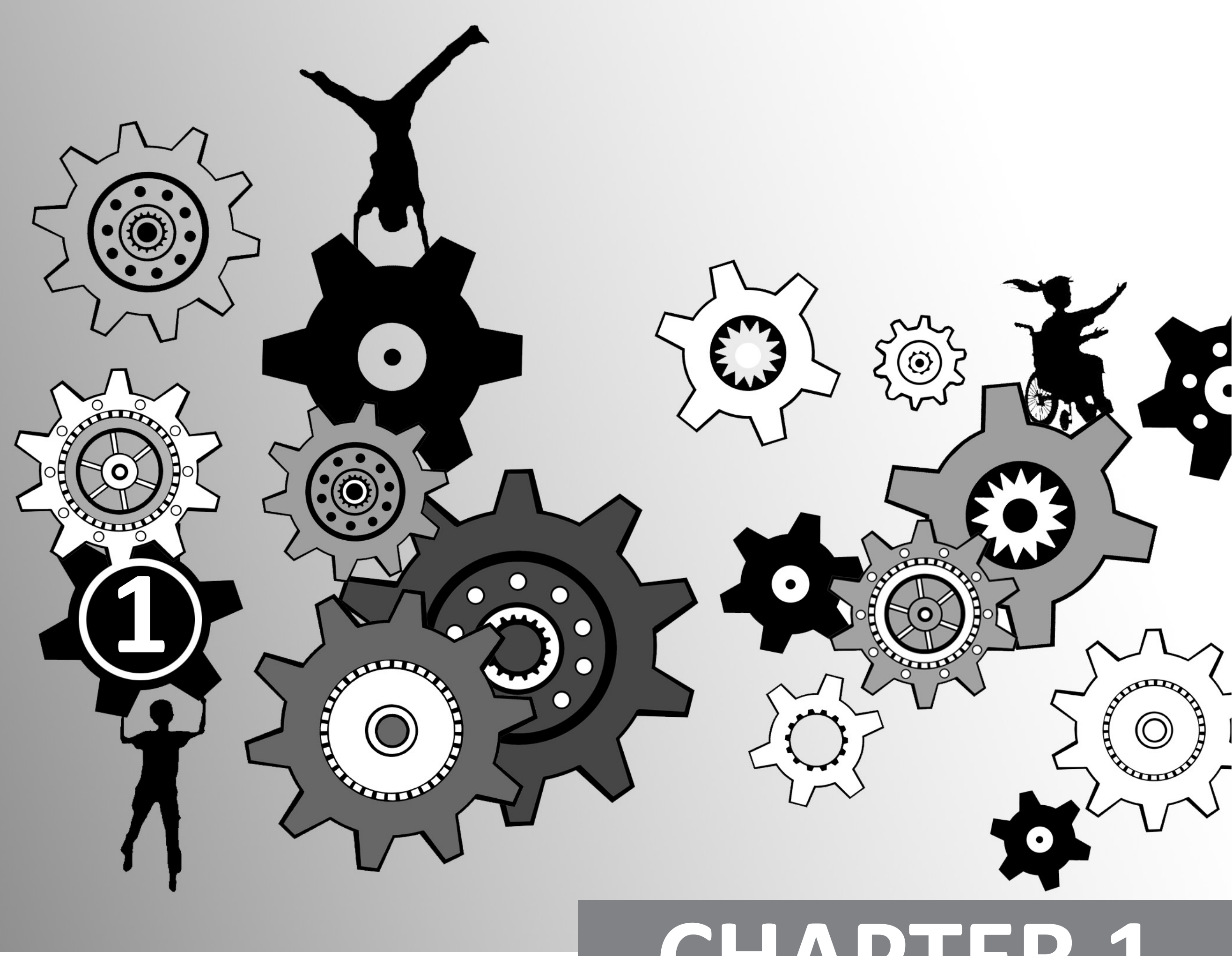
Applied exercise physiology in rehabilitation of children with cerebral palsy

Balemans, A.C.J.

