General introduction
Children and young adults with a physical disability, like cerebral palsy (CP) and spina bifida (SB), often experience problems with walking, such as fatigue during walking, a reduced walking distance and/or a reduced walking speed.\textsuperscript{1,2} These problems are likely to be primarily caused by their motor impairments that can cause a pathological gait.\textsuperscript{3,4} Insight in the underlying physical mechanisms behind these walking problems can direct rehabilitation treatment. Physical examinations\textsuperscript{5} and gait analysis\textsuperscript{6,7} are often used by rehabilitation practitioners to substantiate their treatment for individuals with these walking problems. Studies have suggested that i) increased energy demands of walking and ii) decreased physical fitness values may cause walking problems in children with CP.\textsuperscript{8-11} Still, assessments of these fitness parameters are not part of the clinical routine yet. The energy demands of walking and physical fitness (aerobic and anaerobic fitness) can be measured with clinical exercise tests. When the outcomes of these tests are used to set up a treatment plan, the recommended treatment for individuals may be better targeted to their walking problems. Therefore, the work in this thesis focused on assessing the usefulness of clinical exercise tests for children and young adults with physical disabilities.

**PHYSICAL DISABILITIES**

The group of children and young adults with physical disabilities represents a diverse array of conditions, such as CP, SB, muscular dystrophy, acquired spinal injuries, and amputations. To our knowledge, prevalence or incidence numbers for children and young adults with physical disabilities in the Netherlands have not been described by previous studies. Yet, in Canada 4 – 7% of all children have a physical disability, and the number of children with physical disabilities still increases.\textsuperscript{12} In this thesis, we included mostly individuals diagnosed with CP.

CP occurs in 1.96 per 1000 live births in countries with well-developed health care\textsuperscript{13} and is the most prevalent physical disability in childhood seen by pediatric rehabilitation practitioners, including pediatric rehabilitation physicians and pediatric physical therapists. The definition of CP is: “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”.\textsuperscript{14} The motor impairments are often accompanied by behavioral impairments, epilepsy, impairments of sensation, perception, cognition, communication, and by secondary musculoskeletal problems.\textsuperscript{15} The severity of motor impairments, as well as the cognitive, communicative and behavioral impairments are different for each individual,\textsuperscript{16} resulting in a wide variability in functioning of children and young adults with CP.\textsuperscript{17-19}
GMFCS

Because children and young adults with CP vary considerably in their functional abilities, it is important to classify their abilities. First, to promote consistency in the language we use, and second, to assess whether information from published studies is relevant for an individual. The severity of the gross motor function can be classified using the five-level Gross Motor Function Classification System (GMFCS). Children who walk without limitation are classified as GMFCS level I, children who walk with limitations as GMFCS level II, children who walk with a hand-held mobility device as GMFCS level III, children who might use hand-held mobility devices for short indoor distances but use a wheelchair transportation for community mobility as GMFCS level IV, and children who cannot move around independently as GMFCS level V. This thesis focused on individuals with at least some walking ability; therefore, participants with GMFCS level V were excluded.

WALKING PROBLEMS

Walking problems for individuals with physical disabilities are probably primarily caused by motor impairments that can lead to a pathological gait. Spasticity, decreased range of motion (ROM) caused by decreased muscle length or bony deformities, impaired muscle coordination and lower strength levels may cause these pathological gaits. During growth a mobility decline can occur; around 25% of the adults with CP experience a decline in walking abilities. Children and young adults with physical disabilities often seek medical advice due to walking problems, and an important aim of treatment for rehabilitation practitioners during growth is to improve walking or to maintain walking ability.

