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# Hyperventilation during Exercise in Very Low Birth Weight School-Age Children may Implicate Inspiratory Muscle Weakness

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**Objectives** To study the ventilatory response during exercise in 8- to 10-year-old children born in 1998 to 2000 with a birthweight <1500 g (very low birthweight [VLBW]).

**Study design** We studied 19 VLBW children and 20 full-term children paired for age and sex. A physical activity questionnaire was administered. Lean body mass, spirometry, and maximal inspiratory pressure were assessed at rest. Gas exchange, breathing pattern, and the tension-time index of the inspiratory muscles, a noninvasive indicator of inspiratory muscle effort, were evaluated during a continuous incremental cycling protocol.

**Results** VLBW children had lower weight, height, lean body mass, and maximal inspiratory pressure than control subjects. Their physical activity level was not different. During exercise, they had a higher respiratory rate and minute ventilation for the same metabolic level ( $\text{VCO}_2/\text{kg}$ ) and a higher tension-time index of the inspiratory muscles for the same exercise level (percentage of maximal oxygen consumption).

**Conclusions** The lower inspiratory muscle strength observed in school-age VLBW children resulted in a higher inspiratory effort during incremental exercise. The rapid but not shallow breathing pattern adopted by this population during exercise may have been in response to their lower inspiratory muscle resistance to fatigue. VLBW children complaining of dyspnea should be investigated with exercise testing.

It remains unclear whether the long-term respiratory outcome of very preterm infants has changed with the increased survival rate at lower gestational age and the advances in ventilatory management strategies.<sup>1</sup> Antenatal steroids and surfactant have lowered the mortality rate, especially of more immature children at higher risk for lung injury and long-term respiratory sequelae.<sup>1</sup> However, changes in ventilatory modalities, including the development of noninvasive ventilation techniques and lowered oxygen saturation goals, have modified the short-term respiratory outcomes.<sup>2</sup> To date, the studies assessing the long-term respiratory outcome of very low birthweight (VLBW) children have shown a higher prevalence of airways obstruction and gas trapping<sup>3</sup> and the lower diffusion capacity of the lungs at rest.<sup>4</sup> Exercise performance, evaluated at the end of the first decade with the measurement of maximal oxygen consumption ( $\text{VO}_{2\text{max}}$ ), has been highly variable.<sup>5-9</sup> However, analysis of the physiological systems involved during exercise adaptation has shown normal cardiovascular function,<sup>5,10</sup> but abnormal ventilatory responses.<sup>5-9</sup> These abnormalities were more striking when the children had a history of bronchopulmonary dysplasia (BPD).

The great heterogeneity in the breathing pattern adopted by VLBW children during exercise remains unexplained.<sup>5,7-9</sup> We hypothesized that it may be linked to the variable level of inspiratory muscle effort produced at each breath during exercise. An obstructive syndrome with alveolar hyperinflation may impose an increased load on the inspiratory muscles, which would modify the ventilatory pattern adopted during exercise.<sup>11</sup> The noninvasive tension-time index of the inspiratory muscles ( $\text{TT}_{0.1}$ ) has been proposed to assess inspiratory muscle effort during exercise in children with cystic fibrosis.<sup>12</sup>  $\text{TT}_{0.1}$  integrates all the components that may affect the respiratory muscles during exercise, including breathing cycle timing, inspiratory demand, and maximal inspiratory force reserve. Our goal was to compare the inspiratory function at rest and during exercise in a recent cohort of VLBW children and healthy term-born children paired for age and sex.

