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Comparison of mechanical ventilatory constraints between continuous and intermittent exercises in healthy prepubescent children.

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Keywords:	children, exercise modality, ventilatory response, flow/volume loop



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Title Page

Title: Comparison of mechanical ventilatory constraints between continuous and intermittent exercises in healthy prepubescent children.

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Running title: Mechanical ventilatory constraints in children

1
2
3 1 **Abstract**
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5 2 **Background:** The aim of this study was to evaluate the occurrence and severity of mechanical
6
7 ventilatory constraints in healthy prepubescent children during continuous and intermittent exercise.
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10 4 **Methods:** Twelve prepubescent children (7 – 11 years old) performed 7 exercises on a treadmill: one
11
12 graded test for the determination of maximal aerobic speed (MAS), three continuous exercises (CE)
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14 at 60, 70 and 80% of MAS and three intermittent exercises (IE), alternating 15s of exercise with 15s of
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16 passive recovery, at 90, 100 and 110% of MAS. During each CE and IE, tidal flow/volume loops were
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18 plotted within a maximal flow/volume loop (MFVL) measured at rest before each exercise. Expiratory
19
20 flow limitation (expFL expressed in %Vt) was defined as the part of exercise tidal volume (Vt) meeting
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22 the boundary of MFVL. Breathing strategy was estimated by measuring inspiratory capacity relative
23
24 to forced vital capacity and tidal volume relative to inspiratory capacity. Other breathing pattern
25
26 parameters (ventilation \dot{V}_E , Vt, respiratory frequency f) were continuously recorded during exercise.
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31 13 **Results:** An "intensity" effect was found for \dot{V}_E during CE ($p < 0.001$) but not during IE ($p = 0.08$). The
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33 increase in \dot{V}_E was predominantly assumed by an increase in f for both exercise modalities. During
34
35 each exercise, several children heterogeneously experienced expFL ranging between 10 – 90%Vt. For
36
37 all exercises, Vt was predominantly regulated by an increase in Vt/IC with no change in IC/FVC from
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39 rest to exercise. Finally, no significant "modality" effect was found for mechanical ventilatory
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41 constraint parameters (expFL, VT/IC and IV/FVC).
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45 19 **Discussion:** We could conclude that neither of the modalities studied induced more mechanical
46
47 ventilatory constraints than the other, but that exercise intensities specific to each modality might be
48
49 greater sources of exacerbation for mechanical ventilatory constraints.
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53 22
54 23 **Keywords:** children, exercise modality, ventilatory response, flow/volume loop
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1 Introduction

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8 In the literature, it has been reported that children show specific ventilatory adaptations in
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10 comparison with adults during exercise. In fact, children present a phenomenon of hyperventilation
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12 for a similar level of relative intensity in comparison with adults. This phenomenon of
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14 hyperventilation in children is characterized by a higher respiratory equivalent in oxygen ($\dot{V}E / \dot{V}O_2$)
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16 in children than in adults ¹⁻⁴ and could result from a specific breathing pattern. The latter is
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18 characterized by rapid and shallow breathing in children, defined by higher values of respiratory
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20 frequency and lower values of tidal volume than in adults ⁵.
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27 Moreover, as already shown in adults during incremental exercise, mechanical ventilatory constraints
28
29 were also highlighted in children during exercise ⁶⁻¹². Such constraints represented the balance
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31 between ventilatory demand and ventilatory capacity ⁶ and could easily be identified by estimating
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33 breathing reserve (BR) ⁶. However, BR provides no information on breathing pattern, or on the
34
35 source and type of ventilatory constraints. This type of information could be obtained by using the
36
37 exercise flow/volume loops method, consisting in plotting tidal flow/volume loops within maximal
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39 flow/volume loops during exercise ⁶. By using this method, some studies have assessed mechanical
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41 ventilatory constraints in children during incremental exercise and reported several cases of
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43 expiratory flow limitation during high intensities of the incremental exercise ^{13,14}. Thus, Nourry et al
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45 reported an "intensity" effect for mechanical ventilatory constraint occurrence and severity during a
46
47 maximal graded test in trained or untrained prepubescent children ^{13,14}. From these results, we have
48
49 hypothesized that intermittent exercise could induce higher mechanical ventilatory constraints than
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51 continuous exercise, as the exercise intensities prescribed for intermittent exercises are higher than
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53 those prescribed for continuous exercises. The answers to this question could enlighten us on
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55 specific ventilatory adaptations in children during two exercise modalities frequently encountered
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3 1 during everyday life, contrary to current data from the literature, which is only based on incremental
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5 2 exercise.
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10 4 The aim of this study was 1) to evaluate and compare breathing pattern and tidal flow/volume loops
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12 5 between continuous and intermittent exercises in healthy prepubescent children, so as to determine
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14 6 if both exercise modalities could induce mechanical ventilatory constraints and 2) to determine the
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16 7 effects of the exercise modality on the severity of potential ventilatory constraints, in order to
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18 8 determine if one exercise modality was more restrictive than the other on the children's ventilatory
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20 9 system.
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3 1 **Methods**
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8 3 **Population**
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10 4 Twelve 7 – 11 year old healthy prepubescent children volunteered to participate in this study, which
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12 5 had previously received approval from the local ethics committee. Parents and children were
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14 6 informed as to the modalities of the study and then gave their written, informed consent prior to any
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16 7 involvement in it. All the children were free of respiratory or cardiac diseases and of orthopedic
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18 8 counter indications for physical exercise, performed less than 3h/week of extra academic physical
19
20 9 activity and their sum of pubertal stages was lower than 3. Sexual maturity was evaluated from
21
22 10 pubertal stages, according to Tanner's method: indices of breast, pubic hair and genital
23
24 11 development¹⁵. The same physician made all the observations for all the children.
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31 13 **Study design**
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33 14 All the children came to the laboratory three times within a one-month period, with at least 48 hours
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35 15 between two evaluation days. At the beginning of each visit, a resting ECG and a clinical examination
36
37 16 were performed. During the first visit, spirometry and sexual maturity were evaluated, followed by a
38
39 17 period of familiarization and realization of a maximal graded test on a treadmill. Measurement of
40
41 18 pulmonary gas exchanges allowed the determination of peak oxygen uptake ($\dot{V}O_{2\text{peak}}$) and maximal
42
43 19 aerobic speed (MAS). During the last two visits, the children performed three continuous (continuous
44
45 20 visit) and three intermittent (intermittent visit) exercises on the treadmill in a random order. Prior to
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47 21 the exercises, spirometry was performed and, subsequent to them, measurements of pulmonary gas
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49 22 exchanges, heart rate and exercise flow/volume curves were carried out.
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57 24 **Spirometry**
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3 1 At each visit, the children underwent spirometry before each of the exercises performed (Vmax
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5 2 Encore, Sensormedics, Viasys Healthcare, USA). Each child was seated on a chair and fitted with a
6
7 3 noseclip. All the lung tests were carried out by the same physician respecting American Thoracic
8
9 4 Society recommendations¹⁶. For each child, three measurements of maximal flow/volume loops
10
11 5 (MFVL) were carried out, allowing the determination of forced vital capacity (FVC) and forced
12
13 6 expiratory volume in 1 second (FEV₁). Among the registered measurements, the MFVL with the
14
15 7 greatest combination of FVC and FEV₁ was retained.
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22 9 **Cardio-respiratory parameters**

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24 10 At each visit and during all exercise tests, the children wore a mouthpiece connected to a breath-by-
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26 11 breath gas analyzer (V max Encore laboratory system, Sensormedics, Viasys Healthcare, USA),
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28 12 allowing the measurement of oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), ventilation
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30 13 ($\dot{V}E$), tidal volume (Vt) and respiratory frequency (f). In order to ensure accurate measurements, O₂
31
32 14 and CO₂ analyzers were calibrated before each exercise test, using ambient air and two gases of
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34 15 known O₂ concentration (16% and 26%) and CO₂ concentration (4% and 0%). The calibration of the
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36 16 pneumotachograph was performed using a 3-liter syringe following the manufacturer's
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38 17 recommended procedures.
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43 18 Heart rate (HR) was continuously monitored with a heart rate monitor (Polar S810, Polar Electro Oy,
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45 19 Kempele, Finland). The data acquisition frequency for HR was set at 5 sec.

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47 20 Borg's CR-10 scale¹⁷ (ranging from 0 to 10) was used during all the exercises in order to evaluate
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49 21 dyspnea. This scale was explained to the children at the beginning of each visit and was shown to
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51 22 them at the end of each exercise.
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56 24 **Maximal graded test**

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3 1 A period of familiarization on the treadmill was proposed for all the children, consisting in explaining
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5 2 the security procedures and letting them walk and run on it. After explaining the exercise to the
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7 3 children, the test began with a resting period of three minutes in a standing position on the treadmill.
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9 4 Subsequently, a warm-up period of 3 minutes at $3\text{km}\cdot\text{h}^{-1}$ was performed. The exercise began with
10
11 5 one minute at $4\text{ km}\cdot\text{h}^{-1}$, then the speed was increased by $0.5\text{ km}\cdot\text{h}^{-1}$ every minute. During the whole
12
13 6 exercise, pulmonary gas exchanges and heart rate were continuously recorded and the values were
14
15 7 averaged every 30 seconds. The exercise ended when the children were no longer able to maintain
16
17 8 the imposed running speed. It was judged that they had performed a maximal exercise when 3 or
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19 9 more of the following criteria were obtained: visible exhaustion (excessive hyperpnea, facial flushing,
20
21 10 sweating, discomfort)¹⁸, maximal heart rate $>90\%$ of predicted maximal heart rate $(208-0.7 \times \text{age})$ ¹⁹, a
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23 11 plateau in $\dot{V}\text{O}_2$ despite increasing running speed or a final respiratory exchange ratio (RER) higher
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25 12 than 1.0²⁰. The maximal aerobic speed (MAS), corresponding to the speed at the last completed
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27 13 stage²¹, was used as a reference value for the calculation of the individualized speeds of the
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29 14 continuous and intermittent exercises.
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38 **Continuous and intermittent visits**

