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Anomalous relationship of heart rate to oxygen consumption in children with hemiplegic cerebral palsy.

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Abstract

Background: Co-contraction and spasticity may distort the normal relationship between heart rate and oxygen consumption in cerebral palsy. *Purpose:* To compare cardio-respiratory responses to sustained isometric exercise (SET) at 50% of maximal torque between children with hemiplegic cerebral palsy (CP) and healthy controls. *Methods:* Participants were 10 children with right-sided CP (nine males, one female; age 13 ± 2 years), and 10 age- and sex-matched controls. Muscle volumes were determined by anthropometry, isometric torques were measured by Cybex Norm II dynamometer, and the Cosmed K4b2 metabolic telemeter recorded respiratory gas exchange. *Results:* In children with hemiplegic CP, both affected and unaffected legs had a reduced muscle volume and a low absolute maximal isometric torque. When expressed per litre of muscle volume, torque was reduced in the affected leg, but was normal for the unaffected leg. Oxygen consumptions during SET at 50% of maximal torque were also disproportionately high relative to heart rate and ventilation, whichever leg was being tested. *Conclusions:* During SET, the oxygen consumption is disproportionately high relative to heart rate and ventilation in CP. The added oxygen consumption probably reflects co-contraction and spasticity in muscles where blood flow is not restricted by the primary contraction. This issue complicates estimates of oxygen consumption from heart rate during isometric effort, and may also modify the heart rate/oxygen consumption relationship during aerobic activity. **Health & Fitness Journal of Canada 2014;7(1):14-25.**

Keywords: Co-contraction; Heart rate predictions; Isometric Testing; Rehabilitation; Spastic contractions; Sub-maximal testing

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Introduction

Exercise physiologists commonly use heart rate as a simple method of assessing the intensity of exercise in their clients. During aerobic exercise, there is normally a relatively linear relationship between heart rate and oxygen consumption over the range 50-95% of maximal oxygen intake (Shephard, 1982), although this index becomes unreliable in those with a pacemaker, after the administration of beta-blocking agents and in individuals with other disturbances of autonomic activation. During isometric activity, also, the increase of heart rate is normally proportional to the relative intensity of muscular contraction, with weaker individuals showing a greater increase of heart rate at any absolute increment of muscle force. Children with cerebral palsy (CP) show substantial muscle weakness (Damiano et al., 2000; Engsborg et al., 2000; Ross et al., 2002), and the question thus arises how far heart rate remains a useful marker of increases of oxygen consumption when children with CP undertake muscular activity.

This brief report documents the heart rate/oxygen consumption relationship during isometric exercise in a small sample of children with hemiplegic CP, and it examines both the light that this relationship sheds upon the origins of

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muscular weakness and possible approaches to restoration of more normal function. We have examined maximal voluntary isometric force in relation to anthropometric estimates of muscle volume, and cardio-respiratory responses to sustained contraction at 50% of maximal isometric force. Data for both affected and unaffected legs, collected in children with hemiplegic CP (Gross Motor Function Classification System levels I and II, Palisano et al., 1997; 2007), have been compared with age- and sex-matched values for healthy peers. Our primary working hypothesis was that if performance in CP was substantially hampered by muscle spasticity and co-contraction, then the increase of oxygen consumption during a sustained isometric contraction at a given fraction of maximal force would be disproportionate to the heart rate and ventilatory response.

Methods

Participants

Participants were 9 boys and 1 girl with right-sided CP and 10 age- and sex-matched controls drawn from a public school in Amiens (Tables 1 and 2). Children and parents were informed about all aspects of the study, and written consent was obtained for a protocol approved by the local ethics committee, in accordance with the Helsinki Declarations of 1975 and 1983. Children were excluded if they had undergone a surgical procedure influencing functional mobility during the past year, or were taking medication that could affect muscular function. All children with CP were independently ambulatory and were classified as Gross Motor Function Classification System levels I and II (as expanded and revised for children > 12 years)(Palisano et al., 1997; 2007),

although two children wore ankle-foot orthoses. A physician assessed the spasticity of each child, using the method of Ashworth (1964). Maturity was assessed by Tanner staging (Worley et al., 2002; Henderson et al., 2006).