2014



CHAPTER 1

General Introduction

Astrid CJ Balemans

Children with cerebral palsy are at risk for both low levels of physical fitness and an inactive lifestyle, which can lead to increased health risks later in life.[24] This reduction in physical fitness and physical activity may increase the impact of the disorder on daily functioning. It is therefore important to intervene early in life to break this vicious circle of low physical fitness and low physical activity. This thesis investigates the level of physical fitness and physical activity in walking children with cerebral palsy across the different levels of gross motor function, and the relation between physical fitness and physical activity, with the aim of guiding intervention programs for children with cerebral palsy. The overall project is part of the national 'Learn 2 Move' research study, a randomized controlled trial evaluating the effects of a physical activity stimulation program for children with cerebral palsy.[53]

Cerebral palsy

Cerebral palsy (CP) is the most common cause of physical disability in childhood, with a prevalence of 2.18 per 1000 live births in Western Europe.[29] As the etiology of the disorder is heterogeneous and has variable manifestations, over the years the definition of CP has been the subject of debate.[42] Nowadays, CP is defined as "a group of disorders of the development of movement and posture causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain".[9;20] The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior, and/or by a seizure disorder.[9] CP is diagnosed based on its clinical manifestations.

There are many etiological factors underlying CP and many are typical for a particular time of onset: prenatal (e.g. intoxication), perinatal (e.g. hypoxic-ischemia) and postnatal (e.g. infection). Important risk factors associated with the development of CP are prematurity and low birth weight. The exact cause remains unknown in about 15% of cases.[12]

The motor disorder can be grouped into three subtypes: the spastic, the dyskinetic and the ataxic types.[1] Mixed presentations also occur in which the dominant subtype of the presentation determines the classification of the disorder.[1] The spastic type is most common in CP (around 80%) and it is this type that will be discussed in this thesis.[1;20] The spastic type is defined as a posture- and movement- dependent muscle tone regulation impairment.[12] Impaired muscle function in spastic CP can be classified as either impaired muscle activation or impaired biomechanical muscle properties.[13] Impaired muscle activation results in negative or deficit symptoms (e.g. muscle paresis, reduced selective motor control, increased muscle fatigue) and positive or excessive symptoms (e.g. spasticity, hypertonic muscles, muscle co-contraction, involuntary synergies).[12,34] The changes in biomechanical muscle properties can be subdivided into muscle stiffness and impaired muscle length.[25;30] Spastic CP can be subclassified based on anatomical distribution: persons with a unilateral involvement are affected on one side of the body, while bilateral involved individuals are affected on both sides of the body.[28]

GMFCS

Because CP is an umbrella term for a group of disorders, its clinical manifestations are heterogeneous. Limitations in activity therefore vary between individuals.[42] For that reason, the severity of the motor impairment with regard to gross motor function can be classified according to the Gross Motor Function Classification System (GMFCS).[39] This system was specifically developed for CP and identifies five levels in which distinctions between levels are based on functional performance: children in level I walk independently without restrictions, children in level II walk independently with restrictions, children in level III walk with a walking aid and children in levels IV and V are unable to walk.[39]

ICF-CY

The impact of CP on daily functioning can be described using the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY). This framework serves to describe the consequences of a disorder at the level of body functions and structures, activity and participation (Figure 1.1).[2] The consequences of CP can be present at all domains of the ICF-CY model.[10;20] The impaired muscle activation and impaired biomechanical muscle properties, which may result in decreases in physical fitness, are consequences at the domain body functions and structures.[10] The motor impairments cause limitations in the execution of activities such as walking and running, which can affect the level of daily physical activity.[10] Consequently, the ability to participate in daily life situations may be reduced. The decreased level of daily physical activity can in turn further influence body functions and structures, as deconditioning results in a lower level of physical fitness.[10]