## Methods

The VLBW group was recruited from a cohort of 79 children, 8 to 10 years old, born between 1998 and 2000 before 29 weeks of gestation with a birthweight <1500 g, and observed longitudinally at Montpellier University Hospital Center. Inclusion criteria

BPD	Bronchopulmonary dysplasia	$P_{i\text{max}}$	Maximal inspiratory pressure
FRC	Functional residual capacity	$P_{0.1}$	Occlusion pressure
HR	Heart rate	RR	Respiratory rate
LBM	Lean body mass	$\text{TT}_{0.1}$	Tension-time index of the inspiratory muscles
MAQ	Modifiable Activity Questionnaire	VLBW	Very low birthweight
MET	Metabolic equivalents of task	$\text{VO}_{2\text{max}}$	Maximal oxygen consumption
$\text{PetCO}_2$	Tidal expiratory pressure of carbon dioxide	VT	Tidal volume

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were a need for supplemental oxygen  $\geq 28$  days for the BPD subgroup<sup>13</sup> and a need for supplemental oxygen  $\leq 10$  days for premature infants without BPD (no-BPD). Exclusion criteria were a need for supplemental oxygen for 10 to 27 days, cerebral palsy that precluded exercise testing because of physical or cognitive deficits, relative or absolute contraindication to perform an incremental exercise test referenced by the American Thoracic Society,<sup>14</sup> and use of medications not part of the pharmacological management of BPD and liable to cause exercise limitation (alpha- and beta-blockers, amiodarone, digitalis, and calcium channel blockers).

The control group was recruited through the press and matched for age and sex with the VLBW children. Inclusion criteria were term birth ( $\geq 37$  weeks of gestation), normal birth weight according to the national reference curves, and no cardiac, pulmonary, or muscular disease or overt physical or mental disability. Exclusion criteria were relative or absolute contraindication to perform an incremental exercise test<sup>14</sup> and intensive training defined as sports practice amounting to  $>6$  hours per week.

We obtained informed written consent from all the children and their two parents. The protocol was approved by the local ethics committee (Comité de Protection des Personnes Sud Méditerranée IV).

### Protocol

All participants came to the pulmonary function laboratory at Arnaud de Villeneuve Hospital in Montpellier for a 4-hour assessment. Anthropometric measurements were made and respiratory function was assessed at rest and during a maximal incremental cycling exercise. Physical activity was assessed with a self-administered questionnaire.

**Anthropometric Measurements.** Weight and height were measured, and the body mass index was calculated as weight in kilograms divided by height in square meters ( $\text{kg}/\text{m}^2$ ). Lean body mass (LBM) was assessed with impedance and skinfold measurements. The values given by both methods were averaged to balance the variability of the two methods.

Bicipital, tricipital, subscapular, and suprailiac skinfold thicknesses were measured with a Harpenden skinfold caliper (Eugedia, Cachan, France). Body fat mass was assessed according to the 4-skinfold-thickness measurements of Durnin and Rahaman.<sup>15</sup> LBM was calculated by subtracting body fat mass from total body mass.

Body composition was determined with bioelectrical impedance with a multifrequency impedance analyzer (body impedance analyzer, model BIA 101/S; Akern/RJL Systems, Clinton Township, Michigan) with the following frequencies: 1, 5, 10, 50, and 100 kHz.

**Respiratory Function at Rest.** Spirometry and lung volumes were performed at rest with a body plethysmograph (Bodybox 5500; Medisoft, Lille, France) by skilled pulmonary function technicians who work regularly with children, following the recommendations of the American Thoracic and European Respiratory Societies.

Maximal inspiratory pressure ( $P_{i \text{ max}}$ ) was measured at rest at functional residual capacity (FRC) on seated subjects, with a Validyne MP45 pressure transducer (Validyne Engineering, Northridge, California) ( $\pm 250$  cm  $\text{H}_2\text{O}$ ), with the technique of Black and Hyatt.<sup>16</sup>

**Gas Exchange, Ventilatory Pattern, and  $\text{TT}_{0.1}$  during Exercise.** A maximal incremental exercise test was performed on a cycle ergometer (Ergomeca GP440, La Bayette, France), according to a standardized protocol for children.<sup>17</sup> Inspiratory muscle effort was assessed at each level of exercise with the non-invasive measure of  $\text{TT}_{0.1}$ , as previously described.<sup>12</sup>

**Physical Activity Questionnaire.** Physical activity and energy expenditure over the past year were assessed with the French version of Kriska's Modifiable Activity Questionnaire (MAQ).<sup>18</sup> The MAQ was administered to both parents and child. They were asked to indicate the activities the child had engaged in at least 10 times during the past year from among a list of common leisure activities. They could also report activities that were not included on the list. An estimate of the energy expenditure in the past year was then calculated and expressed in metabolic equivalents of task (MET).

