotid PWV	ms^{-1}	5.1 (0.9)	5.3 (1.0)	5.1 (0.9)	0.235/0.114
Distensibility coefficient	(kPa^{-1})	0.041 (0.017)	0.036 (0.016)	0.039 (0.013)	0.282/0.099
Compliance coefficient	$(mm^2\ kPa^{-1})$	1.4 (.4)	1.3 (.5)	1.3 (.4)	0.791/0.010
Beta stiffness	—	5.6 (1.6)	6.4 (1.9)	6.0 (1.3)	0.050/0.221
Diameter	mm	6.7 (0.7)	6.9 (0.7)	6.7 (0.7)	0.085/0.185
Carotid IMT	mm	0.48 (0.18)	0.50 (0.10)	0.51 (0.09)	0.706/0.025
Stiffness mismatch					
Aortic-brachial PWV ratio	—	0.91 (0.16)	0.83 (0.22)	0.82 (0.24)	0.196/0.138
Brachial-aortic PWV difference	ms^{-1}	1.0 (1.7)	1.7 (2.3)	2.0 (2.4)	0.190/0.140

*Indicates significant differences from pre-intervention.

†Indicates significant differences from MICT.

Data are mean (SD). *P* and *η* are *P* value and partial eta squared for the effect of time on selected variable, respectively.

DBP, diastolic blood pressure; HIIT, high-intensity interval training; IMT, intima-media thickness; MAP, mean arterial pressure; MICT, moderate-intensity continuous training; PP, pulse pressure; PWV, pulse wave velocity; SBP, systolic blood pressure.

(−0.8 ± 0.9 m s^{-1}, $P = 0.013$). Similarly, brachial DBP (−10.5 ± 13.1, $P = 0.031$) and MAP (−11.2 ± 11.7, $P = 0.049$) decreased from pre-intervention values following HIIT, but not MICT. However, changes in central PWV were not associated with changes in MAP ($r = 0.006$, $P = 0.983$) or DBP ($r = 0.041$, $P = 0.890$), nor with respective pre-intervention values (MAP: $r = 0.019$,

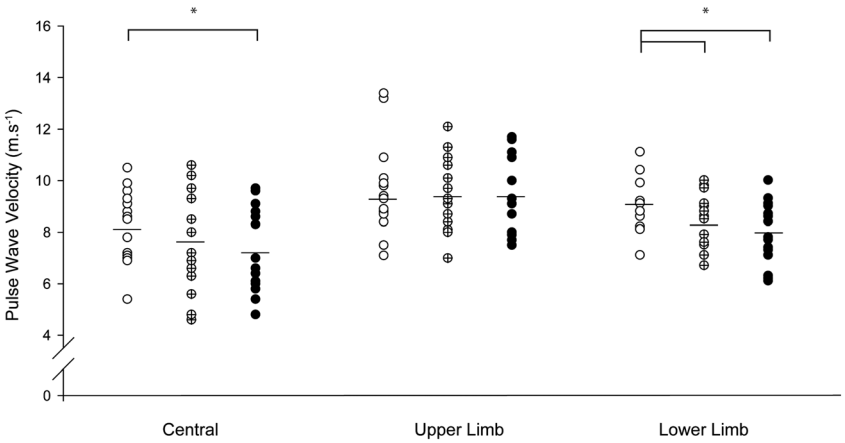

Figure 2. Regional pulse wave velocity before and after a 12-month supervised moderate-intensity continuous aerobic training, and a subsequent 3-month supervised high-intensity interval training. Data are individual values. Horizontal lines represent mean values at each time point '*' indicates significant differences ($P < 0.05$). '*O*' indicates values at pre-intervention (0 months), '⊕' indicates values following moderate-intensity continuous aerobic training (12 months), and '●' indicates values following high-intensity interval training (15 months).