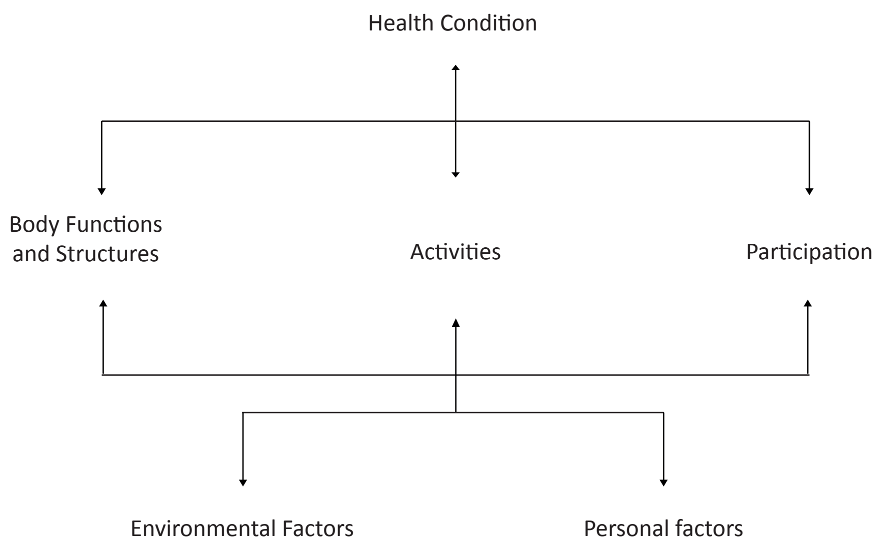


Figure 1.1 The International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY).[2]

Physical fitness, physical activity and exercise

Definitions

The terms *physical fitness* and *physical activity* will be used based on the following definitions: *Physical fitness* is “a set of attributes or characteristics that people have or achieve that relate to the ability to perform physical activity”.[22] The health-related components of physical fitness are defined by the American College of Sports Medicine (ACSM) as cardiorespiratory (aerobic) fitness, body composition, muscular strength and muscular endurance, and flexibility.[3] Anaerobic fitness is not a separate fitness component according to the ACSM. However, in addition to aerobic fitness and muscular strength, anaerobic fitness is an important determinant for physical activity and exercise in children, who have short, intermittent activity patterns.[5;27] *Physical activity* is defined as “any bodily movement produced by the contraction of skeletal muscles that requires energy expenditure”.[60] *Exercise* is defined as “a type of physical activity consisting of planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness”.[3;22]

Decreased physical fitness in cerebral palsy

Although the primary deficit in CP occurs as a lesion in the brain, the impaired muscle function (impaired muscle activation and impaired biomechanical muscle properties) in combination with reduced daily physical activity may affect the level of physical fitness. Physical fitness components such as aerobic fitness[32;36;54], anaerobic fitness[8;27;35;52] and muscle strength[40] are reduced in children and adults[31] with CP. However, it is not clear whether the level of physical fitness is related to the severity of the motor disorder or whether this is a result of inactivity. Exercise capacity as described by Wasserman et al. is dependent on three systems: the muscular system, the cardiovascular system and the ventilatory system (Figure 1.2).[56] Analyzing these systems may contribute to unraveling the physiological factors that are limiting exercise in children with CP.[7] The musculoskeletal system of children with CP has different biomechanical and energetic properties to those of children who are developing typically.[41] For example, children with CP have a smaller muscle volume,[18;38] which may result in decreased muscle strength and peak power as a direct result of impaired muscle function.[7] Lower muscle volume may also impact oxygen extraction in exercising muscles, affecting aerobic fitness. While it is unlikely that ventilatory and cardiovascular systems are directly influenced by the impaired muscle function in walking children with CP, these systems might be influenced by deconditioning resulting from inactivity. However, little is currently known about these systems in children with CP. Although previous studies have reported decreased values of aerobic and anaerobic fitness in walking children with CP, few researchers have investigated how these physical fitness components are influenced by the severity of the motor disorder.[23;32;51] Evaluating the influence of the level of motor impairment may help to identify factors that affect the level of physical fitness and may help clarify the respective roles of physical disability and physical inactivity in the physical fitness of children with CP.[6]