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40 17 At each of the two other visits, the children performed 3 continuous (CE) or 3 intermittent exercises
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42 18 (IE). Figure 1 shows the design for each exercise-testing visit. First, children rested for three minutes.
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44 19 Then, a 6-minute exercise period was carried out, immediately followed by a 4-minute period of
45
46 20 passive recovery, with measurement of gas exchanges. After that, the mouthpiece of the pulmonary
47
48 21 gas exchange apparatus was removed until the next exercise. Between two exercises, a 30-minute
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50 22 rest period was observed, without taking any measurements. For the continuous exercises, the 6-
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52 23 minute exercise period was performed at an individualized and constant speed. For intermittent
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54 24 exercises, the exercise period was divided into periods of 15s of running followed by 15s of passive
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56 25 recovery, except for the last minute of each intermittent exercise which was divided into one 30s
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3 1 period of running and one 30s period of passive recovery, so as to perform exercise tidal
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5 2 flow/volume loop measurement. In order to avoid the inertia of the treadmill for the two exercise
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7 3 modalities, the treadmill belt was set in motion at the adequate running speed before the beginning
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9 4 of the exercise period. The children were instructed to put their feet on both sides of the belt of the
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11 5 treadmill and to get on the belt at the beginning of the exercise period. For intermittent exercises, as
12
13 6 the treadmill was not stopped at the end of each 15-second running period, the children were
14
15 7 instructed to get on or off the treadmill after each 15-second period of running or passive recovery.
16
17 8 Leaving the treadmill consisted in putting their feet on both sides of it. Hence, the children were
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19 9 familiarized with getting on or off the treadmill before the intermittent exercises and were helped by
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21 10 an adult.

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26 11 Continuous exercises intensities corresponded to 60% (CE60), 70% (CE70) and 80% (CE80) of MAS.
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28 12 These intensities were always performed in this order. The intermittent exercise intensities
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30 13 corresponded to 90% (IE90), 100% (IE100) and 110% (IE110) of MAS and here also, this order was
31
32 14 kept for all the subjects. These MAS intensity percentages were chosen as they are frequently used
33
34 15 for continuous and intermittent exercises respectively²². Three intensity levels could be described:
35
36 16 low (CE60 vs. IE90), middle (CE70 vs. IE100) and high (CE80 vs. IE110).
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38 17 For all the continuous and intermittent exercises performed by the children, the mean values of
39
40 18 $\dot{V}O_2$, $\dot{V}E$, v_t , f , $\dot{V}E/\dot{V}O_2$, $\dot{V}E/\dot{V}CO_2$ and HR, reported in the "Results" section, were obtained
41
42 19 by averaging raw data during the first 30 seconds of the last minute of each exercise. This period of
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44 20 measurement corresponded to the time of exercise flow/volume loop measurement.
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52 **Determination of ventilatory constraints**

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54 23 For each continuous and intermittent exercise, ventilatory constraints were firstly determined with
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56 24 the calculation of breathing reserve (BR). BR was calculated based on maximal $\dot{V}E$ reached during
57
58 25 the exercise and the estimated maximal voluntary ventilation (MVV). It corresponded to how closely
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3 1 the maximal $\dot{V}E$ achieved during exercise approached MVV. The BR calculation equation was the
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6 2 following:

$$BR (\%) = [(MVV - \dot{V}E_{\max}) / MVV] \times 100$$

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15 6 where MVV was determined according to the following equation ^{6,23}: $MVV = FEV_1 \times 35$ and $\dot{V}E_{\max}$
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17 7 corresponded to the maximal value of $\dot{V}E$ reached during each continuous or intermittent exercise.
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19 8 The MVV was estimated for each exercise performed, with the FEV_1 measured just before the
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22 9 exercise.

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25 10 In order to evaluate mechanical ventilatory constraints and breathing strategy during the exercise,
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27 11 exercise tidal flow/volume loops (tidal F/V loops) were recorded just once, at the end of the first 30
28
29 12 seconds of the last minute of each exercise using a pneumotachograph. Tidal F/V loops corresponded
30
31 13 to a mean of ten tidal breaths recorded and were computer averaged before a maximal inspiratory
32
33 14 capacity (IC) maneuver. This maneuver allows correction of drift phenomena, as described by
34
35 15 Johnson et al ⁶. During exercise, a drift phenomenon could appear in the volume signal due to
36
37 16 electrical or physiological changes over time. This drift must be corrected in order to obtain correctly
38
39 17 placed tidal F/V loops within MFVL. Thus, the maximal inspiratory capacity maneuver was performed
40
41 18 immediately after tidal F/V loop measurement. This maximal IC maneuver was compared to the
42
43 19 maximal IC determined at rest. After the maneuver, the computer could correctly plot tidal F/V loops
44
45 20 within the MFVL determined before the exercise. For each tidal F/V loop measurement, the mean
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47 21 values of $\dot{V}O_2$, $\dot{V}E$, V_t , f , $\dot{V}E / \dot{V}O_2$, $\dot{V}E / \dot{V}CO_2$ and HR were calculated at the moment of
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49 22 measurement (corresponding to the mean of the first 30 seconds of the last minute of exercise).

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53 23 Expiratory flow limitation (expFL) corresponds to the part of tidal F/V loop that meets or exceeds the
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55 24 expiratory boundary of the MFVL and is expressed as a % of tidal volume (% V_t). In order to
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57 25 determine breathing strategy, the evolution of different ratios was analyzed. Hence, inspiratory
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3 1 capacity (IC) relative to forced vital capacity (IC/FVC)⁶, expiratory reserve volume relative to vital
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5 2 capacity (ERV/FVC), tidal volume relative to inspiratory capacity (Vt/IC)⁶ and inspiratory reserve
6
7 3 volume relative to vital capacity (IRV/FVC) were computed (Figure 2).
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11 5 **Statistical analysis**

12 6 All the values were expressed as means \pm standard deviation (mean \pm SD). For each parameter, data
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14 7 normality was verified with a Kolmogorov-Smirnov test.
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18 9 In order to determine the effect of exercise modality, a two-way repeated measure analysis of
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20 10 variance (ANOVA) was performed for all the parameters. The factors were "exercise intensity" and
21
22 11 "exercise modality". When the ANOVA F ratio was significant, the mean values were compared by
23
24 12 using pairwise multiple comparison procedures (Bonferroni post-hoc test).
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28 14 For intra-modality comparison, a one-way repeated measure analysis of variance (ANOVA) was
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30 15 performed for all the parameters. The factor was "exercise intensity". When the ANOVA F ratio was
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32 16 significant, the mean values were compared by using pairwise multiple comparison procedures
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34 17 (Bonferroni post-hoc test).
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38 19 For rest versus exercise values comparison within the same modality, a "paired t-test" was carried
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40 20 out.
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44 22 For all the tests, significance was set at the 0.05 level.
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1 Results

2 3 **Anthropometric, spirometric and maximal values at incremental exercise**

4 Respiratory data from one subject were unworkable. Thus, anthropometric, spirometric and maximal
5 exercise values of the eleven children were analyzed (8 boys and 3 girls; Table 1). For each child, 3
6 criteria of maximality at least were fulfilled, showing that the graded exercise was maximal.

7
8 Mean cardiorespiratory values ($\dot{V}O_2$, HR, RER) measured during continuous and intermittent
9 exercises for the whole population are shown in Table 2. For $\dot{V}O_2$ only, a significant "intensity x
10 modality" interaction and an "intensity" effect were highlighted. However post-hoc tests revealed no
11 significant difference between continuous and intermittent exercises within the three different
12 intensity levels (ie. CE60 vs. IE90, CE70 vs. IE100 and CE80 vs. IE110), allowing the comparison of the
13 ventilatory data obtained during each exercise modality. For HR, an significant intensity effect was
14 highlighted for both modalities, without "modality" effect. Finally, no effect of the exercise modality
15 and intensity was found for Respiratory Exchange Ratio (RER).

16 17 **Ventilatory response to exercise**

18 19 *Breathing pattern*

20 The mean values of ventilation are shown in Table 3. Two-way ANOVA analysis highlights "intensity"
21 and "modality x intensity" interaction effects for ventilation ($p < 0.05$). An "intensity" effect ($p < 0.001$)
22 was found for $\dot{V}E$ in continuous exercise ($p < 0.001$) but not in intermittent exercise ($p = 0.08$).
23 Following post-hoc tests, for each level of exercise intensity (CE60 vs. IE90, CE70 vs. IE100 and CE80 vs.
24 IE110), ventilation and dyspnea scores were not significantly different between continuous and
25 intermittent exercises. For tidal volume (V_t), no "intensity" or "modality" effects were found for

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3 1 either CE or IE modalities. Concerning respiratory frequency (f), an "intensity" effect was found for IE
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5 2 ($p < 0.05$) and a tendency towards significant effect for CE ($p = 0.06$). No "modality" effect was found
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7 3 for this parameter.
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10 4 11 12 5 *Mechanical ventilatory constraints*

13 14 6 - Expiratory flow limitation

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16 7 Expiratory flow limitation (expFL) was experienced by 1 child during CE60, 6 children during CE70 and
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18 8 6 children during CE80. Concerning intermittent exercise, expFL was observed for 3, 4 and 6 children
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20 9 during IE90, IE100 and IE110 respectively (Figure 3.b). Individual values of ExpFL ranged between 10
21
22 10 – 90% of V_t . Only one child showed expFL during all the continuous and intermittent exercises. Mean
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24 11 values of expFL for the whole population ranged from 5% to 29% of V_t and from 13% to 23% of V_t for
25
26 12 the continuous and intermittent exercises respectively (Figure 3.a).
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31 13 32 33 14 - Flow-limited (FL) vs. non flow-limited (NFL) comparison

