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Reproducibility of energy cost of locomotion in ambulatory children with spina bifida☆

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ABSTRACT

Objectives: Many ambulatory children with Spina Bifida (SB) experience functional decline in ambulation despite stable or even improving motor exams. Improving or maintaining low energy cost of locomotion during childhood and throughout the teenage years, could be an important goal for children and adolescents with SB. Purpose of this study was to determine reproducibility of energy expenditure measures during gait in ambulatory children with SB.
Design: Reproducibility study.
Setting: Child Development and Exercise Center of the University Children's Hospital in Utrecht, the Netherlands.
Participants: Fourteen ambulatory children (6 boys/8 girls) with SB. Mean age was 10.8 years (±3.4).
Interventions: Net and gross energy expenditure measures during locomotion were determined during a six-minute walking test. These measures consisted of energy consumption (ECS), expressed in J/kg/min, and energy cost (EC), expressed in J/kg/m. For reliability, the intra-class coefficient (ICC) was determined. For agreement, the smallest detectable difference (SDD) was calculated.
Results: ICCs vary from 0.86 to 0.96 for both EC and ECS. The SDD ranges from 18–24% for gross measures, up to over 30% for net values.
Conclusion: Reproducibility of energy expenditure during ambulation in children with SB should be considered carefully when using these measures in the evaluation of gait. High reliability of energy expenditure measurements makes these measurements appropriate to use as discriminative tools in children with SB, while agreement of only gross EC seems acceptable to use as a evaluative tool in children with SB. Overall, measures of reliability and agreement seem higher in young children when compared to adolescents. Further research is recommended to determine clinically relevant changes in energy expenditure in children with SB.

1. Introduction

Spina bifida (SB) is the most frequent congenital deformity of the neural tube, with an incidence of approximately one per 1000 live births [1,2]. Depending on both the type and level of lesion of the SB, patients experience a variety of deficits in cognition, motor function, sensory function and bowel and bladder function [3]. Besides medical classification according to type, lesion level and presence of hydrocephalus, children are functionally classified using the adapted Hoffer classification [4]. In this classification community ambulatory children are distinguished from normal ambulatory children, based on the use of a wheelchair or other devices of locomotion for longer distances.

About 20% of the lesions occur at the sacral level, enabling them to be, in most cases, community or normal ambulatory. Looking at prognosis and development of SB, a 25-year cohort study found a decline in ambulation as the main mode of locomotion from 95% at age 0–5 to 46% at age 20–25 in patients with SB, despite stable or even improving motor exams in respectively 73% and 16% of the patients [5]. At the same time, ambulation level during teenage years seemed predictive of ambulation as the main mode of locomotion as young adults. Thus, improving or maintaining

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efficient ambulation during childhood and throughout the teenage years, may be an important goal for ambulatory children and adolescents with SB. Earlier studies have shown higher levels of energy expenditure during ambulation in patients with SB [6–15], compared to healthy children. These studies, however, are hard to interpret and compare, as different protocols were used regarding both modes of testing (treadmill versus level ground), walking speed (self-selected versus imposed), calculation of energy cost, and preparation of the subjects (see Appendix A).

Moreover, they often do not report true energy expenditure in caloric units or Joules, but rather oxygen expenditure (VO_2). Since substrate utilization (fatty acids versus carbohydrates) per liter oxygen results in different amounts of energy expenditure, this is an important distinction. For these reasons, new methodology has been proposed in recent literature to evaluate energy expenditure during gait [16–18]. These changes include [1] use of energetic outcomes versus oxygen utilization and [2] net versus gross outcomes.

Studies in different populations have shown improvement in energy expenditure, again measured in different ways, after training [19,20] or orthopedic interventions [13]. In order to use energy expenditure during locomotion as an outcome measure in the rehabilitation process of children and adolescents with SB, information is needed regarding reproducibility of energy expenditure in this population. In the literature regarding reproducibility of energy expenditure measures in children with CP, new methodology has been proposed [16,18,21]. For energy expenditure measures in children with SB, this new methodology has not yet been applied. Furthermore, information regarding the reproducibility of energy expenditure measures in children with SB is lacking. Therefore, the purpose of this study was to determine the reproducibility of both gross and net energy expenditure during gait in ambulatory children and adolescents with SB.

2. Methods

2.1. Study population

This study was part of a larger study (The ... study) regarding exercise and functional capacity testing in ambulatory children with SB. Study procedures took place at the Child Development and Exercise Center of the University Children's Hospital in Utrecht, the Netherlands. All study procedures were approved by the University Medical Ethics Committee.