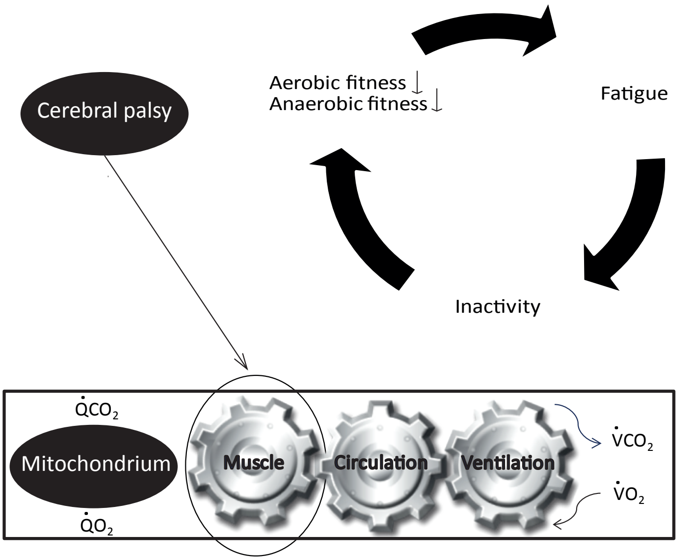


Figure 1.2 The proposed vicious circle of decreased physical fitness, fatigue and inactivity, including the three systems described by Wasserman et al.: the muscular system, the cardiovascular system and the ventilatory system.[56] Printed with permission.

Aerobic fitness, anaerobic threshold and anaerobic fitness

When estimating the level of physical fitness, it is important to measure the different components of physical fitness. Measurement of each of the various physical fitness components requires a specific approach. The approach to measurement depends on the type and duration of exercise to which the physical fitness component is related.[3] The intensity and duration of exercise determine the contribution of the different metabolic systems to the production of the adenosine triphosphate (ATP) that is required for muscle contraction. Of the three metabolic systems, the two anaerobic systems (the creatine phosphate system and the glycolytic system) can be differentiated from the aerobic system (aerobic oxidation) in which oxygen is consumed during the process of ATP generation.[58]

Immediately at the start of exercise, the anaerobic creatine phosphate system supplies ATP to the exercising muscle through the regeneration of ATP from ADP using creatine phosphate as the phosphate donor.[56] Thereafter, the anaerobic glycolytic system generates ATP through the degradation of carbohydrates.[56] The anaerobic glycolytic system allows the muscle to perform exercise with high intensity and short duration (1-2 min).[5] Anaerobic capacity is the maximal amount of ATP that is resynthesized via anaerobic metabolism during short bursts (30-45 s) of high intensity exercise.[27] In order to estimate anaerobic capacity, mean power output can be measured during a short sprint test (20-30 s) on a cycle ergometer.[27,8] Anaerobic capacity is used in this thesis as a measure of anaerobic fitness.

The aerobic system contributes to exercise of moderate intensity. The aerobic system generates ATP through the degradation of fatty acids and/or carbohydrates using oxygen. The maximum amount of oxygen consumed during exercise (VO_2peak) reflects the aerobic capacity.[4;43] The VO_2peak can be measured during a maximal exercise test in which resistance or speed is gradually increased until fatigue limits any further increase in exercise intensity by an individual.[57]

Oxygen transport is able to supply all of the required oxygen to the muscle for the aerobic regeneration of ATP up to a certain exercise intensity threshold. This level of exercise intensity is defined as the anaerobic threshold (AT) (Figure 1.3).[56;11] The AT can be measured using the V-slope method. This method defines AT as the point at which carbon dioxide production increases relatively faster than the increase in oxygen uptake.[11]

The level of the AT and VO_2peak determine the duration and intensity of sustained physical performance and may therefore be important to the physical activity of an individual in daily life. In addition, due to the short and intermittent patterns that characterize activity in children, adequate anaerobic fitness is assumed to be an important prerequisite for performing daily activities in children.[5] In order to properly measure these physical fitness components in children with CP, exercise tests appropriate for children with CP are required.[55] The level of evidence for the clinimetric properties of the available exercise tests has not yet been specifically evaluated for this population.

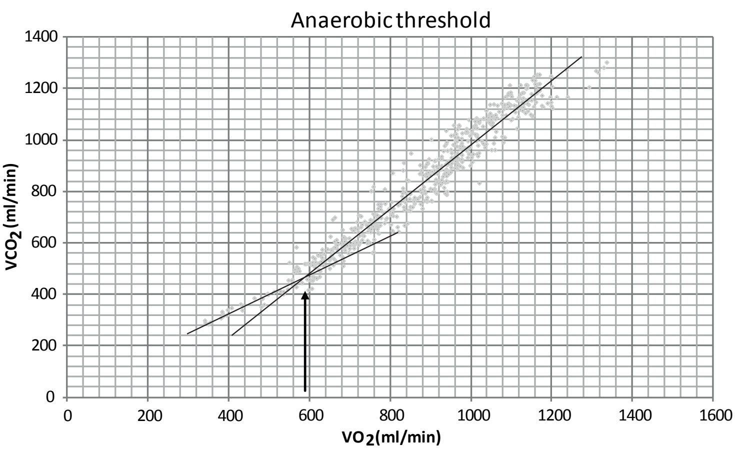


Figure 1.3 Example of the anaerobic threshold (AT) determined by gas exchange with the V-slope method.[11]