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35 15 Within each exercise, the population was divided into two groups according to the presence or
36
37 16 absence of an expiratory flow limitation (expFL) during exercise. The children who presented expFL
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39 17 made up the flow-limited group (FL group). The non flow-limited group (NFL) was composed of the
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41 18 other children.
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44 19 For continuous exercise at 60% of MAS, only one child experienced an expFL versus 10 children
45
46 20 making up the NFL group, which made comparison impossible.
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49 21 No significant difference was highlighted between the two groups for breathing pattern (V_t and f) in
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51 22 any of the exercises.
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54 23 Breathing reserve was significantly lower in the FL than the NFL group during continuous exercise, for
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56 24 CE70 (30.8 ± 11.6 for FL and 48.8 ± 10.2 for NFL; $p = 0.02$) and CE80 (21.8 ± 10.1 for FL and 42.1 ± 10.9
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58 25 for NFL; $p = 0.01$). During all intermittent exercises, no significant difference for BR was found
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3 1 between FL and NFL groups for IE90 (38.8 ± 1.2 for FL and 50.9 ± 10.2 for NFL), IE100 (33.9 ± 7.9 for
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5 2 FL and 45.2 ± 12.2 for NFL) and IE110 (24.2 ± 22.2 for FL and 46.7 ± 13.9 for NFL).
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10 4 - Flow volume loops and tidal volume regulation.
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12 5 The mean values of resting and exercise pulmonary parameters are recapitulated in Table 4. IRV
13 6 decreased significantly from rest to exercise for all continuous or intermittent exercises ($p < 0.05$). ERV
14 7 increased significantly from rest to exercise for CE70, IE100 and IE110 ($p < 0.05$). For IC, a significant
15 8 difference was observed between rest and exercise for CE70, IE100 and IE110 ($p < 0.05$). No significant
16 9 differences were found for IC/FVC and ERV/FVC between rest and exercise values, except for IE110
17 10 ($p < 0.05$). IRV/FVC decreased significantly between rest and exercise for all the exercises. In the same
18 11 way, V_t/IC was significantly higher than at rest for all the exercises except for CE70 and IE100
19 12 ($p < 0.05$).
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33 14 For all the parameters of mechanical ventilatory constraints (expFL, V_t/IC , IC/FVC, IRV/FVC and
34 15 ERV/FVC), there were no significant "modality" and "intensity" effects (Table 4 and Figure 3.a).
35 16 However, an "intensity" effect tended to be significant for expFL during continuous exercise
36 17 ($p = 0.065$).
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3 1 Discussion
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6 2 The purpose of the study was to evaluate the ventilatory response during continuous and
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8 3 intermittent exercises and to determine if one of these two exercise modalities could induce greater
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10 4 mechanical ventilatory constraints than the other. Our results showed that both exercise modalities
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12 5 (continuous and intermittent) could induce mechanical ventilatory constraints in healthy
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14 6 prepubescent children, as several children presented expiratory flow limitation (expFL) during
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16 7 continuous and intermittent exercises with no influence due to exercise modality.
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22 9 Some limits should be considered for this study, mainly concerning recorded exercise flow/volume
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24 10 loops. As mentioned by some authors^{6,13}, expFL assessment is highly dependent on the placement of
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26 11 exercise flow/volume loop within maximal flow/volume loop. This limit has been taken in account
27
28 12 with the realization of inspiratory capacity (IC) maneuvers after exercise flow/volume loop
29
30 13 measurement, allowing drift correction. The IC maneuver has already been used to enhance
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32 14 reproducibility of the flow/volume loop method⁶.
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38 16 As described above, the aim of the study was to compare mechanical ventilatory constraints
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40 17 (expiratory flow limitation and dynamic hyperinflation) and breathing pattern (ventilation, tidal
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42 18 volume and breathing frequency) during continuous and intermittent exercises with exercise
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44 19 intensities inducing similar metabolic demand. Even if a significant interaction for oxygen uptake was
45
46 20 highlighted, it appears that, within the different levels of exercise intensity (low, medium and high),
47
48 21 the metabolic demand ($\dot{V}O_2$) was matching for the pair of tasks concerning the two exercise
49
50 22 modalities. In other words, no significant difference was highlighted for $\dot{V}O_2$ between CE60 vs. IE90,
51
52 23 CE70 vs. IE100 and CE80 vs. IE110, allowing the comparison of the breathing pattern data and
53
54 24 mechanical ventilatory constraints data obtained during each exercise.
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3 1 *Effects of exercise intensity on breathing pattern*
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5 2 As expected, ventilation for the continuous exercise modality increased with greater exercise
6
7 3 intensity. However, during intermittent exercises, ventilation increased slightly, but not significantly,
8
9 4 with the increase in exercise intensity. These specific ventilation evolutions according to exercise
10
11 5 modality could be due to the fact that, during 15s – 15s intermittent exercises performed by the
12
13 6 children in this study, the time of running was rather short. Hence, the ventilatory system would not
14
15 7 seem to have enough time to adapt to the ventilatory demand induced by the exercise intensity.
16
17 8 However, within the three intensity levels (i.e. low, medium or high), no significant difference was
18
19 9 highlighted between continuous and intermittent exercises. These results could logically be
20
21 10 explained since the intensities of intermittent exercises were specifically chosen in order to be
22
23 11 matched with continuous exercise intensities in terms of energy expenditure (i.e. oxygen uptake), as
24
25 12 already reported by Berthoin et al.²⁴ The absence of significant difference for ventilation between
26
27 13 both exercise modalities was also required in order to compare breathing pattern components (V_t
28
29 14 and f) correctly. In fact, several studies have reported that for a particular subject, the regulation of
30
31 15 the breathing pattern at a given level of ventilation is largely independent of the cause of the
32
33 16 increased ventilation^{25,26}.

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35 17 During all the continuous and the intermittent exercises, our results showed that the increase in
36
37 18 ventilation was mainly due to an increase in respiratory frequency. This result supports the findings
38
39 19 in the literature⁵ and revealed that, whatever the exercise modality, children presented rapid and
40
41 20 shallow breathing. However, differences in ventilatory regulation according to exercise modality
42
43 21 seemed to exist, as a "modality" effect was found for ventilatory equivalent in carbon dioxide
44
45 22 ($\dot{V}E/\dot{V}CO_2$). Post-hoc analysis revealed that, in general, intermittent exercise modality induced
46
47 23 higher $\dot{V}E/\dot{V}CO_2$ values than continuous exercise modality. This could be explained firstly, by a
48
49 24 chemical regulation due to a higher acidosis level during intermittent exercise and, secondly, by a
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3 1 movement frequency encountered during intermittent exercise which could induce a greater
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5 2 ventilatory response²⁷.
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10 4 *Effects of exercise intensity on mechanical ventilatory constraints*

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12 5 As described by Johnson et al⁶, the assessment of breathing reserve (BR) could be an indicator of the
13
14 6 occurrence of mechanical ventilatory constraints during exercise. In all the previous studies reporting
15
16 7 BR values in children, the exercise performed has been incremental^{13,14,28-30}. This difference in
17
18 8 protocols makes it impossible to compare our results with the previous studies, which is normal,
19
20 9 since this is the originality of our study. In our study, BR significantly decreased during CE and IE
21
22 10 whereas there was no “intensity” effect for \dot{V}_E during IE. This result is surprising and reinforces the
23
24 11 work of Johnson et al.⁶ asserting that breathing reserve is a general and inappropriate parameter for
25
26 12 the study of mechanical ventilatory constraints during exercise.
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31 13 The study of mechanical ventilatory constraints with exercise flow/volume loops brings more
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33 14 information on the adaptation of the ventilatory system during exercise.
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36 15 In our study, the number of expiratory flow limitation cases increased with exercise intensity in both
37
38 16 exercise modalities. For the highest intensity exercises, more than 50% of the whole population (6 of
39
40 17 the 11 children studied) showed an expiratory flow limitation. Individual expiratory flow limitation
41
42 18 ranged between 10 – 90% of Vt. These values are in accordance with values of expFL found in the
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44 19 literature. In fact, Nourry et al.¹³ reported an increase in the number of observations of expFL in non-
45
46 20 athlete prepubescent children (8 children out of the 18 studied) with the increase in intensity during
47
48 21 the maximal graded test, ranging between 16 – 78% of Vt. The occurrence of expFL during sub-
49
50 22 maximal (CE60, CE70, CE80 and IE90) and supra-maximal (IE100, IE110) exercises is not surprising,
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52 23 since a previous study has reported the case of expFL from 30% of maximal aerobic power¹³ and
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54 24 intensities prescribed in our study were all higher than this threshold value. As with ventilatory
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56 25 response during exercise, the occurrence of expFL in our population was heterogeneous as some
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1 children experienced expFL during IE90 and IE110 but not during IE100 for example. The
2 heterogeneity of expFL occurrence has also previously been described in children¹³ and could be
3 explained by the different levels of ventilatory system maturation.

4 Thus, for both exercise modalities, the increase in ventilation was generally associated with a
5 significant decrease in IRV and IRV/FVC and an increase in Vt/IC from rest to exercise without
6 significant modification of ERV/FVC and IC/FVC ratios, whatever the exercise performed. These
7 results attested to the absence of dynamic hyperinflation. The absence of significant modification of
8 ERV/FVC and IC/FVC ratios during exercise attested to a specific breathing pattern for children,
9 whatever the exercise modality, in comparison with an adult population.