### Statistics

The lung function test results were analyzed as percentages of the reference values.<sup>19</sup> Medians (25th and 75th values) are reported. The Mann-Whitney rank sum test was used for comparisons between VLBW and control groups and between BPD and no-BPD groups. The  $\chi^2$  test was used for categorical data. Forward stepwise analysis was applied to assess factors associated with  $P_{i \text{ max}}$ .

A linear mixed model compared the continuous variables between groups to take in account the multiple observations per patient during the incremental exercise test. All analysis was carried out with the SAS/UNIX statistical software (SAS version 9, SAS Institute, Cary, North Carolina). Statistical significance was defined as a  $P$  value  $<.05$  (two-sided).

## Results

### Perinatal Characteristics of the Study Population

Of the 79 VLBW children who survived to hospital discharge, 51 were eligible: 20 without BPD and 31 with BPD. Thirty-two of these eligible patients were not enrolled: 20 were lost during follow-up, and 12 declined to participate in the study. Nineteen children were thus included in the VLBW: 9 without BPD (no-BPD) and 10 with BPD (BPD). None of the antenatal, neonatal, or postnatal data for known risk factors or markers of BPD differed between the included and non-included children (Table I; available at [www.jpeds.com](http://www.jpeds.com)).

Their gestational age was 27.0 weeks (range, 26.0-27.0 weeks), and the birthweight was 850 g (range, 730-1000 g). Surfactant treatment was given to 84% of the cases, and 32% received a first course of cyclooxygenase inhibitor for persistent ductus arteriosus. The durations of invasive mechanical ventilation and supplemental oxygen were 5.0 days (range, 1.5-11.5,

days) and 21 days (range, 4-50 days), respectively. At 36 weeks, 7 children had mild BPD and 3 had moderate BPD that still required oxygen. As expected, children with BPD had longer mechanical ventilation than children without BPD (12 days [range, 1-23 days] versus 4 days [range, 2-5 days], respectively;  $P < .05$ ) and longer supplemental oxygen exposure (49 days [range, 44-54 days] versus 3 days [range, 1-5 days], respectively,  $P < .001$ ). These children also more frequently received inhaled corticosteroids (90% versus 56%, respectively;  $P < .05$ ) and bronchodilators (70% versus 22%, respectively;  $P < .05$ ) during their first 2 years.

The gestational age and birthweight of control children were 40 weeks (range, 39-41 weeks) and 3460 g (range, 3385-3805 g), respectively.

### Morphologic and Functional Testing at 8 to 10 Years

VLBW and control children were assessed at 8.7 years old (range, 8.4-9.2 years).

Compared with control children, VLBW children had significantly lower weight (25.6 kg [range, 20.0-29.5 kg] versus 29.9 kg [range, 28.5-32.7 kg];  $P < .01$ ), height (127.0 cm [range, 122.8-133.0 cm] versus 135.5 cm [129.3-140.5 cm];  $P < .001$ ), and LBM (20.4 kg [range, 18.9-3.6 kg] versus 24.0 kg [range, 22.7-27.4 kg],  $P < .001$ ). No child had thoracic deformation.

### Respiratory Function at Rest

The VLBW children had significantly lower end tidal expiratory pressure of carbon dioxide ( $P_{\text{etCO}_2}$ ) (32.5 mm Hg [range, 30.8-35.6 mm Hg] versus 36.6 mm Hg [range, 35.9-37.6 mm Hg] in control subjects;  $P < .01$ ), and forced expiratory flow at 75% of forced vital capacity ( $FEF_{75\%}$ ). The other spirometric data and lung volumes were not significantly different in the groups (Table II).