Children were included when they were (1) at least community ambulatory, (2) able to follow instructions regarding testing and (3) between six and 18 years of age. Parents and children signed informed-consent forms prior to testing. Exclusion criteria were medical events that might interfere with the outcomes of the testing and/or medical status that did not allow maximum exercise testing.

2.2. Measurements

2.2.1. Demographics

Data concerning medical history were obtained from medical records. These data included type of SB, motor level of lesion, use of orthotics, ambulation level, age, pubertal staging and sex.

2.2.2. Energy expenditure

During rest and ambulation, physiologic responses were measured using a heart rate (HR) monitor (polar) and calibrated mobile gas analysis system (Cortex Metamax B^3, Cortex Medical GmbH, Leipzig, Germany) for breath-by-breath analysis. All measurements and calibration were performed according to the manufacturer's instructions and guidelines. The mask was checked for possible leakage throughout the test. The Cortex Metamax is a valid and reliable system for measuring gas-exchange parameters during exercise [22,23].

2.2.3. Test protocol

Each test consisted of a resting measurement and measurements during ambulation. Resting measurements were recorded while participants were seated in a chair for five minutes. Energy expenditure during locomotion was measured during a six-minute walking test (6 MWT). The test was performed on a twenty-meter track in a straight corridor. Patients were instructed to cover the largest possible distance in six minutes at a self-selected walking speed. The test and encouragements during the test were performed in accordance with the American Thoracic Society guidelines [24]. The distance walked was recorded to calculate speed. Retest took place two weeks later, with the children being tested during the same time of day.

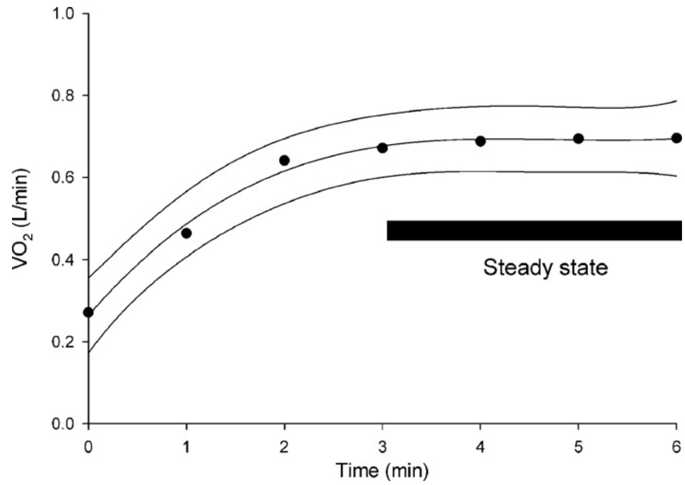

Fig. 1. Determination of steady state.

2.2.4. Energy expenditure analysis

Steady state (SS) normalized oxygen consumption (VO_2/kg/min) was calculated as the average value over the period during which oxygen consumption changed 5% or less. For this purpose, VO_2 was plotted for visual inspection (see Fig. 1). Within the period of least differences, a SS of two minutes was determined. Respiratory exchange ratio (RER) was calculated as VCO_2/VO_2 during steady state. Speed (m/min) was calculated as distance (m)/6 (min). Subsequently the following parameters were derived: resting energy consumption (ECS_{rest}), and gross energy consumption (ECS_{gross}). Net energy consumption (ECS_{net}) was calculated as the difference between ECS_{gross} and ECS_{rest}. ECS was expressed in J/kg/min, using VO_2 and RER in the following equation: J/kg/min = (4.960 × RER during steady state + 16.040) × VO_2/kg [25]. Furthermore gross energy cost (EC_{gross}) and net energy cost (EC_{net}), expressed in J/kg/m, were calculated, dividing respectively ECS_{gross} and ECS_{net} by speed.

2.3. Statistical analysis

For initial analyses, data were checked for normality and heteroscedasticity, the latter referring to the degree of variability depending on the outcome of the measurement. Heteroscedasticity was defined as a correlation coefficient between the differences of test–retest and the mean of the observations greater than 0.3 [26]. At the same time, a visual interpretation of Bland and Altman plots was performed to check for heteroscedasticity. All data were distributed normally and heteroscedasticity was not present.