11 *Effects of exercise modality on mechanical ventilatory constraints*

12 The exercise modality had no effect on breathing reserve, as similar values were found during
13 continuous and intermittent exercises for the three intensity levels. Tidal volume regulation was not
14 influenced by a "modality" effect either. Following statistical analysis, exercise modality was noted to
15 have no effect on the occurrence and/or the severity of expFL. This absence of "modality" effect
16 invalidated our hypothesis. In fact, as higher intensities are frequently used during intermittent
17 exercises, we had hypothesized that the higher ventilatory demand induced by the high-intensity
18 intermittent exercises would induce greater mechanical ventilatory constraints. The absence of a
19 "modality" effect for ventilation could be an explanation for the absence of a "modality" effect on
20 mechanical ventilatory constraints.

21
22 In the present study, the assessment of the ventilatory response corresponded to an intermittent
23 exercise design comprising 15s of exercise followed by 15s of passive recovery. However many
24 modalities of intermittent exercises exist, such as 30s – 30s, with passive or active recovery²⁴. Our
25 results may only be relevant for this intermittent exercise design. In fact, any change in parameters

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3 1 defining intermittent exercises could modify the ventilatory response values and so alter the
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5 2 breathing pattern, breathing strategy and the occurrence of mechanical ventilatory constraints
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7 3 during intermittent exercises. Yet, on the other hand, the 15s – 15s design was chosen as this
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9 4 intermittent exercise design has previously been used quite often in the literature and has generally
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11 5 been well accepted by children^{24,31}.
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38 7 In conclusion, exercise modality does not seem to be a predominant factor in mechanical ventilatory
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40 8 constraint occurrence during exercise. Nevertheless, the exercise intensity seems to be an important
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42 9 factor in inducing mechanical ventilatory constraints, as the number of occurrences and the severity
43
44 10 increased with intensity increased. We could conclude that neither of the modalities studied induced
45
46 11 more or greater mechanical ventilatory constraints than the other, but exercise intensities specific to
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48 12 each modality might be greater sources of exacerbation for mechanical ventilatory constraints.
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43
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Figure legends

Figure 1: Design of continuous and intermittent exercise tests.

With MAS: maximal aerobic speed. For intermittent modality, each vertical band corresponds to a 15 sec exercise period.

Figure 2: Exercise tidal volume plotted within maximal flow/volume loop

With MFVL: maximal flow/volume loop determined at rest; ExpFL : expiratory flow limitation corresponding to the part of tidal flow/volume loop that meets or exceeds MFVL; EELV : end-expiratory lung volume determined by inspiratory capacity relative to forced vital capacity; EILV : end-inspiratory lung volume determined by tidal volume relative to inspiratory capacity; Vt : tidal volume; IRV: inspiratory reserve volume; ERV : expiratory reserve volume; FVC : forced vital capacity; IC : inspiratory capacity.

Figure 3: Expiratory flow limitation during the six performed exercises.

Values are expressed as mean \pm SD. Graph 3.a : mean expiratory flow limitation for the whole population. Graph 3.b : mean expiratory flow limitation for the flow-limited group. ExpFL corresponds to expiratory flow limitation expressed in percentage of tidal volume that meets or exceeds maximal flow/volume loop. Thus, the flow limit group was composed of the children who showed an expFL during exercise.

CE60, CE70 and CE80 correspond to continuous exercise at 60%, 70% and 80% of maximal aerobic speed; IE90, IE100 and IE110 to intermittent exercise at 90%, 100% and 110% of maximal aerobic speed.

Title Page

Title: Comparison of mechanical ventilatory constraints between continuous and intermittent exercises in healthy prepubescent children.

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Running title: Mechanical ventilatory constraints in children

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3 1 **Abstract**

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6 2 **Background:** The aim of this study was to evaluate the occurrence and severity of mechanical
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8 3 ventilatory constraints in healthy prepubescent children during continuous and intermittent exercise.

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10 4 **Methods:** Twelve prepubescent children (7 – 11 years old) performed 7 exercises on a treadmill: one
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12 5 graded test for the determination of maximal aerobic speed (MAS), three continuous exercises (CE)
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14 6 at 60, 70 and 80% of MAS and three intermittent exercises (IE), alternating 15s of exercise with 15s of
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16 7 passive recovery, at 90, 100 and 110% of MAS. During each CE and IE, tidal flow/volume loops were
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18 8 plotted within a maximal flow/volume loop (MFVL) measured at rest before each exercise. Expiratory
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20 9 flow limitation (expFL expressed in %Vt) was defined as the part of exercise tidal volume (Vt) meeting
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22 10 the boundary of MFVL. Breathing strategy was estimated by measuring inspiratory capacity relative
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24 11 to forced vital capacity and tidal volume relative to inspiratory capacity. Other breathing pattern
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26 12 parameters (ventilation \dot{V}_E , Vt, respiratory frequency f) were continuously recorded during exercise.

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29 13 **Results:** An "intensity" effect was found for \dot{V}_E during CE ($p < 0.001$) but not during IE ($p = 0.08$). The
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31 14 increase in \dot{V}_E was predominantly assumed by an increase in f for both exercise modalities. During
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33 15 each exercise, several children heterogeneously experienced expFL ranging between 10 – 90%Vt. For
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35 16 all exercises, Vt was predominantly regulated by an increase in Vt/IC with no change in IC/FVC from
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37 17 rest to exercise. Finally, no significant "modality" effect was found for mechanical ventilatory
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39 18 constraint parameters (expFL, VT/IC and IV/FVC).

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42 19 **Discussion:** We could conclude that neither of the modalities studied induced more mechanical
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44 20 ventilatory constraints than the other, but that exercise intensities specific to each modality might be
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46 21 greater sources of exacerbation for mechanical ventilatory constraints.

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54 23 **Keywords:** children, exercise modality, ventilatory response, flow/volume loop
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Introduction

In the literature, it has been reported that children show specific ventilatory adaptations in comparison with adults during exercise. In fact, children present a phenomenon of hyperventilation for a similar level of relative intensity in comparison with adults. This phenomenon of hyperventilation in children is characterized by a higher respiratory equivalent in oxygen ($\dot{V}E / \dot{V}O_2$) in children than in adults¹⁻⁴ and could result from a specific breathing pattern. The latter is characterized by rapid and shallow breathing in children, defined by higher values of respiratory frequency and lower values of tidal volume than in adults⁵.

Moreover, as already shown in adults during incremental exercise, mechanical ventilatory constraints were also highlighted in children during exercise⁶⁻¹². Such constraints represented the balance between ventilatory demand and ventilatory capacity⁶ and could easily be identified by estimating breathing reserve (BR)⁶. However, BR provides no information on breathing pattern, or on the source and type of ventilatory constraints. This type of information could be obtained by using the exercise flow/volume loops method, consisting in plotting tidal flow/volume loops within maximal flow/volume loops during exercise⁶. By using this method, some studies have assessed mechanical ventilatory constraints in children during incremental exercise and reported several cases of expiratory flow limitation during high intensities of the incremental exercise^{13,14}. Thus, Nourry et al reported an "intensity" effect for mechanical ventilatory constraint occurrence and severity during a maximal graded test in trained or untrained prepubescent children^{13,14}. From these results, we have hypothesized that intermittent exercise could induce higher mechanical ventilatory constraints than continuous exercise, as the exercise intensities prescribed for intermittent exercises are higher than those prescribed for continuous exercises. The answers to this question could enlighten us on specific ventilatory adaptations in children during two exercise modalities frequently encountered

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3 1 during everyday life, contrary to current data from the literature, which is only based on incremental
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5 2 exercise.
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10 4 The aim of this study was 1) to evaluate and compare breathing pattern and tidal flow/volume loops
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12 5 between continuous and intermittent exercises in healthy prepubescent children, so as to determine
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14 6 if both exercise modalities could induce mechanical ventilatory constraints and 2) to determine the
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16 7 effects of the exercise modality on the severity of potential ventilatory constraints, in order to
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18 8 determine if one exercise modality was more restrictive than the other on the children's ventilatory
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20 9 system.
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3 1 **Methods**
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8 3 **Population**
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10 4 Twelve 7 – 11 year old healthy prepubescent children volunteered to participate in this study, which
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12 5 had previously received approval from the local ethics committee. Parents and children were
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14 6 informed as to the modalities of the study and then gave their written, informed consent prior to any
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16 7 involvement in it. All the children were free of respiratory or cardiac diseases and of orthopedic
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18 8 counter indications for physical exercise, performed less than 3h/week of extra academic physical
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20 9 activity and their sum of pubertal stages was lower than 3. Sexual maturity was evaluated from
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22 10 pubertal stages, according to Tanner's method: indices of breast, pubic hair and genital
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24 11 development¹⁵. The same physician made all the observations for all the children.
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31 13 **Study design**
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33 14 All the children came to the laboratory three times within a one-month period, with at least 48 hours
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35 15 between two evaluation days. At the beginning of each visit, a resting ECG and a clinical examination
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37 16 were performed. During the first visit, spirometry and sexual maturity were evaluated, followed by a
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39 17 period of familiarization and realization of a maximal graded test on a treadmill. Measurement of
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41 18 pulmonary gas exchanges allowed the determination of peak oxygen uptake ($\dot{V}O_{2\text{peak}}$) and maximal
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43 19 aerobic speed (MAS). During the last two visits, the children performed three continuous (continuous
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45 20 visit) and three intermittent (intermittent visit) exercises on the treadmill in a random order. Prior to
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47 21 the exercises, spirometry was performed and, subsequent to them, measurements of pulmonary gas
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49 22 exchanges, heart rate and exercise flow/volume curves ~~was~~ were carried out.
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57 24 **Spirometry**
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3 1 At each visit, the children underwent spirometry before each of the exercises performed (Vmax
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5 2 Encore, Sensormedics, Viasys Healthcare, USA). Each child was seated on a chair and fitted with a
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7 3 noseclip. All the lung tests were carried out by the same physician respecting American Thoracic
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9 4 Society recommendations¹⁶. For each child, three measurements of maximal flow/volume loops
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11 5 (MFVL) were carried out, allowing the determination of forced vital capacity (FVC) and forced
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13 6 expiratory volume in 1 second (FEV₁). Among the registered measurements, the MFVL with the
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15 7 greatest combination of FVC and FEV₁ was retained.
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22 9 **Cardio-respiratory parameters**

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24 10 At each visit and during all exercise tests, the children wore a mouthpiece connected to a breath-by-
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26 11 breath gas analyzer (V max Encore laboratory system, Sensormedics, Viasys Healthcare, USA),
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28 12 allowing the measurement of oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), ventilation
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30 13 ($\dot{V}E$), tidal volume (Vt) and respiratory frequency (f). In order to ensure accurate measurements, O₂
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32 14 and CO₂ analyzers were calibrated before each exercise test, using ambient air and two gases of
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34 15 known O₂ concentration (16% and 26%) and CO₂ concentration (4% and 0%). The calibration of the
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36 16 pneumotachograph was performed using a 3-liter syringe following the manufacturer's
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38 17 recommended procedures.
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43 18 Heart rate (HR) was continuously monitored with a heart rate monitor (Polar S810, Polar Electro Oy,
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45 19 Kempele, Finland). The data acquisition frequency for HR was set at 5 sec.