Inspiratory muscle testing showed lower  $P_{i \text{ max}}$  in VLBW children compared with control subjects (82 cm H<sub>2</sub>O [range, 68-116 cm H<sub>2</sub>O] versus 112 cm H<sub>2</sub>O [97-159 cm H<sub>2</sub>O];  $P = .005$ ). Significant correlations were found between  $P_{i \text{ max}}$  and birthweight ( $r^2 = 0.566$ ,  $P < .001$ ), height ( $r^2 = 0.413$ ,  $P < .01$ ), LBM ( $r^2 = 0.525$ ,  $P < .001$ ), and forced expiratory volume in 1 second ( $FEV_1$ ,  $r^2 = 0.368$ ,  $P < .05$ ). With forward stepwise regression, only LBM was independently correlated with  $P_{i \text{ max}}$  ( $r^2 = 0.32$ ,  $P < .01$ ). When corrected for LBM,  $P_{i \text{ max}}$  was not significantly different between VLBW and control children ( $4.5 \pm 1.6$  cm H<sub>2</sub>O/kg versus  $5.3 \pm 2.0$  cm H<sub>2</sub>O/kg;  $P = .181$ ).

### Data at Submaximal Exercise

In the VLBW group, respiratory rate (RR) and minute ventilation indexed to LBM ( $VE_{\text{LBM}}$ ) increased more rapidly with carbon dioxide production indexed to LBM ( $VCO_{2 \text{ LBM}}$ ). This hyperventilation resulted in lower values of end  $P_{\text{etCO}_2}$  than in control group (Figure 1).

$TT_{0.1}$  increased more rapidly with oxygen consumption ( $VO_2$ ) in VLBW children compared with control subjects. This result was the direct consequence of the lower  $P_{i \text{ max}}$  in these children, because the occlusion pressure ( $P_{0.1}$ ) and the ratio of the inspiratory time to the total time of the breathing cycle ( $T_i/T_{\text{tot}}$ ) were comparable in the groups (Figure 2).

**Table II.** Respiratory function at rest in VLBW and control children

	Control n = 20	VLBW n = 19
FVC	98 (92-103)	104 (95-112)
FEV <sub>1</sub>	98 (92-103)	105 (94-110)
FEV <sub>1</sub> /FVC	101 (95-106)	100 (94-106)
FEF <sub>75%</sub>	96 (89-105)	85 (72-92)*
FEF <sub>50%</sub>	89 (80-107)	82 (75-98)
FEF <sub>25%</sub>	73 (62-101)	83 (55-96)
TLC	96 (91-106)	100 (94-109)
RV	108 (88-121)	100 (93-125)
RV/TLC (%)	106 (94-120)	107 (96-125)

FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 second; FEF<sub>75%, 50%, and 25%</sub>, forced expiratory flow at 75%, 50%, and 25% of forced vital capacity; TLC, total lung capacity; RV, residual volume.

Values are expressed as median (Q25-Q75) and are percent predicted for height, age, and sex. \* $P < .01$  with a Mann and Whitney rank sum test.

### Data at Maximal Exercise

The maximal workload was lower in VLBW children, but comparable with that of control subjects when expressed as a percentage of the maximal predicted workload.  $VO_{2 \text{ max}}$  and  $VCO_{2 \text{ max}}$  indexed to body weight or LBM, the first ventilatory threshold, and the ventilation data, including  $VE_{\text{LBM}}$ , RR, and  $VT_{\text{LBM}}$ , were comparable in the groups. The maximal heart rate (HR) was lower in the VLBW group, but the increase in HR with oxygen uptake ( $HR/VO_2$ ) was not different in the groups (Table III).