Table 1: Clinical characteristics and sex of children with hemiplegic cerebral palsy. In all cases the hemiplegia affected the right limb. The Gross Motor Function Classification System (GMFCS) was used (Palisano et al., 1997; 2007), and spasticity was rated by the attending physician on a scale of 1-2 using the method of Ashworth (1964).

Subject	GMFCS	Degree of Spasticity	Knee Joint angle (°)	Sex
1	I	2	45	girl
2	I	1	60	boy
3	II	2	57	boy
4	I	1	70	boy
5	I	2	68	boy
6	I	1	45	boy
7	II	1	70	boy
8	I	1	80	boy
9	II	1	60	boy
10	I	1	68	boy

Anthropometric Measurements

Standing height, body mass, and body mass index were determined by standard anthropometric techniques. Fat mass, limb volumes and limb muscle volumes for the legs were estimated from the individual's leg length (L), skin fold thicknesses (S, measured over the mid-thigh and mid-calf), 5 limb circumferences (C, ankle, mid-calf, knee, mid-thigh and groin), and the skinfold-corrected inter-condylar diameter (D), as detailed elsewhere (Shephard et al., 1988; Samson-Fang et al., 2000):

$$\text{Total leg volume} = (\sum C^2) L / 62.8$$

$$\text{Leg fat volume} = (\sum C / 5) (\sum S / 4) L$$

$$\text{Bone volume} = (0.235D)^2 3.14L$$

$$\text{Muscle volume} = \text{Total leg volume} - (\text{fat} + \text{bone volumes})$$

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Muscle Function Assessment

Maximum voluntary isometric force and static endurance time at 50% of maximum force were determined using a Cybex dynamometer (Cybex Norm II; Lumex Inc., Ronkonkoma, NY)(Nsenga Leunkeu et al., 2009; 2010). Several studies have established the safety of such testing in CP (Damiano et al., 2000; 2002; Nsenga Leunkeu et al., 2010). Chest and knee strapping maintained a consistent position; controls were tested at knee and hip angles of 60° and 120° respectively; angles for children with CP varied slightly, depending on available joint ranges. A practice trial ensured that the child understood procedures before definitive evaluations were made. Three sets of 5 maximal contractions were then performed. Verbal encouragement was provided and the child watched the force developed on a computer monitor. A 20-sec recovery interval was allowed for each repetition, and a 1-minute interval for each set of contractions. The maximal force was considered as the average of the highest readings from each of the 3 sets.

During the static endurance test, children maintained the contraction at a computer reference mark corresponding to 50% of their personal maximal force. Timing began as soon as the target force was attained, and subjects were informed of the elapsed time every 15 seconds. The test was halted when the child could no longer maintain the contraction within 5% of the target value. A final 3 minutes of passive recovery was allowed following such testing.

Cardio-respiratory Measurements

Cardio-respiratory measurements were made during Cybex testing. All tests followed an identical protocol;

measurements were made in the same laboratory, at the same time of day, with a physician always in attendance. Oxygen consumption ($\dot{V}O_2$), heart rate (HR) and ventilation ($\dot{V}E$), during the static endurance test were monitored using a Cosmed K4 gas analyzer (Cosmed Srl, Rome, Italy). Inspiratory air flows and expired gas concentrations were computed from the final breathing cycles of each minute, and peak values were established for oxygen consumption, heart rate, and respiratory minute volume. Tests ended when the force developed by the subject dropped more than 5% below the target value.

Statistical Analyses

All data were analyzed using StatView Software (SAS Institute Inc, SAS Campus Dr, Cary, North Carolina 27513, USA). Statistical significance was set at $p < .05$ throughout. Values are expressed as means \pm SDs. Comparisons between affected and unaffected limbs and between children with CP and control children were made by analyses of variance (ANOVA), and a Schéffe *post-hoc* test was used to identify significant differences.

Results

Physical and Anthropometric Characteristics

There was no significant difference of age between those with CP (13.0 ± 1.0 years) and controls (14.0 ± 0.6 years). Tanner staging showed a similar average maturity status (Stage 2) for both groups.