Vicious circle of decreased physical fitness and physical inactivity

Maintaining or improving one or more components of physical fitness requires regular exercise. An adequate level of physical fitness and regular participation in physical activity brings significant health benefits,[60] contributes to the development of the musculoskeletal system in children and helps prevent secondary health conditions such as high blood pressure, obesity and osteoporosis.[19;26] Persons with CP have impaired muscle function and a higher risk of developing these secondary conditions.[24] Children with CP can become trapped in a vicious circle[21] of higher energy expenditure when executing activities[32;33;51;54;59] and decreased physical fitness,[32;51;54] which may result in a lower level of physical activity.[16;50] This may then lead to deconditioning and a further decrease in physical fitness.

When performing activities such as walking, children with CP expend more energy.[37;49] This high energy expenditure per meter may result in a high exercise intensity.[17;23;48] Children with CP also show lower levels of physical fitness, as indicated by the lower values for VO_2peak.[32;36;54] A low physical fitness, together with the high energy expenditure, results in a high relative exercise intensity when performing activities.[23] Therefore, children with CP might experience fatigue earlier than children without CP,[15] leading to a reduction in physical activity as a compensatory mechanism to prevent fatigue and resulting in deconditioning and a further reduction in physical fitness[24] (Figure 1.2). However, these relations are currently speculative and whether they actually exist in children with CP is not yet clear.[37]

Children with CP are known to have lower levels of physical activity.[21] Despite high energy expenditure during walking[17], children with CP also show a lower overall energy expenditure during the day.[14;37;50] In addition, previous studies have found that children with CP take fewer steps during the day and show a reduced total amount of activity counts over the day compared with typically developing children.[16;21;45] In adults with CP, a lower level of daily physical activity is associated with a higher physical strain.[44] Physical strain is the O_2 consumption during walking expressed as a percentage of the VO_2peak.[23;44] The relation between physical strain and physical activity suggests that adequate physical fitness might contribute to higher physical activity or vice versa. A cross-sectional relation between the level of VO_2peak and physical activity has not been demonstrated in children with CP.[37] Similarly, the longitudinal relationship between physical fitness and physical activity has not yet been investigated. Interestingly, increasing VO_2peak does result in a decrease in physical strain. If an increase in VO_2peak can be established through training, the subsequent reduction in physical strain might have a positive impact on the level of physical activity. This could potentially lead to a greater ability to participate in daily activities, with a concomitant further improvement in physical fitness and prevention of secondary conditions.

In summary, children with CP are at risk for a reduced level of physical fitness and physical activity. Since inactive children are more likely to become inactive adults,[46;47] adequate physical fitness and an active lifestyle should be stimulated at early ages. However, it is not yet clear whether the level of physical fitness and physical activity are related to the severity of the motor disorder as classified by the GMFCS level. It is also not yet clear whether decreased physical fitness might increase the impact of the disorder on the capacity for executing the activities of daily living. Furthermore, it is not known to what extent the lower levels of physical activity relate to the higher exercise intensity during walking and whether increased physical fitness contributes to an improved physical activity. The aim of the studies described in this thesis was therefore to investigate the level of physical fitness and physical activity in walking children with cerebral palsy across the different levels of gross motor function I-III, and then to determine the relations between physical fitness and physical activity.