### Analyses in the VLBW Subgroups

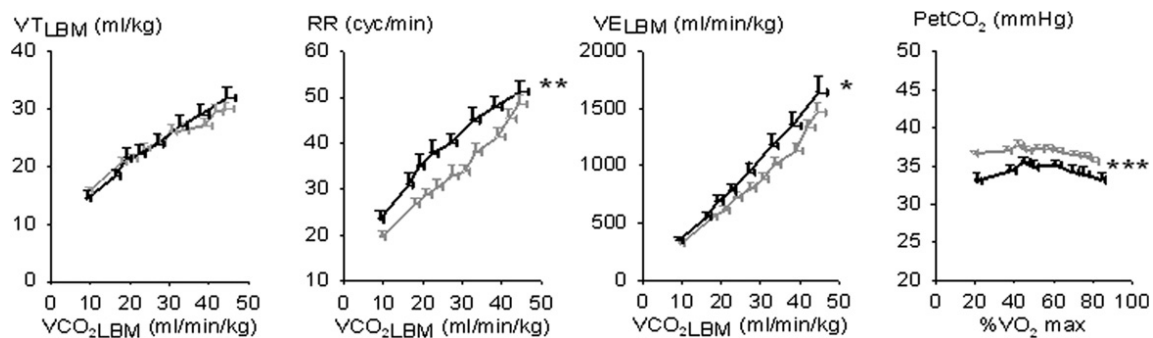
No difference was observed in anthropometric measurements, inspiratory muscle strength, respiratory function at rest, and performance at submaximal and maximal exercise between ex-preterm children with and without BPD.

### Physical Activity

There was no significant difference in the groups in weekly extracurricular physical activity: 2.0 hours/week (range, 1.0-2.9 hours/week) in VLBW children versus 1.0 hours/week (range, 0.1-2.0 hours/week) in control subjects ( $P = .25$ ). The estimate of the past year's energy expenditure calculated from the MAQ questionnaire was also comparable in the groups: 29.5 MET-hours per week (range, 12.7-71.8 MET-hours per week) in VLBW children versus 29.6 MET-hours per week (range, 4.2-88.2 MET-hours per week) in control subjects ( $P = .78$ ).

## Discussion

We report inspiratory muscle function in the interpretation of long-term respiratory outcome of VLBW children. At school age, their respiratory function at rest and their exercise performance as evaluated by  $VO_{2 \text{ max}}$  were not altered. However, their lower maximal inspiratory muscle strength required greater inspiratory effort, which may explain the rapid but not shallow breathing during submaximal exercise and be responsible for respiratory discomfort. We recommend that the



**Figure 1.** Breathing pattern during submaximal exercise in VLBW (in *black*) and control (control, in *gray*) children. At each exercise power, VT, RR, minute ventilation (VE),  $PetCO_2$ , carbon dioxide production ( $VCO_2$ ), and oxygen consumption ( $VO_2$ ) were measured. VT, VE and  $VCO_2$  were indexed to LBM. Each *dot* represents the mean value of each variable measured at an exercise power. \* $P < .05$ . \*\* $P < .01$ . \*\*\* $P < .001$  using a linear mixed model.

exploratory studies of VLBW children complaining of dyspnea during exercise systematically include the measure of  $P_{i\ max}$  to enhance the interpretation of exercise tests.