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47 20 Borg's CR-10 scale¹⁷ (ranging from 0 to 10) was used during all the exercises in order to evaluate
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49 21 dyspnea. This scale was explained to the children at the beginning of each visit and was shown to
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51 22 them at the end of each exercise.
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56 24 **Maximal graded test**

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3 1 A period of familiarization on the treadmill was proposed for all the children, consisting in explaining
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5 2 the security procedures and letting them walk and run on it. After explaining the exercise to the
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7 3 children, the test began with a resting period of three minutes in a standing position on the treadmill.
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9 4 Subsequently, a warm-up period of 3 minutes at $3\text{km}\cdot\text{h}^{-1}$ was performed. The exercise began with
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11 5 one minute at $4\text{ km}\cdot\text{h}^{-1}$, then the speed was increased by $0.5\text{ km}\cdot\text{h}^{-1}$ every minute. During the whole
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13 6 exercise, pulmonary gas exchanges and heart rate were continuously recorded and the values were
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15 7 averaged every 30 seconds. The exercise ended when the children were no longer able to maintain
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17 8 the imposed running speed. It was judged that they had performed a maximal exercise when 3 or
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19 9 more of the following criteria were obtained: visible exhaustion (excessive hyperpnea, facial flushing,
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21 10 sweating, discomfort)¹⁸, maximal heart rate $>90\%$ of predicted maximal heart rate $(208-0.7 \times \text{age})^{19}$, a
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23 11 plateau in $\dot{V}\text{O}_2$ despite increasing running speed or a final respiratory exchange ratio (RER) higher
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25 12 than 1.0²⁰. The maximal aerobic speed (MAS), corresponding to the speed at the last completed
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27 13 stage²¹, was used as a reference value for the calculation of the individualized speeds of the
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29 14 continuous and intermittent exercises.
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38 **Continuous and intermittent visits**

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40 17 At each of the two other visits, the children performed 3 continuous (CE) or 3 intermittent exercises
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42 18 (IE). Figure 1 shows the design for each exercise-testing visit. ~~A resting period of three minutes was~~
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44 19 ~~firstly observed~~ **First, children rested for three minutes.** Then, a 6-minute exercise period was carried
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46 20 out, immediately followed by a 4-minute period of passive recovery, with measurement of gas
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48 21 exchanges. After that, the mouthpiece of the pulmonary gas exchange apparatus was removed until
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50 22 the next exercise. Between two exercises, a 30-minute rest period was observed, without taking any
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52 23 measurements. For the continuous exercises, the 6-minute exercise period was performed at an
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54 24 individualized and constant speed. For intermittent exercises, the exercise period was divided into
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56 25 periods of 15s of running followed by 15s of passive recovery, except for the last minute of each
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3 1 intermittent exercise which was divided into one 30s period of running and one 30s period of passive
4
5 2 recovery, so as to perform exercise tidal flow/volume loop measurement. In order to avoid the
6
7 3 inertia of the treadmill for the two exercise modalities, the treadmill belt was set in motion at the
8
9 4 adequate running speed before the beginning of the exercise period. The children were instructed to
10
11 5 put their feet on both sides of the belt of the treadmill and to get on the belt at the beginning of the
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13 6 exercise period. For intermittent exercises, as the treadmill was not stopped at the end of each 15-
14
15 7 second running period, the children were instructed to get on or off the treadmill after each 15-
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17 8 second period of running or passive recovery. Leaving the treadmill consisted in putting their feet on
18
19 9 both sides of it. Hence, the children were familiarized with getting on or off the treadmill before the
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21 10 intermittent exercises and were helped by an adult.
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26 11 Continuous exercises intensities corresponded to 60% (CE60), 70% (CE70) and 80% (CE80) of MAS.
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28 12 These intensities were always performed in this order. The intermittent exercise intensities
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30 13 corresponded to 90% (IE90), 100% (IE100) and 110% (IE110) of MAS and here also, this order was
31
32 14 kept for all the subjects. These MAS intensity percentages were chosen as they are frequently used
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34 15 for continuous and intermittent exercises respectively²². Three intensity levels could be described:
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36 16 low (CE60 vs. IE90), middle (CE70 vs. IE100) and high (CE80 vs. IE110).
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40 17 For all the continuous and intermittent exercises performed by the children, the mean values of
41
42 18 $\dot{V}O_2$, $\dot{V}E$, v_t , f , $\dot{V}E/\dot{V}O_2$, $\dot{V}E/\dot{V}CO_2$ and HR, reported in the "Results" section, were obtained
43
44 19 by averaging raw data during the first 30 seconds of the last minute of each exercise. This period of
45
46 20 measurement corresponded to the time of exercise flow/volume loop measurement.
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51 22 **Determination of ventilatory constraints**

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53 23 For each continuous and intermittent exercise, ventilatory constraints were firstly determined with
54
55 24 the calculation of breathing reserve (BR). BR was calculated based on maximal $\dot{V}E$ reached during
56
57 25 the exercise and the estimated maximal voluntary ventilation (MVV). It corresponded to how closely
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3 1 maximal $\dot{V}E$ achieved during exercise approached MVV. The BR calculation equation was the
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6 2 following:

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$$BR (\%) = [(MVV - \dot{V}E_{\max}) / MVV] \times 100$$

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15 6 where MVV was determined according to the following equation ^{6,23}: $MVV = FEV_1 \times 35$ and $\dot{V}E_{\max}$
16
17 7 corresponded to the maximal value of $\dot{V}E$ reached during each continuous or intermittent exercise.
18
19 8 The MVV was estimated for each exercise performed, with the FEV_1 measured just before the
20
21
22 9 exercise.

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24
25 10 In order to evaluate mechanical ventilatory constraints and breathing strategy during the exercise,
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27 11 exercise tidal flow/volume loops (tidal F/V loops) were recorded just once, at the end of the first 30
28
29 12 seconds of the last minute of each exercise using a pneumotachograph. Tidal F/V loops corresponded
30
31 13 to a mean of ten tidal breaths recorded and were computer averaged before a maximal inspiratory
32
33 14 capacity (IC) maneuver. This maneuver allows correction of drift phenomena, as described by
34
35 15 Johnson et al ⁶. During exercise, a drift phenomenon could appear in the volume signal due to
36
37 16 electrical or physiological changes over time. This drift must be corrected in order to obtain correctly
38
39 17 placed tidal F/V loops within MFVL. Thus, the maximal inspiratory capacity maneuver was performed
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41 18 immediately after tidal F/V loop measurement. This maximal IC maneuver was compared to the
42
43 19 maximal IC determined at rest. After the maneuver, the computer could correctly plot tidal F/V loops
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45 20 within the MFVL determined before the exercise. For each tidal F/V loop measurement, the mean
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47 21 values of $\dot{V}O_2$, $\dot{V}E$, V_t , f , $\dot{V}E / \dot{V}O_2$, $\dot{V}E / \dot{V}CO_2$ and HR were calculated at the moment of
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49 22 measurement (corresponding to the mean of the first 30 seconds of the last minute of exercise).

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53 23 Expiratory flow limitation (expFL) corresponds to the part of tidal F/V loop that meets or exceeds the
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55 24 expiratory boundary of the MFVL and is expressed as a % of tidal volume (% V_t). In order to
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57 25 determine breathing strategy, the regulation evolution of different ratios was analyzed. Hence,
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3 1 inspiratory capacity (IC) relative to forced vital capacity (IC/FVC)⁶, expiratory reserve volume relative
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5 2 to vital capacity (ERV/FVC), tidal volume relative to inspiratory capacity (Vt/IC)⁶ and inspiratory
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7 3 reserve volume relative to vital capacity (IRV/FVC) were ~~estimated~~ **computed** (Figure 2).
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11 12 5 **Statistical analysis**

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14 6 All the values were expressed as means \pm standard deviation (mean \pm SD). For each parameter, data
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16 7 normality was verified with a Kolmogorov-Smirnov test.
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18

19 8 In order to determine the effect of exercise modality, a two-way repeated measure analysis of
20
21 9 variance (ANOVA) was performed for all the parameters. The factors were "exercise intensity" and
22
23 10 "exercise modality". When the ANOVA F ratio was significant, the mean values were compared by
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25 11 using pairwise multiple comparison procedures (Bonferroni post-hoc test).
26
27

28 12 For intra-modality comparison, a one-way repeated measure analysis of variance (ANOVA) was
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30 13 performed for all the parameters. The factor was "exercise intensity". When the ANOVA F ratio was
31
32 14 significant, the mean values were compared by using pairwise multiple comparison procedures
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34 15 (Bonferroni post-hoc test).
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37 16 For rest versus exercise values comparison within the same modality, a "paired t-test" was carried
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39 17 out.
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42 18 For all the tests, significance was set at the 0.05 level.
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Results

Anthropometric, spirometric and maximal values at incremental exercise

Respiratory data from one subject were unworkable. Thus, anthropometric, spirometric and maximal exercise values of the eleven children were analyzed (8 boys and 3 girls; Table 1). For each child, 3 criteria of maximality at least were fulfilled, showing that the graded exercise was maximal.