Outline of the thesis

The studies focus on children with a spastic CP and consist of three main parts:

1. Clinimetric properties of physical fitness measurement
   (Chapters 2 and 3)
2. The level of physical fitness
   (Chapters 4 and 5)
3. Daily physical activity and the relationship with physical fitness
   (Chapters 6 and 7)

Chapter 2 systematically identifies aerobic and anaerobic fitness measures for children with CP described in the literature, and evaluates the level of evidence for the clinimetric properties of these tests. **Chapter 3** investigates the reliability of a progressive maximal aerobic cycling test for children with CP. **Chapter 4** compares the maximal aerobic and anaerobic exercise responses of children with CP with those of children who show typical development. **Chapter 5** describes the relationship between changes in exercise responses and how this relates to changes in gross motor function and walking capacity. **Chapter 6** addresses the intensity of daily physical activity through measurement of stride rate activity and exercise intensity during the day. **Chapter 7** combines physical fitness and physical activity by evaluating the change over time in physical fitness in relation to changes in daily walking physical activity. In **chapter 8,** findings and clinical implications are discussed.

References

1. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). *Dev Med Child Neurol.* 2000;42(12):816-24.
2. World Health Organization. International Classification of Functioning, Disability and Health (ICF). Geneva, Swiss. http://www.who.int/classifications/icf/en/ 2001.
3. American College of Sports Medicine. Benefits and risks associated with physical activity. *ACSM's Guidelines for Exercise Testing and Prescription*. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
4. Armstrong N, Welsman JR. Assessment and interpretation of aerobic fitness in children and adolescents. *Exerc Sport Sci Rev.* 1994;22:435-76.
5. Bailey RC, Olson J, Pepper SL, Porszasz J, Barstow TJ, Cooper DM. The level and tempo of children's physical activities: an observational study. *Med Sci Sports Exerc.* 1995;27(7): 1033-41.
6. Baquet G, Van Praagh E, Berthoin S. Endurance training and aerobic fitness in young people. *Sports Med.* 2003;33(15):1127-43.
7. Bar-Or O. Pathophysiological factors which limit the exercise capacity of the sick child. *Med Sci Sports Exerc.* 1986;18(3):276-82.
8. Bar-Or O. The Wingate anaerobic test. An update on methodology, reliability and validity. *Sports Med.* 1987;4(6):381-94.
9. Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N, Dan B, Jacobsson B, Damiano D. Proposed definition and classification of cerebral palsy, April 2005. *Dev Med Child Neurol.* 2005;47(8):571-6.
10. Bax MC, Flodmark O, Tydeman C. Definition and classification of cerebral palsy. From syndrome toward disease. *Dev Med Child Neurol Suppl.* 2007;109:39-41.
11. Beaver WL, Wasserman K, Whipp BJ. A new method for detecting anaerobic threshold by gas exchange. *J Appl Physiol.* 1986;60(6):2020-7.
12. Becher J, Gorter JW, Vermeulen RJ. Cerebrale Parese. *Kinderrevalidatie*. 2009. p. 255.
13. Becher JG, Harlaar J, Lankhorst GJ, Vogelaar TW. Measurement of impaired muscle function of the gastrocnemius, soleus, and tibialis anterior muscles in spastic hemiplegia: a preliminary study. *J Rehabil Res Dev.* 1998;35(3):314-26.
14. Bell KL, Davies PS. Energy expenditure and physical activity of ambulatory children with cerebral palsy and of typically developing children. *Am J Clin Nutr.* 2010;92(2):313-9.
15. Berrin SJ, Malcarne VL, Varni JW, Burwinkle TM, Sherman SA, Artavia K, Chambers HG. Pain, fatigue, and school functioning in children with cerebral palsy: a path-analytic model. *J Pediatr Psychol.* 2007;32(3):330-7.
16. Bjornson KF, Belza B, Kartin D, Logsdon R, McLaughlin JF. Ambulatory physical activity performance in youth with cerebral palsy and youth who are developing typically. *Phys Ther.* 2007;87(3):248-57.
17. Brehm MA, Becher J, Harlaar J. Reproducibility evaluation of gross and net walking efficiency in children with cerebral palsy. *Dev Med Child Neurol.* 2007;49(1):45-8.
18. Brooke MH, Engel WK. The histographic analysis of human muscle biopsies with regard to fiber types. 4. Children's biopsies. *Neurology.* 1969;19(6):591-605.
19. Byun W, Sieverdes JC, Sui X, Hooker SP, Lee CD, Church TS, Blair SN. Effect of positive health factors and all-cause mortality in men. *Med Sci Sports Exerc.* 2010;42(9):1632-8.