T-tests were performed for test and retest data, with significance level set at $p < 0.05$. Reproducibility encompasses both reliability and agreement [27]. For reliability, the intra-class correlation$_{consistency}$ (ICC) was calculated using the following formula: $\text{variance}^2_{patient}/\text{variance}^2_{patient} + \text{variance}^2_{residual}$ [27]. An ICC of 0.8 or higher was considered good [28].

For agreement, the Standard Error of Measurement (SEM) and the Smallest Detectable Difference (SDD) were calculated, using the following equations: $SEM = SD \times \sqrt{1 - ICC_{consistency}}$ and $SDD = 1.96 \times \sqrt{2} \times SEM$. SDD was also expressed as a percentage of the mean score [27,28].

Secondary analysis included (1) *t*-tests between normal and ambulatory children and between prepubertal children and pubertal adolescents and (2) recalculation of ICC and SDD for the pubertal groups.

Statistical analyses were performed using SPSS for Windows (version 15.0, SPSS Inc., Chicago, Ill).

3. Results

3.1. Population

The study population consisted of 14 ambulatory children (6 boys/8 girls) with SB. Mean age was 10.8 years (±3.4), height 1.0 m (±0.2) and weight 38.4 kg (±18.7). The motor level of lesion (classified according to the American Spine Injury Association guidelines [29]), and the ambulation level are presented in Table 1.

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Table 1
Level of lesion and functional ambulation level.

	Number (%)
Level of lesion	
L3–L4	1 (7)
L4–L5	10 (72)
S1–S4	1 (7)
No motor loss	2 (14)
Ambulation level	
Normal ambulatory	8 (57)
Community ambulatory	6 (43)
Anthropometrics	Mean (SD)
Height (m)	1.0 (0.2)
Weight (kg)	38.4 (18.7)
BMI (kg/m^2)	18.6 (3.0)
Z-scores BMI	+1.1 (1.2)

Table 2
Mean energy expenditure outcomes during test and retest.

	Test (SD)	Retest (SD)	Difference (test–retest)
Speed (m/min)	70.0 (13.8)	70.4 (14.8)	−0.4
ECS rest (J/kg/min)	162.9 (62.1)	160.5 (70.5)	2.4
ECS gross (J/kg/min)	441.6 (99.6)	465.1 (107.4)	−23.4
EC gross (J/kg/m)	6.5 (1.8)	6.8 (2.2)	−0.3
ECS net (J/kg/min)	278.7 (94.9)	304.4 (93)	−25.8
EC net (J/kg/m)	4.0 (1.4)	4.4 (1.6)	−0.4

ECS = energy consumption; EC = energy cost.

3.2. Energy expenditure during ambulation

All children completed the six-minute walking test and retest without difficulties. Results include data from all children. Outcomes from both test and retest can be found in Table 2. *T*-tests showed no significant differences between test and retest for any of the outcome measures ($p < 0.05$ for all measures).

3.3. Reproducibility of energy expenditure during ambulation

Reproducibility measures for speed and both gross and net energy expenditure can be found in Table 3. ICCs vary from 0.86 and 0.88 for net EC and ECS to 0.96 for resting ECS. ICC for speed is 0.97. The SDD for speed is 6.8 m/min. SDDs for ECS range from 36.8 to 89.4 kJ/kg/min and from 1.5 to 1.7 kJ/m for EC.

To gain more insight in the clinical value of the SDDs, unpaired *t*-tests were performed to analyze differences between community ($n = 6$) and normal ambulators ($n = 8$). Only gross EC and speed differed significantly among the groups. The difference in speed was 20.8 m/min ($p = 0.01$) while the difference in gross EC was 2.4 J/kg/m ($p = 0.02$), with normal ambulatory children walking faster at a lower cost.

Table 3
Reproducibility data for speed and energy expenditure in children with SB.

	ICC	Pearson	SEM	SDD	SDD%
Speed	0.97	0.97	2.5	6.8	9.7
ECS rest	0.96	0.96	13.3	36.8	22.8
ECS gross	0.91	0.91	31.0	86.1	18.9
EC gross	0.91	0.92	0.6	1.7	24.8
ECS net	0.88	0.88	32.3	89.4	30.5
EC net	0.86	0.86	0.6	1.5	37.0

ECS = energy consumption; EC = energy cost.