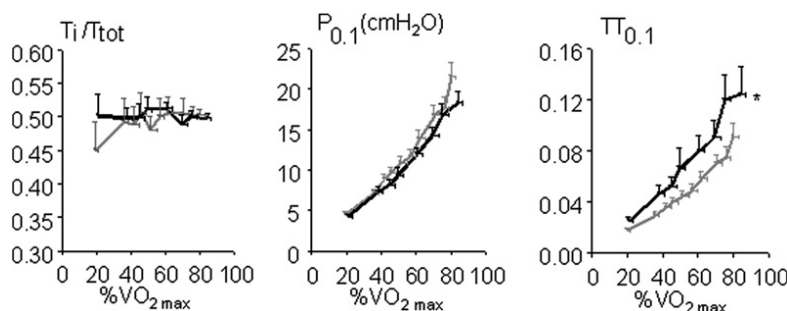
Although the average age of the children was 9 years, this cohort was representative of the current treatment of VLBW infants, because approximately 80% of them had received antenatal corticosteroids and postnatal surfactant treatments. Our inclusion criteria were chosen to test whether the severity of neonatal respiratory disease was correlated with more severe long-term respiratory outcomes. This hypothesis required the selection of VLBW children with less severe respiratory distress, explaining the trend toward shorter mechanical ventilation and supplemental oxygen exposure compared with all the VLBW survivors. However, our sample had risk factors comparable with those of the entire cohort of chronic lung disease, including intrauterine growth restriction, chorioamnionitis, and male sex, and a similar respiratory outcome during their first 2 years.<sup>20</sup>

The decrease in  $FEF_{75\%}$  only, with no other differences in pulmonary flows or volumes at rest, probably had little clinical relevance. Earlier studies in children of comparable age have reported a higher prevalence of airway obstructive disease and gas trapping, with lower  $FEV_1$  and forced vital capacity and higher residual volume and FRC in

ex-premature children compared with term-born children.<sup>6-8</sup> The nearly normal respiratory function at rest observed in our VLBW cohort may be explained by the higher rates of prenatal corticosteroid therapy, postnatal surfactant administration, and shorter periods of invasive mechanical ventilatory support than in earlier studies in children born before 1995. However, we recently reported that BPD in a similar population of VLBW children born in our center was associated with higher respiratory resistance, lower compliance, and lower forced vital capacity at the age of 9 months.<sup>21</sup> There are very few longitudinal studies on the respiratory outcome of VLBW children, but some also indicate an improvement in lung function with increasing age.<sup>22,23</sup>

Consistent with earlier studies, we found that exercise performance, as evaluated with  $VO_{2\ max}$  per kg and the maximal power expressed in percentage of the predicted maximal power, were not significantly different between VLBW children and control children.<sup>7</sup> Contradictory conclusions have been drawn about  $VO_{2\ max}$  in ex-preterm children, probably linked to the heterogeneous neonatal characteristics and physical activity levels in the previously studied cohorts.<sup>14</sup>

In the study of Pianosi et al, a lower  $VO_{2\ max}$  indexed to body weight was recorded in VLBW children, but the  $VO_{2\ max}$  of their VLBW cohort was within the reference range, and the



**Figure 2.** Inspiratory muscle performance during submaximal exercise in VLBW (in *black*) and control (control, in *gray*) children. Each *dot* represents the mean value of each variable measured at an exercise power.  $T_i/T_{tot}$ , ratio of inspiratory time to total time of the breathing cycle. \* $P < .05$  using a linear mixed model.

**Table III.** Power, gas exchange, breathing pattern, and cardiac parameters at maximal exercise in VLBW and control children