20. Cans C, Guillem P, Arnaud C, Baille F, Chalmers J, McManus V, Cussen G, Parkes J, Dolk H, Hagberg B, Hagberg G, Jarvis S, Colver A, Johnson A, Surman G, Krageloh-Mann I, Michaelis R, Platt MJ, Pharoah P, Topp M, Udall P, Torrioli MG, Miceli M, Wichers M. Prevalence and characteristics of children with cerebral palsy in Europe. *Dev Med Child Neurol.* 2002;44(9):633-40.
21. Carlon SL, Taylor NF, Dodd KJ, Shields N. Differences in habitual physical activity levels of young people with cerebral palsy and their typically developing peers: a systematic review. *Disabil Rehabil.* 2013;35(8):647-55.
22. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* 1985;100(2): 126-31.
23. Dallmeijer AJ, Brehm MA. Physical strain of comfortable walking in children with mild cerebral palsy. *Disabil Rehabil.* 2011;33(15-16):1351-7.
24. Fowler EG, Kolobe TH, Damiano DL, Thorpe DE, Morgan DW, Brunstrom JE, Coster WJ, Henderson RC, Pitetti KH, Rimmer JH, Rose J, Stevenson RD. Promotion of physical fitness and prevention of secondary conditions for children with cerebral palsy: section on pediatrics research summit proceedings. *Phys Ther.* 2007;87(11):1495-510.
25. Fry NR, Gough M, Shortland AP. Three-dimensional realisation of muscle morphology and architecture using ultrasound. *Gait Posture.* 2004;20(2):177-82.
26. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43(7):1334-59.
27. Green S. A definition and systems view of anaerobic capacity. *Eur J Appl Physiol Occup Physiol.* 1994;69(2):168-73.
28. Hagberg B, Hagberg G. The changing panorama of cerebral palsy--bilateral spastic forms in particular. *Acta Paediatr Suppl.* 1996;416:48-52.
29. Himmelmann K, Hagberg G, Uvebrant P. The changing panorama of cerebral palsy in Sweden. X. Prevalence and origin in the birth-year period 1999-2002. *Acta Paediatr.* 2010;99(9):1337-43.
30. Hof AL. Changes in muscles and tendons due to neural motor disorders: implications for therapeutic intervention. *Neural Plast.* 2001;8(1-2):71-81.
31. Hombergen SP, Huisstede BM, Streur MF, Stam HJ, Slaman J, Bussmann JB, van den Berg-Emons R. Impact of cerebral palsy on health-related physical fitness in adults: systematic review. *Arch Phys Med Rehabil.* 2012;93(5):871-81.
32. Hoofwijk M, Unnithan VB, Bar-Or O. Maximal Treadmill Performance of Children With Cerebral Palsy. *Pediatr Exerc Sci.* 1995;7(3):305-13.
33. Kurz MJ, Arpin DJ, Corr B. Differences in the dynamic gait stability of children with cerebral palsy and typically developing children. *Gait Posture.* 2012;36(3):600-4.
34. Lance JW. Spasticity: Disorderd Motor Control. *Year Book Medical Publishers*. Chicago: 1980. p. 485-95.
35. Laurent CMJ, Meyers MC, Robinson CA, Green JM. Cross-validation of the 20- versus 30-s Wingate anaerobic test. *Eur J Appl Physiol.* 2007;100(6):645-51.
36. Lundberg A. Maximal aerobic capacity of young people with spastic cerebral palsy. *Dev Med Child Neurol.* 1978;20(2):205-10.
37. Maltais DB, Pierrynowski MR, Galea VA, Bar-Or O. Physical activity level is associated with the O2 cost of walking in cerebral palsy. *Med Sci Sports Exerc.* 2005;37(3):347-53.

38. Noble J, Fry N, Lewis A, Keevil S, Gough M, Shortland A. Lower limb muscle volumes in bilateral spastic cerebral palsy. *Brain Dev.* 2014.

39. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev Med Child Neurol.* 1997;39(4):214-23.

40. Rimmer JH. Physical fitness levels of persons with cerebral palsy. *Dev Med Child Neurol.* 2001;43(3):208-12.

41. Rose J, Haskell WL, Gamble JG, Hamilton RL, Brown DA, Rinsky L. Muscle pathology and clinical measures of disability in children with cerebral palsy. *J Orthop Res.* 1994;12(6): 758-68.