The children with CP were shorter than the controls (1.49 ± 0.12 vs. 1.65 ± 0.09 m, $p < .01$). They also tended to have a lower body mass (44 ± 9 vs. 55 ± 11 kg, ns), although body mass indices were more comparable for the two groups

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(19.7 ± 2.7 vs. 18.5 ± 2.9 kg.m⁻², ns).

The fat content of the paralyzed leg was greater than that of either the unaffected leg ($p < .05$) or the right leg of control subjects ($p < .01$); however, the fat content of the unaffected leg did not differ from control data (Table 2). The estimated total leg volume and muscle volume were lower in the affected leg than in either the unaffected leg or the right limb of control subjects ($p < .05$ and $p < .01$, respectively), and volumes also differed significantly between the unaffected leg and the right limb of control subjects (Table 2).

Table 2: Anthropometric characteristics of subjects (mean \pm SD).

Variable	Control Subjects (n =10)	Children with Cerebral Palsy (n =10)	
	Right leg	Unaffected leg	Affected leg
Leg fat (%)	13.7 \pm 6.0	12.5 \pm 5.8	18.9 \pm 5.2 *
Leg volume (L)	11.3 \pm 2.2	9.2 \pm 1.8*	8.3 \pm 2.3 *
Leg Muscle Volume (L)	7.4 \pm 2.4	5.6 \pm 1.6*	5.0 \pm 1.7 **
* p< 0.01 **p< 0.001			

Muscle function. *Maximal Voluntary Isometric Torque.* Whether considering data for the affected leg (62.8 ± 11.0 Nm) or the unaffected leg (115.0 ± 18.5 Nm), the children with CP developed a much lower quadriceps maximal voluntary torque than that seen in control subjects (171.1 ± 23.8 Nm) ($p < .0001$ and $p < .01$, respectively) (Fig. 1A). Maximal torque values were also significantly smaller for the affected than for the

unaffected leg ($p < .01$). However, there were no significant inter-group differences in endurance times at 50% of maximal isometric effort.

Maximal voluntary isometric force per litre of muscle volume

The deficit of maximal isometric force observed in the affected leg persisted when data were expressed per liter of muscle in the lower limb: affected leg versus control ($p = .004$), affected versus unaffected leg ($p = .021$). However, data for the unaffected limb did not differ significantly from control values (Fig. 1B).