$P = 0.948$; DBP: $r = 0.115$, $P = 0.696$), and the same was true for lower limb PWV ($P > 0.05$). Changes in central and peripheral PWV were also not associated with changes in absolute or relative peak VO_2 nor with respective pre-intervention values ($P > 0.05$). No significant effects of time were observed in carotid indices of arterial stiffness and haemodynamics and in stiffness mismatch.

Discussion

This is the first study to evaluate the effects of a 12-month MICT on indices of arterial stiffness and CRF in adults with IDD and to test whether improvements in indices of arterial stiffness and CRF responsiveness could be enhanced by adding 3 months of HIIT. We found that HIIT improved CRF responsiveness and reductions in central PWV in adults with IDD, suggesting the presence of different regulatory mechanisms and time courses based on type of exercise employed. Still, both MICT and HIIT led to similar decreases in lower limb PWV.

Effects of exercise training in vascular stiffness in people with intellectual and developmental disabilities

There is limited evidence on the effect of exercise training on arterial stiffness in adults with IDD. In a study enrolling 24 men with IDD, randomly assigned to 12 weeks of aerobic exercise, half-bath or control treatment groups, the author found that PWV, as measured by vessel compliance (PWV 3.0-K_M TEC, Korea), was significantly reduced in both the exercise and half-bath groups from that in the control group (Kim 2017). Results from randomised controlled trials suggest a generalised effect of exercise training (≥4 weeks) on PWV in adults without IDD (Ashor *et al.* 2014; Huang *et al.* 2016; Zhang *et al.* 2018), with a larger effect size related to longer duration of training and in those with lower a priori levels of arterial stiffness (Ashor *et al.* 2014). Our findings add to the existing knowledge by comparing aerobic training performed at different intensity levels, on vascular stiffness and structure in adults with IDD. Compared with MICT, HIIT was more efficacious for decreasing central PWV in adults with IDD, and these adaptations were not influenced by changes in blood pressure, body composition or CRF. Only recently, a systematic review with meta-analyses compared the effect of HIIT versus MICT on central arterial stiffness (Way *et al.* 2019). Although earlier reviews (Ashor *et al.* 2014; Huang *et al.* 2016) found an inverse relationship between exercise intensity and reductions in arterial stiffness, suggesting that HIIT could be a more effective modality than MICT, the results from this meta-analyses of 10 pooled studies (≥4 weeks) found no significant difference between HIIT and MICT for changes in PWV (Way *et al.* 2019). Given that every 1 m s^{-1} increase in central PWV leads to a 7% increase of the hazard for cardiovascular events (Vlachopoulos *et al.* 2014), and there is an increase in PWV by 7.5–12.8% per decade in 30- to 59-year-old adults without hypertension (Reference Values for Arterial Stiffness' Collaboration 2010), our finding of a decrease in central PWV by 0.8 m s^{-1} is likely to have important clinical implications in the 10-year risk classification of adults with IDD. In the absence of associations between changes in central and peripheral blood pressure or peak VO_2 with changes in central PWV, the mechanisms by which HIIT significantly reduced central PWV in our study more than MICT could be associated with the intensity-dependent relationship between exercise intensity and hyperemia (Green *et al.* 2017). Alternatively, it could be related to the induced reactive oxygen species-dependent fragmentation of the ryanodine receptor, which is implicated in the post-exercise increase in intracellular Ca2+ concentration (MacInnis and Gibala 2017), a regulator of the stiffness of vascular smooth muscle cells by a mechanism involving myosin contractile apparatus (Zhu *et al.* 2019). It is also possible that HIIT required longer time for PWV to recover from repeated HIIT bouts, thereby providing a different representation of the cumulative effect of exercise (Ramírez-Vélez *et al.* 2019). Larger reductions in peripheral PWV compared with central PWV have also been reported (Ashor *et al.* 2014). Although we did not find central and peripheral PWV following MICT to be significantly different from that following HIIT, exercise-derived adaptations in lower limb PWV were observed immediately following MICT. Possibly, more muscular, stiffer peripheral arteries allow for larger and faster adaptations of arterial wall properties in response to exercise training, compared with central, more elastic arteries (Green *et al.* 2017).