Mean cardiorespiratory values ($\dot{V}O_2$, HR, RER) measured during continuous and intermittent exercises for the whole population are shown in Table 2. For $\dot{V}O_2$ only, a significant "intensity x modality" interaction and an "intensity" effect were highlighted. However, post-hoc tests revealed no significant difference between continuous and intermittent exercises within the three different intensity levels (ie. CE60 vs. IE90, CE70 vs. IE100 and CE80 vs. IE110), allowing the comparison of the ventilatory data obtained during each exercise modality. For HR, an significant intensity effect was highlighted for both modalities, without "modality" effect. Finally, no effect of the exercise modality and intensity was found for Respiratory Exchange Ratio (RER).

Ventilatory response to exercise

Breathing pattern

The mean values of ventilation are shown in Table 3. Two-way ANOVA analysis highlights "intensity" and "modality x intensity" interaction effects for ventilation ($p < 0.05$). An "intensity" effect ($p < 0.001$) was found for $\dot{V}E$ in continuous exercise ($p < 0.001$) but not in intermittent exercise ($p = 0.08$). Following post-hoc tests, for each level of exercise intensity (CE60 vs. IE90, CE70 vs. IE100 and CE80 vs. IE110), ventilation and dyspnea scores were not significantly different between continuous and intermittent exercises. For tidal volume (V_t), no "intensity" or "modality" effects were found for

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2
3 1 either CE or IE modalities. Concerning respiratory frequency (f), an "intensity" effect was found for IE
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5 2 ($p < 0.05$) and a tendency towards significant effect for CE ($p = 0.06$). No "modality" effect was found
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7 3 for this parameter.
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10 4 11 12 5 *Mechanical ventilatory constraints*

13 14 6 - Expiratory flow limitation

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16 7 Expiratory flow limitation (expFL) was experienced by 1 child during CE60, 6 children during CE70 and
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18 8 6 children during CE80. Concerning intermittent exercise, expFL was observed for 3, 4 and 6 children
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20 9 during IE90, IE100 and IE110 respectively (Figure 3.b). Individual values of ExpFL ranged between 10
21
22 10 – 90% of V_t . Only one child showed expFL during all the continuous and intermittent exercises. Mean
23
24 11 values of expFL for the whole population ranged from 5% to 29% of V_t and from 13% to 23% of V_t for
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26 12 the continuous and intermittent exercises respectively (Figure 3.a).
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33 14 - Flow-limited (FL) vs. non flow-limited (NFL) comparison

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35 15 Within each exercise, the population was divided into two groups according to the presence or
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37 16 absence of an expiratory flow limitation (expFL) during exercise. The children who presented expFL
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39 17 made up the flow-limited group (FL group). The non flow-limited group (NFL) was composed of the
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41 18 other children.
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45 19 For continuous exercise at 60% of MAS, only one child experienced an expFL versus 10 children
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47 20 making up the NFL group, which made comparison impossible.
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50 21 No significant difference was highlighted between the two groups for breathing pattern (V_t and f) in
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52 22 any of the exercises.
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54
55 23 Breathing reserve was significantly lower in the FL than the NFL group during continuous exercise, for
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57 24 CE70 (30.8 ± 11.6 for FL and 48.8 ± 10.2 for NFL; $p = 0.02$) and CE80 (21.8 ± 10.1 for FL and 42.1 ± 10.9
58
59 25 for NFL; $p = 0.01$). During all intermittent exercises, no significant difference for BR was found
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3 1 between FL and NFL groups for IE90 (38.8 ± 1.2 for FL and 50.9 ± 10.2 for NFL), IE100 (33.9 ± 7.9 for
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5 2 FL and 45.2 ± 12.2 for NFL) and IE110 (24.2 ± 22.2 for FL and 46.7 ± 13.9 for NFL).
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10 4 - Flow volume loops and tidal volume regulation.
11

12 5 The mean values of resting and exercise pulmonary parameters are recapitulated in Table 4. IRV
13 6 decreased significantly from rest to exercise for all continuous or intermittent exercises ($p < 0.05$). ERV
14 7 increased significantly from rest to exercise for CE70, IE100 and IE110 ($p < 0.05$). For IC, a significant
15 8 difference was observed between rest and exercise for CE70, IE100 and IE110 ($p < 0.05$). No significant
16 9 differences were found for IC/FVC and ERV/FVC between rest and exercise values, except for IE110
17 10 ($p < 0.05$). IRV/FVC decreased significantly between rest and exercise for all the exercises. In the same
18 11 way, V_t/IC was significantly higher than at rest for all the exercises except for CE70 and IE100
19 12 ($p < 0.05$).
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33 14 For all the parameters of mechanical ventilatory constraints (expFL, V_t/IC , IC/FVC, IRV/FVC and
34 15 ERV/FVC), there were no significant "modality" and "intensity" effects (Table 4 and Figure 3.a).
35 16 However, an "intensity" effect tended to be significant for expFL during continuous exercise
36 17 ($p = 0.065$).
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1 Discussion

2 The purpose of the study was to evaluate the ventilatory response during continuous and
3 intermittent exercises and to determine if one of these two exercise modalities could induce greater
4 mechanical ventilatory constraints than the other. Our results showed that both exercise modalities
5 (continuous and intermittent) could induce mechanical ventilatory constraints in healthy
6 prepubescent children, as several children presented expiratory flow limitation (expFL) during
7 continuous and intermittent exercises with no influence due to exercise modality.

8
9 Some limits should be considered for this study, mainly concerning recorded exercise flow/volume
10 loops. As mentioned by some authors^{6,13}, expFL assessment is highly dependent on the placement of
11 exercise flow/volume loop within maximal flow/volume loop. This limit has been taken in account
12 with the realization of inspiratory capacity (IC) maneuvers after exercise flow/volume loop
13 measurement, allowing drift correction. The IC maneuver has already been used to enhance
14 reproducibility of the flow/volume loop method⁶.

15
16 As described above, the aim of the study was to compare mechanical ventilatory constraints
17 (expiratory flow limitation and dynamic hyperinflation) and breathing pattern (ventilation, tidal
18 volume and breathing frequency) during continuous and intermittent exercises with exercise
19 intensities inducing similar metabolic demand. Even if a significant interaction for oxygen uptake was
20 highlighted, it appears that, within the different levels of exercise intensity (low, medium and high),
21 the metabolic demand ($\dot{V}O_2$) was matching between the pair of tasks concerning the two exercise
22 modalities. In other words, no significant difference was highlighted for $\dot{V}O_2$ between CE60 vs. IE90,
23 CE70 vs. IE100 and CE80 vs. IE110, allowing the comparison of the breathing pattern data and the
24 mechanical ventilatory constraints data obtained during each exercise.

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3 1 *Effects of exercise intensity on breathing pattern*
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5 2 As expected, ventilation for the continuous exercise modality increased with greater exercise
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7 3 intensity. However, during intermittent exercises, ventilation increased slightly, but not significantly,
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9 4 with the increase in exercise intensity. These specific ventilation evolutions according to exercise
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11 5 modality could be due to the fact that, during 15s – 15s intermittent exercises performed by the
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13 6 children in this study, the time of running was rather short. Hence, the ventilatory system would not
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15 7 seem to have enough time to adapt to the ventilatory demand induced by the exercise intensity.
16
17 8 However, within the three intensity levels (i.e. low, medium or high), no significant difference was
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19 9 highlighted between continuous and intermittent exercises. These results could logically be
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21 10 explained since the intensities of intermittent exercises were specifically chosen in order to be
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23 11 matched with continuous exercise intensities in terms of energy expenditure (i.e. oxygen uptake), as
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25 12 already reported by Berthoin et al.²⁴ The absence of significant difference for ventilation between
26
27 13 both exercise modalities was also required in order to compare breathing pattern components (V_t
28
29 14 and f) correctly. In fact, several studies have reported that for a particular subject, the regulation of
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31 15 the breathing pattern at a given level of ventilation is largely independent of the cause of the
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33 16 increased ventilation^{25,26}.

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35 17 During all the continuous and the intermittent exercises, our results showed that the increase in
36
37 18 ventilation was mainly due to an increase in respiratory frequency. This result supports the findings
38
39 19 in the literature⁵ and revealed that, whatever the exercise modality, children presented rapid and
40
41 20 shallow breathing. However, differences in ventilatory regulation according to exercise modality
42
43 21 seemed to exist, as a "modality" effect was found for ventilatory equivalent in carbon dioxide
44
45 22 ($\dot{V}E/\dot{V}CO_2$). Post-hoc analysis revealed that, in general, intermittent exercise modality induced
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47 23 higher $\dot{V}E/\dot{V}CO_2$ values than continuous exercise modality. This could be explained firstly, by a
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49 24 chemical regulation due to a higher acidosis level during intermittent exercise and, secondly, by a
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3 1 movement frequency encountered during intermittent exercise which could induce a greater
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5 2 ventilatory response²⁷.
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10 4 *Effects of exercise intensity on mechanical ventilatory constraints*

11
12 5 As described by Johnson et al⁶, the assessment of breathing reserve (BR) could be an indicator of the
13
14 6 occurrence of mechanical ventilatory constraints during exercise. In all the previous studies reporting
15
16 7 BR values in children, the exercise performed has been incremental^{13,14,28-30}. This difference in
17
18 8 protocols makes it impossible to compare our results with the previous studies, which is normal,
19
20 9 since this is the originality of our study. In our study, BR significantly decreased during CE and IE
21
22 10 whereas there was no “intensity” effect for \dot{V}_E during IE. This result is surprising and reinforces the
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24 11 work of Johnson et al.⁶ asserting that breathing reserve is a general and inappropriate parameter for
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26 12 the study of mechanical ventilatory constraints during exercise.
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31 13 The study of mechanical ventilatory constraints with exercise flow/volume loops brings more
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33 14 information on the adaptation of the ventilatory system during exercise.
34