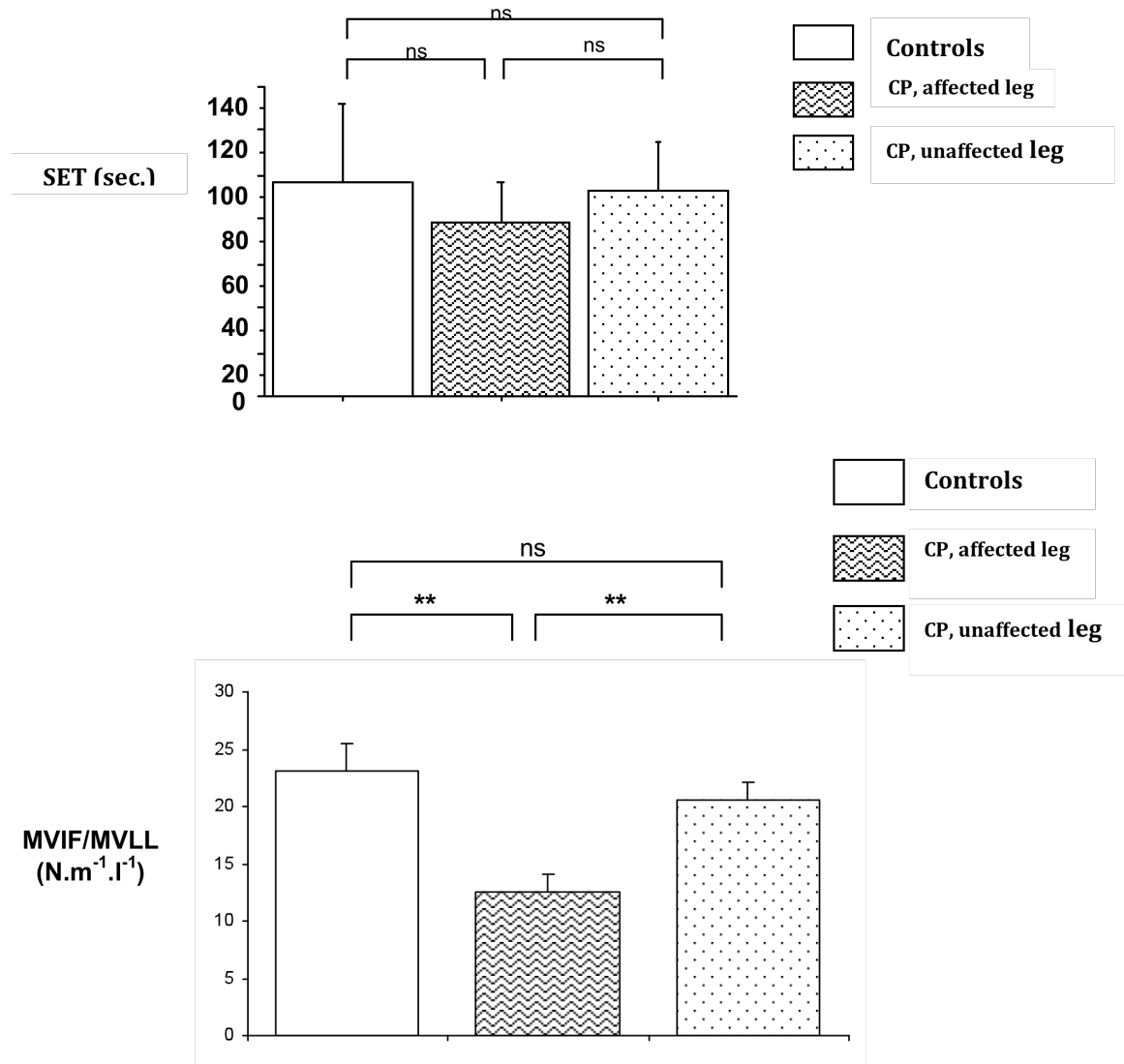
Cardio-respiratory data

Oxygen consumption values for the final 30 s of static effort showed no inter-group differences when contractions were maintained at 50% of maximal effort, despite the much lower force being developed by the children with CP. However, heart rates were lower in the children with CP than in controls (when using the affected leg, $p < 0.05$; when using the unaffected leg, $p < 0.05$), although heart rates were similar whether the isometric effort was made by the affected or the unaffected leg.

The respiratory minute volume during static effort was also lower in children with CP than in controls (affected leg, $p < 0.001$; unaffected leg $p < 0.01$). On the other hand, respiratory minute volumes were similar whether isometric efforts were made by the affected or the unaffected leg (Fig. 2).