Cardiorespiratory fitness response to exercise training

Several studies demonstrated the effectiveness of HIIT on CRF and HR response in apparently healthy participants (Slettaløkken and Rønnestad 2014), those with cardiometabolic (Way *et al.* 2020), and CVD (Koufaki *et al.* 2014), and even in people with IDD (Boer *et al.* 2014). HIIT has been shown to increase stroke volume by augmenting cardiac contractibility (Helgerud *et al.* 2007) and skeletal muscle diffusive capacity (Slørdahl *et al.* 2005). These adaptations translate to clinical relevance as, in our study, HIIT increased CRF by an average of 4.7 mL kg^{-1} min^{-1}, which is suggested to be equivalent to a reduction ≥15% in risk for all-cause mortality and ≥19% in cardiovascular mortality (Lee *et al.* 2011) in people without IDD, but also to have clinical implications in those with IDD, as CRF has been found to be independently associated with survival (Oppewal and Hilgenkamp 2019), and to be the cause for the high incidence of limitations in daily functioning (Oppewal *et al.* 2014, 2015). In addition, a 12.2- to 12.6-mmHg increase in MAP in adults 35–64 years of age is associated with 1.71 and 1.66 adjusted hazard ratio for all stroke incidence in men and women, respectively (Miura *et al.* 2004). Thus, the 11.2-mmHg decrease in MAP following HIIT is also of clinical interest as the stroke risk among adults with IDD is similar to that of the general population (Erickson *et al.* 2016). Overall, our findings fundamentally challenge the notion of CRF non-response to exercise training in adults with IDD, as the incidence of CRF non-response, as determined by peak VO_2, was almost abolished following a successive 12-week HIIT programme. This suggest that CRF is more a function of exercise activity intensity and not volume (Nokes 2009) and that exercise intensity, even of a shorter duration, is an effective strategy to improve CRF in people with IDD as in those without IDD (Milanović *et al.* 2015). This is useful as there are several risk factors to improve simultaneously in people with IDD, and this evidence highlights HIIT as part of lifestyle modification strategy with low rates of CRF non-response and high rates of improvements in blood pressure and arterial stiffness, regardless of improvements in body composition and arterial structure. Still, future studies should examine the long-term feasibility and efficacy of HIIT in adults with IDD.

Limitations

This study is not without limitations. We are unable to determine causality in our interpretation of the observed exercise-induced improvements in indices of arterial stiffness and CRF because we lack a true control group that did not perform HIIT. We used a convenience sample that improved exercise adherence at the expense of representativeness. The sample size was small but believed acceptable given the population of interest. A strict randomisation of the participants following MICT was not possible, not only because of the limited number of participants, but also in order keep the participants motivated, to respect their will and at the same time, to respect the schedule of the institution. Because of these and other limitations (e.g., single site design), it is important to not over-interpret the results of this study, as epidemiological evidence suggests that the largest impact on vascular risk occurs from the adoption of lower volumes and intensities of physical activity (Green *et al.* 2017), and concerns about the potential health risks of HIIT have not yet been ruled out (Keteyian 2012). Other limitations of this study include the lack of control over diet.

Conclusion

Individual CRF responsiveness and reductions in PWV to a 12-month MICT period in adults with IDD were greater following a shorter period of HIIT. These data suggest that HIIT programmes could be very effective for producing favourable health outcomes in persons with IDD.

Acknowledgements

We would like to acknowledge the contributions of Rita Gonçalves and Teresa Gomes to this study and to praise the dedication of CERCIOEIRAS and all the participants throughout the study.

Author contributions

All authors have made substantial contributions to all the following: (1) the conception and design of the study, or acquisition of data, or analysis and

interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be submitted.

Source of funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Conflict of interest

The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. The authors report no conflict of interest. All authors had full access and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Accepted 6 October 2021