42. Rosenbaum P. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol.* 2007;49(6):480.

43. Rowland TW. Does peak VO2 reflect VO2max in children?: evidence from supramaximal testing. *Med Sci Sports Exerc.* 1993;25(6):689-93.

44. Slaman J, Bussmann J, van der Slot WM, Stam HJ, Roebroeck ME, van den Berg-Emons R. Physical strain of walking relates to activity level in adults with cerebral palsy. *Arch Phys Med Rehabil.* 2013;94(5):896-901.

45. Stevens SL, Holbrook EA, Fuller DK, Morgan DW. Influence of age on step activity patterns in children with cerebral palsy and typically developing children. *Arch Phys Med Rehabil.* 2010;91(12):1891-6.

46. Telama R, Yang X, Viikari J, Valimaki I, Wanne O, Raitakari O. Physical activity from childhood to adulthood: a 21-year tracking study. *Am J Prev Med.* 2005;28(3):267-73.

47. Twisk JWR, Kemper HCG, van Mechelen W. The relationship between physical fitness and physical activity during adolescence and cardiovascular disease risk factors at adult age. The Amsterdam Growth and Health Longitudinal Study. *Int J Sports Med.* 2002;23 Suppl 1:S8-14.

48. Unnithan VB, Dowling JJ, Frost G, Bar-Or O. Role of cocontraction in the O2 cost of walking in children with cerebral palsy. *Med Sci Sports Exerc.* 1996;28(12):1498-504.

49. Unnithan VB, Dowling JJ, Frost G, Bar-Or O. Role of mechanical power estimates in the O2 cost of walking in children with cerebral palsy. *Med Sci Sports Exerc.* 1999;31(12):1703-8.

50. Van den Berg-Emons HJG, Saris WHM, de Barbanson DC, Westerterp KR, Huson A, van Baak MA. Daily physical activity of schoolchildren with spastic diplegia and of healthy control subjects. *J Pediatr.* 1995;127(4):578-84.

51. Van Den Berg-Emons RJ, van Baak MA, de Barbanson DC, Speth L, Saris WH. Reliability of tests to determine peak aerobic power, anaerobic power and isokinetic muscle strength in children with spastic cerebral palsy. *Dev Med Child Neurol.* 1996;38(12):1117-25.

52. Van Praagh E. Anaerobic fitness tests: what are we measuring? *Med Sport Sci.* 2007;50: 26-45.

53. Van Wely L, Becher JG, Reinders-Messelink HA, Lindeman E, Verschuren O, Verheijden J, Dallmeijer AJ. LEARN 2 MOVE 7-12 years: a randomized controlled trial on the effects of a physical activity stimulation program in children with cerebral palsy. *BMC Pediatr.* 2010;10:77.

54. Verschuren O, Takken T. Aerobic capacity in children and adolescents with cerebral palsy. *Res Dev Disabil.* 2010;31(6):1352-7.

55. Verschuren O, Ketelaar M, Keefer D, Wright V, Butler J, Ada L, Maher C, Reid S, Wright M, Dalziel B, Wiart L, Fowler E, Unnithan V, Maltais DB, van den Berg-Emons R, Takken T. Identification of a core set of exercise tests for children and adolescents with cerebral palsy: a Delphi survey of researchers and clinicians. *Dev Med Child Neurol.* 2011;53(5):449-56.

56. Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ. Exercise Testing and Interpretation: An Overview. *Principles of exercise testing and interpretation*. 4th ed. Lippincott Williams & Wilkins; 2005. p. 1-9.

57. Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ. Measurements During Integrative Cardiopulmonary Exercise Testing. *Principles of exercise testing and interpretation*. 4th ed. Lippincott Williams & Wilkins; 2005. p. 76-110.

58. Wasserman K, Whipp BJ, Koyl SN, Beaver WL. Anaerobic threshold and respiratory gas exchange during exercise. *J Appl Physiol.* 1973;35(2):236-43.

59. Waters RL, Mulroy S. The energy expenditure of normal and pathologic gait. *Gait Posture.* 1999;9(3):207-31.

60. World Health Organization. *Global Recommendations on Physical Activity for Health*. WHO Press, World Health Organization; 2010. 16.