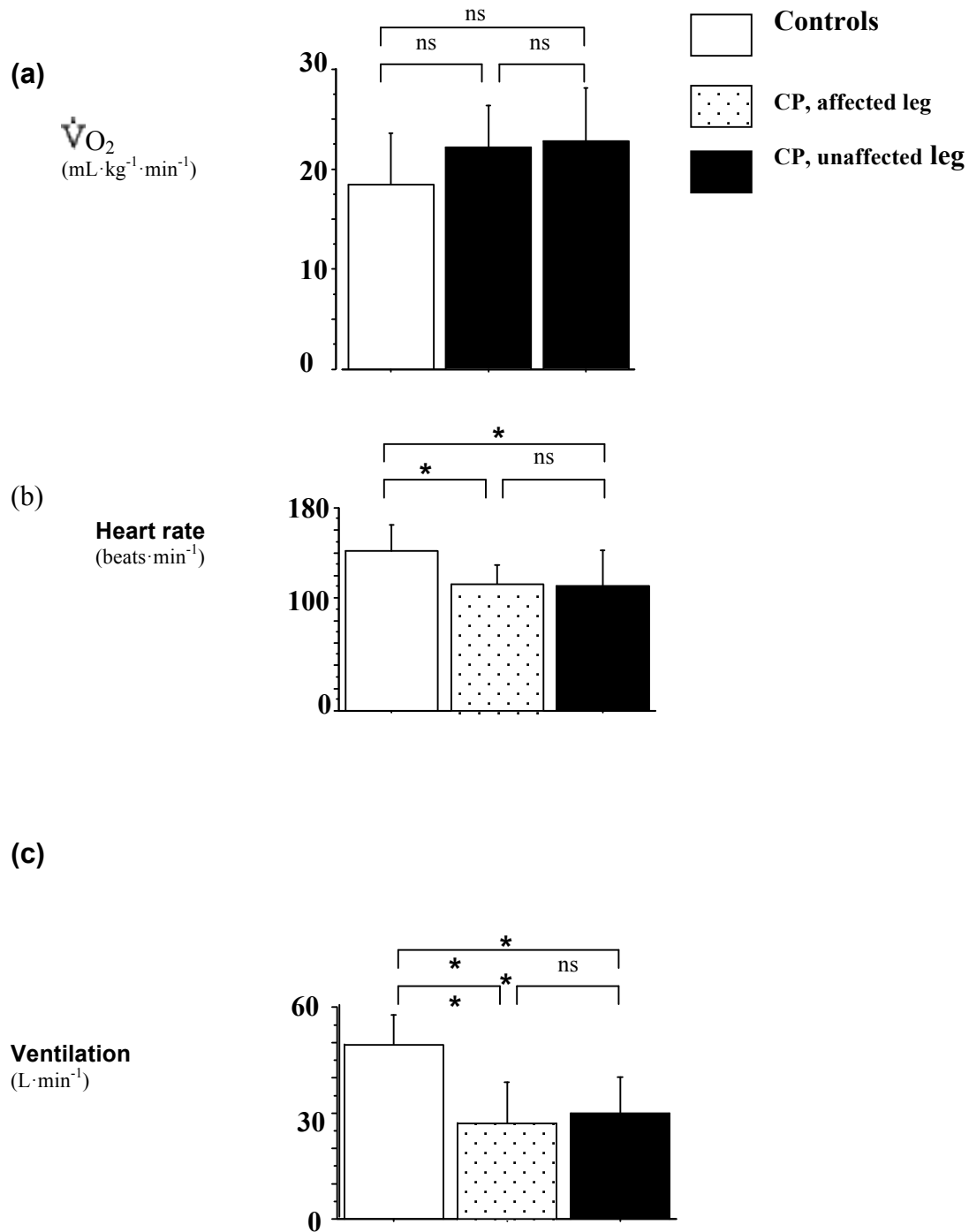
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Figure 1: (A) Endurance times (SET, sec) and (B) maximal voluntary isometric torque of quadriceps muscle expressed per litre of muscle volume (MVIF/MVLL) during contractions at 50% of maximum voluntary isometric torque in children with cerebral palsy (CP) (data for affected and unaffected legs) and controls (data for right leg). Mean \pm SD. ns = not significant, ** = $p < 0.01$.



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Figure 2: Peak cardio-respiratory values during static endurance test at 50% of maximum voluntary isometric force for controls and children with cerebral palsy (CP): (a) oxygen consumption ($\dot{V}O_2$) (b) heart rate, (c) respiratory minute ventilation (means \pm SD). ns = not significant, * = $p < 0.05$.



Discussion

Isometric Muscle Strength and Volume

Estimates of muscle volumes in chronic conditions such as CP and chronic respiratory disease have been criticized, whether based on anthropometry or on more sophisticated techniques such as DXA (Mathur et al., 2008; Modlesky et al., 2010). Anthropometric estimates are somewhat vulnerable to retarded bone development, since muscle volume is obtained by subtracting bone volume from total limb volume. Nevertheless, our data underline that the method is adequate to show a significant difference of muscle volumes between control limbs and the affected limbs of children with hemiplegic cerebral palsy. In accord with the earlier observations of Elder et al. (2003), Samson-Fang et al. (2000), van den Berg-Emons et al. (1998) and Van Mil et al. (1996), values for the affected limb were smaller than those for either control subjects or for the unaffected limbs of the children with CP.