	Control n = 20	VLBW n = 19
Power (W)	110 (100-120)	90 (70-90) <sup>†</sup>
Power (% predicted)	99 (85-116)	99 (84-106)
VO <sub>2</sub> BW (ml/min/kg)	45.2 (41.7-51.3)	45.4 (37.6-55.8)
VO <sub>2</sub> LBM (ml/min/kg)	56.7 (52.7-62.1)	56.4 (51.0-64.9)
VCO <sub>2</sub> BW (ml/min/kg)	46.1 (41.5-53.3)	43.4 (34.8-51.1)
VCO <sub>2</sub> LBM (ml/min/kg)	56.7 (53.1-66.9)	51.0 (47.0-64.3)
RER	1.02 (0.93-1.03)	0.98 (0.88-1.03)
ΔVO <sub>2</sub> /ΔW (mL/min/W)	12.0 (11.3-13.9)	12.3 (11.0-14.2)
VE <sub>LBM</sub> (L/min/kg)	45.2 (41.7-51.3)	45.4 (37.6-55.8)
RR (cyc/min)	54 (49-64)	60 (49-67)
V <sub>T</sub> LBM (mL/kg)	33.9 (31.0-37.0)	30.8 (26.7-33.4)
V <sub>T</sub> LBM/T <sub>i</sub> (mL/kg/s)	62.9 (57.6-68.5)	58.7 (43.9-67.4)
V <sub>E</sub> /VO <sub>2</sub>	30.5 (29.0-34.6)	29.2 (24.5-36.1)
V <sub>E</sub> /VCO <sub>2</sub>	31.6 (29.3-34.6)	32.2 (28.4-34.7)
HR (beat/min)	191 (182-193)	176 (168-187)*
HR/VO <sub>2</sub>	9.4 (7.9-10.2)	10.8 (8.0-12.4)
First ventilatory threshold (%VO <sub>2</sub> max pred)	72.3 (65.0-76.8)	66.0 (61.0-73.5)

VO<sub>2</sub>, oxygen consumption; VCO<sub>2</sub>, carbon dioxide production; RER, respiratory exchange ratio (VCO<sub>2</sub> max/VO<sub>2</sub> max); VE, minute ventilation; T<sub>i</sub>, inspiratory time. Values were indexed to body weight, LBM, or both.

The first ventilatory threshold was determined by the first increase in the slope of the relationship between VE and VCO<sub>2</sub>. Values are expressed as median (Q25-Q75) or percent predicted for height, age, and sex.

\*P < .01.

†P < .001 with a Mann and Whitney rank sum test.

physical activity level of their control population was not mentioned.<sup>5</sup> The lower VO<sub>2</sub> max found by Welsh et al in the EPICure population at the age of 11 years is quite specific, because this study was designed to assess the outcome of the most immature neonates, born before 25 weeks of gestational age.<sup>8</sup>

We did not find peripheral muscular limitation in the VLBW children. Consistent with other studies performed at a similar age,<sup>5-7</sup> the first ventilatory threshold was comparable between the VLBW and control groups, suggesting similar physical activity levels.<sup>6</sup> The physical activity level estimated by the French version of Kriska's MAQ showed no significant difference in the groups. Vrijlandt et al found a lower ventilatory threshold in their VLBW young adult cohort, consistent with fewer hours of exercise per week.<sup>9</sup>

Finally, there was no difference in minute ventilation, RR, or tidal volume (VT) at maximal exercise in the groups. At maximal exercise, ventilation is mainly dependent on a chemical stimulus, metabolic acidosis, caused by predominant anaerobic metabolism. In practice, the individual data of each patient showed a second inflection point in the VE<sub>LBM</sub>/VCO<sub>2</sub> LBM ratio, indicating that the second ventilatory threshold had been reached. We suggest that the stimulation of the respiratory center by metabolic acidosis was comparable in the two groups.

During submaximal exercise, below the point of lactate accumulation (also called the second ventilatory threshold), ventilation is dependent on carbon dioxide production and the neural drive from the respiratory center.<sup>24</sup> Thus, submaximal exercise reveals differences in ventilatory adaptation to exercise that may be masked by the metabolic acidosis that

occurs during the maximal phase. In our study, the ventilatory adaptation of the VLBW children during submaximal exercise was characterized by hyperventilation, with lower PetCO<sub>2</sub>. The ventilatory response was not appropriate for the metabolic demand, as suggested by the higher increase in VE<sub>LBM</sub> with VCO<sub>2</sub> LBM compared with control subjects. A lower CO<sub>2</sub> set point may have contributed to the greater values of VE<sub>LBM</sub> observed in the VLBW children. This hypothesis could be tested in further studies with a rebreathing method during exercise, as used in healthy children and children with cystic fibrosis by Pianosi and Wolstein.<sup>25</sup> However, although this physiological process was plausible to explain the higher values of VE<sub>LBM</sub> in the VLBW children, it failed to explain why only breathing frequency was higher, whereas VT<sub>LBM</sub> was comparable in the groups.<sup>26</sup>