35 15 In our study, the number of expiratory flow limitation cases increased with exercise intensity in both
36
37 16 exercise modalities. For the highest intensity exercises, more than 50% of the whole population (6 of
38
39 17 the 11 children studied) showed an expiratory flow limitation. Individual expiratory flow limitation
40
41 18 ranged between 10 – 90% of V_t . These values are in accordance with values of expFL found in the
42
43 19 literature. In fact, Nourry et al.¹³ reported an increase in the number of observations of expFL in non-
44
45 20 athlete prepubescent children (8 children out of the 18 studied) with the increase in intensity during
46
47 21 the maximal graded test, ranging between 16 – 78% of V_t . The occurrence of expFL during sub-
48
49 22 maximal (CE60, CE70, CE80 and IE90) and supra-maximal (IE100, IE110) exercises is not surprising,
50
51 23 since a previous study has reported the case of expFL from 30% of maximal aerobic power¹³ and
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53 24 intensities prescribed in our study were all higher than this threshold value. As with ventilatory
54
55 25 response during exercise, the occurrence of expFL in our population was heterogeneous as some
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1 children experienced expFL during IE90 and IE110 but not during IE100 for example. The
2 heterogeneity of expFL occurrence has also previously been described in children¹³ and could be
3 explained by the different levels of ventilatory system maturation.

4 Thus, for both exercise modalities, the increase in ventilation was generally associated with a
5 significant decrease in IRV and IRV/FVC and an increase in Vt/IC from rest to exercise without
6 significant modification of ERV/FVC and IC/FVC ratios, whatever the exercise performed. These
7 results attested to the absence of dynamic hyperinflation. The absence of significant modification of
8 ERV/FVC and IC/FVC ratios during exercise attested to a specific breathing pattern for children,
9 whatever the exercise modality, in comparison with an adult population.

11 *Effects of exercise modality on mechanical ventilatory constraints*

12 The exercise modality had no effect on breathing reserve, as similar values were found during
13 continuous and intermittent exercises for the three intensity levels. Tidal volume regulation was not
14 influenced by a "modality" effect either. Following statistical analysis, exercise modality was noted to
15 have no effect on the occurrence and/or the severity of expFL. This absence of "modality" effect
16 invalidated our hypothesis. In fact, as higher intensities are frequently used during intermittent
17 exercises, we had hypothesized that the higher ventilatory demand induced by the high-intensity
18 intermittent exercises would induce greater mechanical ventilatory constraints. The absence of a
19 "modality" effect for ventilation could be an explanation for the absence of a "modality" effect on
20 mechanical ventilatory constraints.

21
22 In the present study, the assessment of the ventilatory response corresponded to an intermittent
23 exercise design comprising 15s of exercise followed by 15s of passive recovery. However many
24 modalities of intermittent exercises exist, such as 30s – 30s, with passive or active recovery²⁴. Our
25 results may only be relevant for this intermittent exercise design. In fact, any change in parameters

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2
3 1 defining intermittent exercises could modify the ventilatory response values and so alter the
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5 2 breathing pattern, breathing strategy and the occurrence of mechanical ventilatory constraints
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7 3 during intermittent exercises. Yet, on the other hand, the 15s – 15s design was chosen as this
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9 4 intermittent exercise design has previously been used quite often in the literature and has generally
10
11 5 been well accepted by children^{24,31}.
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17 7 In conclusion, exercise modality does not seem to be a predominant factor in mechanical ventilatory
18
19 8 constraint occurrence during exercise. Nevertheless, the exercise intensity seems to be an important
20
21 9 factor in inducing mechanical ventilatory constraints, as the number of occurrences and the severity
22
23 10 increased with intensity increased. We could conclude that neither of the modalities studied induced
24
25 11 more or greater mechanical ventilatory constraints than the other, but exercise intensities specific to
26
27 12 each modality might be greater sources of exacerbation for mechanical ventilatory constraints.
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38
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42
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44
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3 **Figure legends**
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6 Figure 1: Design of continuous and intermittent exercise tests.
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9 With MAS: maximal aerobic speed. For intermittent modality, each vertical band corresponds to a 15 sec
10 exercise period.
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15 Figure 2: Exercise tidal volume plotted within maximal flow/volume loop
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18 With MFVL: maximal flow/volume loop determined at rest; ExpFL : expiratory flow limitation corresponding to
19 the part of tidal flow/volume loop that meets or exceeds MFVL; EELV : end-expiratory lung volume determined
20 by inspiratory capacity relative to forced vital capacity; EILV : end-inspiratory lung volume determined by tidal
21 volume relative to inspiratory capacity; Vt : tidal volume; IRV: inspiratory reserve volume; ERV : expiratory
22 reserve volume; FVC : forced vital capacity; IC : inspiratory capacity.
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28 Figure 3: Expiratory flow limitation during the six performed exercises.
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31 Values are expressed as mean \pm SD. Graph 3.a : mean expiratory flow limitation for the whole population.
32 Graph 3.b : mean expiratory flow limitation for the flow-limited group. ExpFL corresponds to expiratory flow
33 limitation expressed in percentage of tidal volume that meets or exceeds maximal flow/volume loop. Thus, the
34 flow limit group was composed of the children who showed an expFL during exercise.
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37 CE60, CE70 and CE80 correspond to continuous exercise at 60%, 70% and 80% of maximal aerobic speed; IE90,
38 IE100 and IE110 to intermittent exercise at 90%, 100% and 110% of maximal aerobic speed.
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Table 1: Anthropometric, spirometric and maximal values at incremental exercise.

Parameter (units)	Mean \pm SD
Age (years)	8.6 \pm 1.4
Height (cm)	135.2 \pm 9.4
Body mass (kg)	29.0 \pm 5.8
BMI (kg.cm ⁻²)	15.7 \pm 1.5
FVC (L)	2.1 \pm 0.4
FVC (% of theoretical value)	99.6 \pm 11.5
FEV ₁ (L)	1.8 \pm 0.4
FEV1 (% of theoretical value)	101.8 \pm 12.3
VO _{2 max} (L.min ⁻¹)	1.5 \pm 0.4
VO _{2 max} (mL.min ⁻¹ .kg ⁻¹)	50.3 \pm 8.2
HR max (bpm)	186.5 \pm 10.6
RER max	1.0 \pm 0.1
MAS (km.h ⁻¹)	10.0 \pm 1.6

With BMI : Body Mass Index ; FVC : Forced Vital Capacity ; FEV₁ : Forced Expiratory Volume in 1 Second ; VO_{2 peak} : peak oxygen uptake ; HRmax : maximal heart rate ; RERmax : maximal respiratory exchange ratio ; MAS : maximal aerobic speed.

Table 2 : Cardio-respiratory data during continuous and intermittent exercises

Intensity level	Low		Medium		High	
Exercise	CE60	IE90	CE70	IE100	CE80	IE110
VO ₂ (L.min ⁻¹)	0.92 ± 0.27 \$μ	1.03 ± 0.22 μ	1.10 ± 0.27 §	1.19 ± 0.31	1.27 ± 0.33	1.17 ± 0.35
HR (bpm)	135.0 ± 11.9 \$μ	146.4 ± 17.3 μ	152.1 ± 10.6 §	151.2 ± 8.1	163.6 ± 16.8	158.2 ± 11.3
RER	0.94 ± 0.05	0.94 ± 0.07	0.96 ± 0.04	0.92 ± 0.06	0.98 ± 0.04	0.96 ± 0.06

Values are expressed in mean ± SD. CE60, CE70 and CE80 represented continuous exercises at 60%, 70% and 80% of maximal aerobic speed (MAS). IE90, IE100 and IE110 represented intermittent exercises at 90%, 100% and 110% of MAS. VO₂: oxygen uptake; HR : heart rate; RER : Respiratory exchange ratio.

\$: p<0.05 for CE60 vs. CE70

§ : p<0.05 for CE70 vs. CE80

μ : p<0.05 for CE60 vs. CE80 or IE90 vs. IE110 comparisons

Table 3: Respiratory parameters for the continuous and intermittent exercises.

Intensity level	Low		Middle		High	
Exercise	CE60	IE90	CE70	IE100	CE80	IE110
$V_E (L.min^{-1})$	28.6 ± 7.5 $\$ \mu$	33.1 ± 6.5	33.7 ± 7.8 $\$$	36.6 ± 8.7	38.7 ± 8.4	36.8 ± 9.7
$V_t (mL)$	616.8 ± 230.4	665.6 ± 224.8	665.5 ± 317.5	603.1 ± 145.5	687.1 ± 350.0	585.1 ± 194.8
$f (cycles.min^{-1})$	49.8 ± 16.5	51.8 ± 12.2 μ	57.4 ± 19.5	63.0 ± 18.4	64.4 ± 22.7	67.4 ± 23.6
V_E/VO_2	31.8 ± 3.3	32.3 ± 3.0	31.2 ± 2.9	31.0 ± 3.4	31.6 ± 3.3	33.2 ± 4.8
V_E/VCO_2	32.4 ± 2.6	32.9 ± 2.9	32.1 ± 3.1	33.2 ± 3.0	31.6 ± 2.7	33.0 ± 2.9
BR (%)	51.4 ± 12.4 $\$ \mu$	46.9 ± 9.7 μ	39.0 ± 14.0 $\$$	41.1 ± 11.8	31.1 ± 14.5	34.5 ± 21.5
Dyspnea	1.1 ± 1.2 $\$$	1.1 ± 1.5 μ	3.1 ± 2.4	2.2 ± 2.2	3.6 ± 2.7	3.5 ± 2.2

Values are expressed in mean ± SD. CE60, CE70 and CE80 represented continuous exercises at 60%, 70% and 80% of maximal aerobic speed (MAS). IE90, IE100 and IE110 represented intermittent exercises at 90%, 100% and 110% of MAS. VO_2 : oxygen uptake; mean VO_2 : mean oxygen uptake of the last two minutes of exercise; V_E : ventilation at tidal FV loop measurement; V_t : tidal volume; f : respiratory frequency; V_E/VO_2 and V_E/VCO_2 : respiratory equivalent in oxygen and in carbon dioxide; BR: breathing reserve.