Looking at pubertal groups, only ECS_{rest} differed significantly among the pubertal versus prepubertal children (120 J/kg/min (SD 26.4) versus 193.1 J/kg/min (SD 71)). In this population, all prepubertal children were younger than 12 years of age and those in later stages of puberty older than 12 years of age. Further analysis showed higher ICCs and lower %SDD for all energy expenditure measures in the younger children compared to the adolescents (see Table 4).

4. Discussion

The purpose of this study was to determine the two aspects of reproducibility (reliability and agreement) of both gross and net energy expenditure during gait in ambulatory children and adolescents with SB. Reliability of all energy expenditure measurements and speed in ambulatory children with SB can be considered good to excellent, with ICCs varying from 0.86 for net EC to 0.97 for speed. This means that measurement of energy expenditure during gait can correctly distinguish higher scores from lower scores. These ICCs are comparable with those reported in the literature, ranging from 0.82 to 0.99 in children with CP and from 0.59 to 0.89 in healthy children [18].

For clinicians, agreement of the measurements is more of interest, because they look to determine meaningful improvements in a single patient. From the results of this study, we can conclude that improvements of 86.1 kJ/kg/min (19%) and 1.7 kJ/m (25%) are needed for respectively ECS_{gross} and EC_{gross} to interpret a change as true improvement. For net energy expenditure, improvements even need to exceed 30%, while the SDD for speed remained below 10% or 6.8 m/min. Again, these outcomes are comparable to the existing literature regarding agreement for energy expenditure in children with ambulatory difficulties, except for a much lower SDD reported for EC_{gross} [18]. In healthy children, Thomas et al. [21] have shown the coefficient of variation (CV) for gross ECS and EC in healthy children to be around 9–10%, while variability in net measures increased to 14–15%. To deal with the moderate agreement of energy expenditure in patients with ambulatory difficulties, modifications have been proposed to improve reproducibility of energy expenditure of locomotion [16]. While these methodological changes might improve scientific outcomes, questions remain regarding the practical implications of needing several repetitions of these expensive and "high-tech"

Table 4
Differences between normal and community ambulatory children.

	Normal ambulatory (SD)	Community ambulatory (SD)	Difference	*p* value
Speed (m/min)	77.9 (8.4)	57.1 (12.5)	20.8	0.01*
ECS rest (J/kg/min)	148.7 (39.9)	179.1 (91.4)	30.4	0.41
ECS gross (J/kg/min)	443.2 (56.9)	467.0 (147.3)	23.8	0.68
EC gross (J/kg/m)	5.7 (0.6)	8.1 (2.4)	2.4	0.02*
ECS net (J/kg/min)	294.5 (64.9)	287.8 (125.1)	6.6	0.89
EC net (J/kg/m)	3.7 (0.7)	4.9 (2.04)	1.2	0.13

ECS = energy consumption; EC = energy cost.
* Significant differences between normal and community ambulatory children.

measurements for four weeks in a row, to establish a baseline measurement in the clinical setting. Schwartz et al. [30] have shown a reduction in variation of energy expenditure in healthy adults and adolescents by calculating a non-dimensional speed, using leg length. In our current randomized clinical trial, we are using this simple modification for the assessment of net non-dimensional consumption and cost.

Another important issue, when looking at the SDD, is its relation to clinical relevant change (CRC). What we do not know is how ECS and/or EC relate to improvement or deterioration in functional status of patients with ambulatory difficulties and this should be a topic of future intervention research. Secondary analysis in our group showed significant differences of 2.4 J/kg/m for gross EC between normal and community ambulation levels. In light of these findings, an SDD of 1.7 J/kg/m for gross EC seems acceptable to use as a clinical marker. In a longitudinal study of Thomas et al., including children with both thoracic and lumbar lesions, gross oxygen cost – not energy cost—was more than 100% higher in children who became non ambulatory, compared to those who remained ambulatory in a three-year period [9]. Recalculating the data from the children with lumbar and sacral lesions only, it is interesting to see a 30% difference in gross oxygen cost between the future walkers and non-walkers at the beginning of the three-year period. It seems that in this context as well, the SDD of 24.8% of gross EC might be small enough to mark clinically important differences.

As in other studies, gross measurements seem less variable than net measurements. This is probably due to the high variability in measuring resting ECS. Net values are particularly important when interested in follow-up over a period of years, as growth and maturation change oxygen utilization and speed of walking [31–33], where gross values can be used in shorter follow-up [16].