The children with CP also had substantially lower leg strength than their peers. Was this simply an expression of low levels of habitual physical activity (and thus potentially susceptible to rehabilitation), or did the poor performance reflect some combination of a reduced activation of prime movers, spasticity and co-activation of antagonist muscles (Damiano et al., 2000; Ross and Engsborg, 2002; Elder et al., 2003; van den Linden et al., 2004; Stackhouse et al., 2005)? When data for the unaffected limb were expressed per unit of muscle volume, values were normalized, suggesting that weakness was entirely attributable to under-development and/or muscle wasting. Our patients were all attending a school for students with special needs, and were involved in a

variety of forms of regular physical activity such as swimming, cycling, handball, walking and horse riding, but repeated immobilization mandated by multiple operative procedures may nevertheless have brought about some loss of lean tissue in these children (Chad et al., 2000).

The force per unit volume of muscle was also low in the affected limb, emphasizing the added role of other factors, including some possible effects from the altered knee angle, together with inability to activate the muscles maximally (Elder et al., 2003), co-contraction, increased stretch reflexes and muscle tone, and diminished motor control. All of these factors probably reduce the capacity to perform vigorous movements in the affected limb (Chad et al., 2000), and our clinical experience suggests that such issues may be even more important in rhythmic contraction than during an isometric test (van den Linden et al. (2004).

Muscular Endurance

The static endurance time at 50% of the individual's maximal voluntary torque was essentially unchanged in CP, although it must be underlined that when using the affected leg, the children with CP were developing only about a half of the torque realized by the controls. Because of a combination of reduced muscle volume and a lower maximal aerobic power (Nsenga Leunku et al., 2012), we may presume that the concentration of metabolites that eventually leads to a cessation of effort was increasing at much the same rate as in a healthy child, despite the weaker muscular effort that they were making. This in turn might suggest that cardio-respiratory training could enhance the ability of a child with CP to sustain

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isometric contractions.

Cardio-respiratory Responses to Exercise

The present findings support our main hypothesis in showing that despite a much smaller limb volume and lesser muscle strength, the oxygen consumption during a sustained isometric contraction at a given percentage of maximal isometric force was as at least as high in children with CP as in control subjects. Although the oxygen consumption that is attained reflects important aspects of the child's overall functional ability (Buckon et al., 2002), it does not provide an accurate index of the isometric effort developed with respect to the required task. Seemingly normal oxygen consumption was attained despite the fact that the children with CP were developing a substantially lower isometric force than their peers. Moreover, the cardiovascular and ventilatory responses to the isometric effort were much less than would have been anticipated from the observed oxygen consumption. This disparity is particularly surprising, given the low level of aerobic fitness in children with this condition (Nsenga Leuenku et al., 2009, 2012). Further, we observed no significant difference of resting values for heart rate or respiration between children with CP and the control subjects, and it thus seems unlikely that the lesser cardio-respiratory response to exercise could be explained on this basis.

In the healthy child, the heart rate and ventilation increase more during isometric contraction than during a similar intensity of rhythmic exercise, because during a vigorous isometric contraction there is difficulty in perfusing the tensed muscles; the resulting pressor reflexes stimulate a strong cardio-

respiratory response (Shephard, 1982). The most plausible explanation of our findings in the children with CP is that when such a child makes an isometric effort, a part of the total observed oxygen consumption is arising not from the isometric contraction itself, but rather from muscle spasticity and a greater than normal co-contraction of other muscle groups. In the children with CP, perfusion of the isometrically contracting muscle occurs more readily than in controls, in part because a much lower force is developed; compression of the muscle arteries is therefore less and pressor reflexes are correspondingly smaller. Moreover, a much larger part of the observed oxygen consumption is likely being incurred by co-contraction and spasticity in other muscle groups, where blood flow is not impeded by an isometric contraction. This same factor could explain why fatiguability of repeated contractions at a given fraction of peak torque is less in children with CP than in normal individuals, and is linked to the extent of weakness, spasticity, co-contraction and stiffness (Moreau et al., 2007; 2008).