For this hyperventilation, we confirmed that the VLBW children adopted rapid but not shallow breathing<sup>5</sup> during exercise, characterized by normal VT and higher RR. However, earlier studies described a different breathing pattern adaptation during exercise with rapid and shallow breathing.<sup>7,8</sup> The discrepancy could be explained by more severe neonatal respiratory disease in these cohorts. Our VLBW cohort had no obstruction at rest. Consistent with this finding, VT, respiratory timing, and the mean inspiratory flow rate were within reference ranges and not different from control values. We thus hypothesized that our VLBW children did not have alveolar hyperinflation during exercise.

In the term-born children, the values of P<sub>i</sub> max at rest showed a range and dispersion similar to those described in the literature by Gaultier and Zinman for children of comparable age with the same measurement method.<sup>27</sup> However, the VLBW children had significantly lower P<sub>i</sub> max. Maximal respiratory pressure measurement can be affected by several factors, including anthropometric characteristics, sex, age, and alveolar hyperinflation.<sup>12</sup> We did not observe any difference in the groups for age, sex, or FRC. A significant correlation was observed between P<sub>i</sub> max and height, body mass index, and LBM, but only this last variable was independently correlated with P<sub>i</sub> max. Thus, the decrease in LBM may be the main explanatory factor of the lower inspiratory muscle strength observed in the VLBW children. For the same exercise intensity, the VLBW children had higher TT<sub>0.1</sub> values. Because of the comparable changes in P<sub>0.1</sub> and T<sub>i</sub>/T<sub>tot</sub> during exercise in our 2 groups, we concluded that this result was the direct consequence of their lower inspiratory muscle strength (P<sub>i</sub> max).

The rapid but not shallow breathing pattern observed in our VLBW cohort may be explained by a greater susceptibility to inspiratory muscle fatigue. For the same exercise intensity, the VLBW children had to sustain a higher relative inspiratory load at each breath than the control subjects. As a consequence, their inspiratory muscles were probably more susceptible to fatigue. Although we were not able to directly measure inspiratory muscle fatigue, we suggest that neural inputs from the fatiguing inspiratory muscles of VLBW might stimulate the central respiratory drive, resulting in the rapid, but not shallow, breathing

strategy observed in adults during maximal exercise.<sup>11,28</sup> Moreover, inspiratory muscle weakness may lead to breathing discomfort.<sup>29</sup> In Welsh's study, ex-premature children perceived themselves as less capable of exercise than their friends and perceived more difficulty in breathing during daily exercise than control subjects.<sup>8</sup> Further studies are required to assess the relationship between inspiratory muscle strength and dyspnea during maximal exercise testing in VLBW children. ■

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**Table I.** Perinatal characteristics of the included and the non-included VLBW children

	Included patients n = 19	Non-included patients n = 32
Chorioamnionitis, n (%)	6 (32%)	9 (28%)
Antenatal steroids, n (%)	15 (79%)	29 (91%)
Gestational age, weeks	27 (26-27)	27 (26-27)
Birthweight, g	850 (730-1000)	880 (757-1020)
SGA, n (%)	8 (42%)	9 (28%)
Male, n (%)	7 (37%)	19 (59%)
Persistent ductus arteriosus, n (%)	6 (32%)	8 (25%)
Invasive mechanical ventilation, days	5 (2-12)	10 (5-22)
Supplemental oxygen, days	21 (4-50)	42 (4-69)
At 36 weeks PMA		
Supplemental oxygen, n (%)	3 (16%)	10 (31%)
nCPAP, n (%)	0	1 (3%)

SGA, small for gestational age; PMA, postmenstrual age; nCPAP, nasal continuous positive airway pressure.

Values are median (Q25-Q75) or absolute frequencies (percentage).

None of the differences between groups was significant.