$\$$: $p < 0.05$ for CE60 vs. CE70 or IE90 vs. IE100 comparisons

$\$$: $p < 0.05$ for CE70 vs. CE80 or IE100 vs. IE110 comparisons

μ : $p < 0.05$ for CE60 vs. CE80 or IE90 vs. IE110 comparisons

Table 4: Ventilatory response at rest and during exercise.

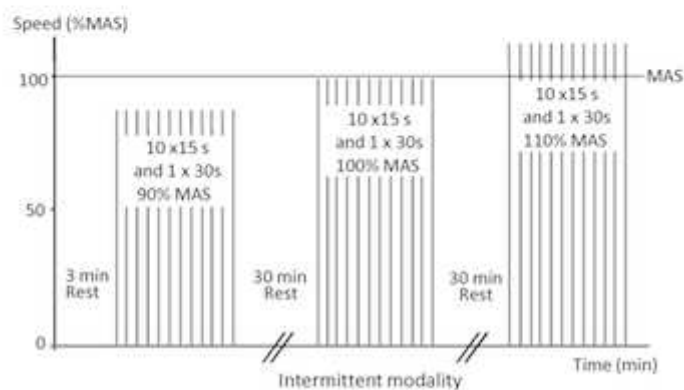
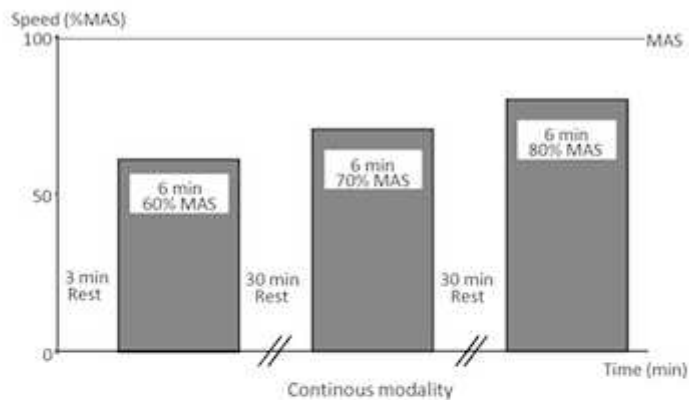
	Continuous exercise					
	CE60		CE70		CE80	
	Rest	Exercise	Rest	Exercise	Rest	Exercise
Vt	0.49 ± 0.23	0.62 ± 0.23	0.55 ± 0.29	0.67 ± 0.32	0.51 ± 0.25	0.69 ± 0.35 *
IRV	1.00 ± 0.25	0.79 ± 0.19 **	0.91 ± 0.28	0.68 ± 0.25 *	0.95 ± 0.18	0.67 ± 0.17 **
ERV	0.65 ± 0.24	0.74 ± 0.26	0.63 ± 0.22	0.74 ± 0.23 *	0.64 ± 0.25	0.74 ± 0.29
IC	1.49 ± 0.26	1.40 ± 0.24	1.47 ± 0.31	1.35 ± 0.27 *	1.45 ± 0.30	1.35 ± 0.35
Vt/IC	0.32 ± 0.14	0.43 ± 0.11 *	0.37 ± 0.19	0.48 ± 0.16	0.34 ± 0.12	0.49 ± 0.13 **
IC/FVC	0.70 ± 0.08	0.66 ± 0.07	0.70 ± 0.07	0.65 ± 0.07	0.70 ± 0.08	0.65 ± 0.11
IRV/FVC	0.47 ± 0.09	0.38 ± 0.09 **	0.44 ± 0.13	0.34 ± 0.13 *	0.47 ± 0.09	0.33 ± 0.12 **
ERV/FVC	0.30 ± 0.08	0.34 ± 0.07	0.30 ± 0.07	0.35 ± 0.07	0.30 ± 0.08	0.35 ± 0.11
	Intermittent exercise					
	IE90		IE100		IE110	
	Rest	Exercise	Rest	Exercise	Rest	Exercise
Vt	0.55 ± 0.24	0.67 ± 0.23	0.58 ± 0.30	0.60 ± 0.15	0.48 ± 0.16	0.59 ± 0.20
IRV	0.96 ± 0.24	0.76 ± 0.20 *	0.88 ± 0.24	0.72 ± 0.23 *	0.97 ± 0.18	0.72 ± 0.11 **
ERV	0.61 ± 0.24	0.71 ± 0.32	0.66 ± 0.18	0.80 ± 0.18 *	0.60 ± 0.22	0.74 ± 0.23 *
IC	1.51 ± 0.36	1.42 ± 0.31	1.45 ± 0.33	1.32 ± 0.31 *	1.45 ± 0.20	1.31 ± 0.25 *
Vt/IC	0.36 ± 0.10	0.47 ± 0.10 *	0.38 ± 0.17	0.46 ± 0.08	0.33 ± 0.09	0.44 ± 0.08*
IC/FVC	0.72 ± 0.09	0.68 ± 0.11	0.69 ± 0.07	0.62 ± 0.07	0.72 ± 0.07	0.64 ± 0.08 *
IRV/FVC	0.46 ± 0.10	0.36 ± 0.10 *	0.42 ± 0.09	0.34 ± 0.07 *	0.48 ± 0.10	0.36 ± 0.08 **
ERV/FVC	0.28 ± 0.09	0.32 ± 0.11	0.31 ± 0.07	0.38 ± 0.07	0.28 ± 0.07	0.36 ± 0.08 *

Values are expressed by mean ± SD. CE60, CE70 and CE80 correspond to continuous exercise at 60%, 70% and 80% of maximal aerobic speed; IE90, IE100 and IE110 to intermittent exercise at 90%, 100% and 110% of maximal aerobic.

Vt: tidal volume (liters), IRV: inspiratory reserve volume (liters), ERV: expiratory reserve volume (liters), IC: inspiratory capacity (liters), FVC: forced vital capacity (liters). * : p<0.05, ** : p<0.01.

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Figure 1

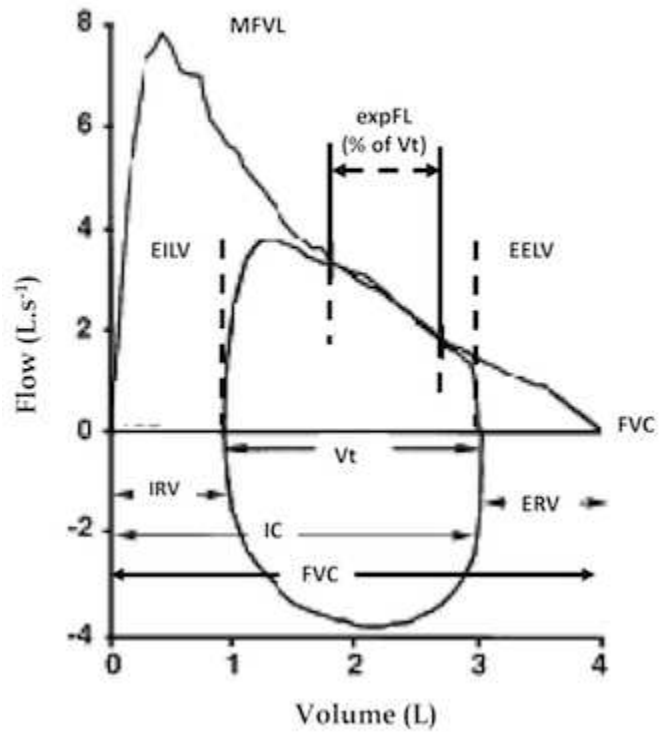


32x40mm (300 x 300 DPI)



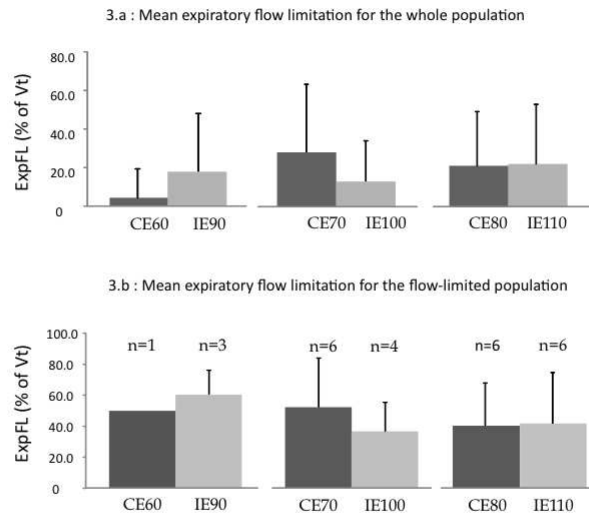
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Figure 2



28x40mm (300 x 300 DPI)





Values are expressed as mean \pm SD. Graph 3.a : mean expiratory flow limitation for the whole population. Graph 3.b : mean expiratory flow limitation for the flow-limited group. ExpFL corresponds to expiratory flow limitation expressed in percentage of tidal volume that meets or exceeds maximal flow/volume loop. Thus, the flow limit group was composed of the children who showed an expFL during exercise.

CE60, CE70 and CE80 correspond to continuous exercise at 60%, 70% and 80% of maximal aerobic speed; IE90, IE100 and IE110 to intermittent exercise at 90%, 100% and 110% of maximal aerobic speed.

352x264mm (72 x 72 DPI)