A part of the rise of heart rate during vigorous endurance exercise also arises from difficulty in perfusing the active muscles, and it will thus be interesting to examine children with CP to determine whether the heart rate/oxygen consumption relationship is abnormal during endurance activity, leading to errors in the prediction of maximal oxygen intake from sub-maximal data.

Overall Health

Often, CP is characterized by poor overall health, with impaired growth, nutritional impairment (Fung et al., 2002), a risk of osteopenia and overall

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changes in body composition (Chad et al., 2000). However, this was not a major issue in our sample; indeed, the children with hemiplegia had a relatively normal body mass index. But despite an equivalent level of maturity on the Tanner scale, our subjects were significantly shorter than the controls, as others have noted previously (Van den Berg-Emons et al., 1998; Chad et al., 2000; Samson-Feng and Stevenson, 2000). This is probably due in part to postural abnormalities and/or weakness and contracture of the affected limb. In our subjects, the limb that was affected by CP tended to be both shorter and slimmer than the unaffected limb.

Practical Implications

Given that the children with CP that we tested were already engaged in a vigorous physical activity programme yet showed substantial weakness in both affected and unaffected limbs, we would agree with Eek (2009) and Scianni et al; (2009) that it is often a difficult matter to increase their muscular strength. Although attempts have been made to enhance performance through better coordination, increased recruitment of motor units and/or an increased firing rate, this would plainly be of little help in the unaffected leg, where the force per unit of muscle volume already does not differ significantly from normal. Here, improvement could only come from a stimulation of muscle growth, whether by a rigorous programme of resisted exercise or enhanced nutrition. Such measures might be beneficial in the affected leg, but if (as we suspect) surgical immobilization is also a factor, this should be kept to a minimum, possibly with electrical stimulation of the limb muscles during periods when the leg is

immobilized.

Limitations

Our sample of patients was relatively small, but nevertheless it was sufficient to demonstrate differences in the relationship of heart rate and ventilation to oxygen consumption between normal children and those with CP. The duration of the isometric effort was also relatively short, so that subjects did not achieve a total steady state, but since endurance times were similar for those with CP and for the control subjects, this seems unlikely as a source of the greater relative oxygen consumption in the children with CP. Both patient and control groups only included one girl, and given the difference in pubertal development of strength between the two sexes, it remains necessary to examine how far our findings will be replicated in female subjects. There is also a need to extend observations to other age groups and to those with differing degrees of disease severity, relating the extent of the excess oxygen consumption to objective data on each individual's spasticity. Finally, more information is needed regarding the possible influence of altered knee joint angles on the force developed in those with CP.

Conclusions

In children with hemiplegic CP, both the affected and the unaffected legs show a smaller muscle volume and a reduced maximal isometric force relative to control subjects. The disadvantage of the unaffected limb disappears if data are expressed relative to muscle mass, showing the influence of muscle wasting. However, in the affected limb, the force developed is also low per unit volume of muscle, underlining other causes such as

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repeated immobilization, spasticity, excessive co-activation of antagonists, increased joint stiffness, poor coordination, inadequate recruitment of motor units and/or an inappropriate firing rate. The isometric endurance time at a fixed fraction of the individual's maximal isometric force does not differ substantially between those with CP and controls; the absolute effort exerted by those with CP is much smaller, but the oxygen intake is similar to that of control subjects, and is high relative to cardiac and ventilatory responses. Additional oxygen consumption is incurred from co-contraction and spasticity, distorting the anticipated relationship of heart rate to oxygen consumption. The reduced muscle volumes point to scope for improvement of muscle function by rehabilitation, although this is unlikely to reverse the adverse effects of spasticity and co-contraction.

Authors' Qualifications

The authors' qualifications are as follows: Angeline Nsenga Leunkeu: Ph.D.; Roy J. Shephard: M.B.B.S., M.D. [Lond.], Ph.D., D.P.E., LL.D., D.Sc., F.A.C.S.M., F.F.I.M.S.; Said Ahmaidi: PhD, P.U.

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