Because our resting energy values were high compared to those mentioned in the literature [18,34], we tested differences of resting as well as gross and net energy expenditure between children younger than 12 years of age and those older than 12 years of age, coinciding with prepubertal versus pubertal staging. One interesting finding from this analysis was a much higher agreement of both net and gross energy expenditure measures in children under 12 years of age compared to the older children. Looking at these results, changes of 15% and 11% in, respectively, gross ECS and EC can be detected in young children. The adolescents still showed a larger intra-variability. This is an interesting finding in itself because it raises the question of whether this increased variability of energy cost might be an indicator or marker of (future) decline in ambulatory function often seen during the adolescent years. Considering the small sample size of both groups, these results should be interpreted with caution, but yield for future research looking into these differences.

4.1. Limitations of the study

The large variability and poor reproducibility of resting ECS, make further discussion about net values unnecessary, except that these measures need further improvements. Our protocol consisted of five minutes of sitting in a chair, without talking or moving around, with children refraining from eating or drinking at least one hour before measurements. The mean resting ECS in this study is higher than reported by Littlewood et al. [34]. They reported a resting metabolism of approximately 120 J/kg/min in children with SB, measured with a fasting protocol and lying down for 10 min. Despite their strict protocol, a large inter-subject variability was reported in children with SB, which is in line with the findings in our study. Higher resting values are most likely due to our protocol and the younger age group included in our study. Measures to increase reproducibility could include lying down, longer familiarization with the equipment and a longer fasting period. Again, while of interest for scientific purposes, these measures are harder to implement in the daily clinical practice.

Further questions could be raised regarding the use of the six-minute walking test (6 MWT) for measuring steady state energy expenditure. In healthy populations, encouragement to cover the largest possible distance could result in discontinuous fast speed, not appropriate for determining steady state. Ambulatory children with SB are limited in their speed by decreased coordination and motor control. In this study, a constant walking velocity throughout the 6 MWT was observed, consistent with other gait studies including pathologic gait patterns [31].

Finally, increased variability in EC compared to variability in ECS contrasts with results in other studies [16,18,21], where EC shows less variability than ECS. This could be due to a fast and uncomfortable walking velocity or leakage from the mask. Looking at the secondary analysis though, this only seems to be the case for the older children, limiting the role of the procedures used in this study.

5. Conclusion

Reproducibility of energy expenditure during ambulation in ambulatory children with SB should be considered carefully, when using these measures in the assessment or evaluation for this population. Reliability of energy expenditure measurements in ambulatory children with SB is good to excellent, supporting the use of these measures for discriminative purposes in this population. Agreement for gross energy cost seems acceptable to use in the clinical evaluation of energy expenditure in children with SB, with a SDD of 1.7 J/kg/m. Overall, measures of reliability and agreement are superior in younger children compared to adolescents.

While the concept of measuring energy expenditure during ambulation is a promising concept, future research should focus on (1) how changes in energy consumption and/or energy cost relate to improvement or deterioration in functional status of patients with ambulatory difficulties and (2) the possible increased variability of measurements of ECS in adolescents with SB.

Conflict of interest

None.

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Appendix A. Overview of protocols to measure energy expenditure in children with SB.

Authors	Subjects (n)	Age in years	Test protocol	Outcome measures*
De Groot et al. [14]	23	6–18	Walking a six-minute walk test in a straight corridor	Gross oxygen expenditure
Bartonek et al. [6]	8	5–14	Walking as far as possible	$HR_{walk} - HR_{rest}$
Bartonek et al. [11]	53	3–11	Walking as far as possible	$(HR_{walk} - HR_{rest})$/speed
Bare et al. [8]	14	7–12	Treadmill walking at four different velocities: 75–100–150% of self-selected speed and velocity of an aged matched healthy peer	Gross oxygen expenditure
Thomas et al. [9]	23		Walking on an oval track at self-selected speed	Gross oxygen expenditure
Duffy et al. [13]	12	6–16	Walking 10 m laps in the gait lab until steady state was reached	Gross oxygen expenditure
Duffy et al. [12]	21	5–12	Walking 10 m laps in the gait lab at a self-selected speed	Gross oxygen expenditure
Williams et al. [10]	15	5–12	Walking outside on a 60.5 m oval level track at a faster velocity than their own choice	Gross oxygen expenditure
Evans and Tew [15]	22	10–16	Walking at their customary walking speed over a standardized flat, tiled floor course	Gross energy expenditure (kcal/min and kcal/m), not normalized for body mass

* Gross oxygen expenditure includes both oxygen consumption (ml/kg/min) and oxygen cost (ml/kg/m).

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