Associated with their pathological gait, the energy demands of walking of children and young adults with physical disabilities are often increased compared to typically developing (TD) peers. Consequently, walking can be a strenuous activity. Therefore, during daily life activities, individuals may walk less, and this may result in lower levels of physical activity. A decrease in physical activities may prevent fatigue, which is a major problem for individuals with physical disabilities. Lower levels of physical activity may result in lower levels of physical fitness. It is well known that children and young adults with physical disabilities have lower levels of physical fitness. Because individuals with CP have reduced levels of physical activity and lower levels of physical fitness they are at higher risk for developing metabolic and cardiovascular diseases.
Within the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) model, physical fitness quantifies the ability to perform bodily functions and activities of daily living, and to participate. Increased energy demands of walking and decreased physical fitness at the domain of body functions and structures according to the ICF-CY, both may cause problems in daily life activities, such as walking. Using more energy for walking combined with a reduced aerobic capacity leads to higher levels of physical strain of walking. The physical strain is expressed as the oxygen uptake of walking (VO_{2walk}) as a percentage of the maximal oxygen uptake (VO_{2peak}), an outcome of the aerobic capacity. The physical strain reflects the relative intensity of walking and an increased physical strain may lead to fatigue during activities of daily living. In adults with CP an increased physical strain relates to less daily walking time. Consequently, the ability to participate in daily life situations may be reduced, and interventions to improve the physical strain may consequently reduce walking problems and increase daily walking time.

The last decades, the energy demands of walking and especially the physical fitness have been subjects of increasing interest in research. However, both outcomes are scarcely

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**Panel 1.1 Definitions**

Physical activity is any bodily movement produced by the contraction of skeletal muscles that results in energy expenditure.1

Physical fitness is a set of attributes or characteristics that people have or achieve that relate to the ability to perform physical activity.1 The American College of Sports Medicine (ACSM) defined the components of physical fitness as cardiorespiratory (aerobic) fitness, body composition, muscular strength and endurance, and flexibility.2

Fatigue is the experience of feeling tired, weak or lacking energy.3 Often fatigue is described as a complex, subjective and multidimensional phenomenon.4

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used in rehabilitation settings to improve the diagnostic process for individuals with physical disabilities, while the treatment options for a rehabilitation practitioner may depend on these outcomes. Orthotics and orthopedic surgeries have, for example, the potential to reduce the energy demands of walking of ambulatory children with CP. Whereas fitness training has the potential to improve the physical fitness in children and young adults with physical disabilities. So, when both outcomes are measured, the rehabilitation practitioner may set a better treatment plan in order to improve walking problems.

**FATIGUE**

Many individuals with physical disabilities consult a rehabilitation practitioner with complaints about fatigue during or after walking, further referred to as walking-induced fatigue. In the literature, fatigue is often described as the experience of feeling tired, weak or lacking energy, further referred to as general fatigue. Questions of care related to general fatigue are: “I can’t go to school for an entire day because I’m too tired” and “When I’m home after a full school day I can’t do anything anymore because I’m too tired”. General fatigue is typically measured with questionnaires such as the Checklist Individual Strength (CIS). As children have difficulty of recalling their perception over a past period the Children’s OMNI Scale of Perceived Exertion (OMNI), instead of a questionnaire, can be used to measure the rate of perceived exertion real-time for a specific task. Using the OMNI after walking (OMNIwalk) can be considered as a task-specific way to measure this walking-induced fatigue. High physical strain values might cause the onset of early fatigue and while we assume that there is a relation between fatigue (both walking-induced fatigue and general fatigue) and increased physical strain values, no studies reported this.

**EXERCISE PHYSIOLOGY**

The source of energy to perform a motor task, such as walking, is adenosine triphosphate (ATP), because ATP is required for muscle contraction. There are three metabolic systems for producing ATP. Two anaerobic systems, namely the creatine phosphate system and anaerobic glycolytic system, and one aerobic system in which oxygen is consumed during the process of ATP generation. Immediately at the start of a task, the anaerobic creatine phosphate system supplies ATP to the muscles through the regeneration of ATP from adenosine diphosphate (ADP) using creatine phosphate as the phosphate donor.
donor. Then the anaerobic glycolytic system generates ATP through the degradation of carbohydrates. The anaerobic system allows muscles to perform high intensity exercise with short duration (1 – 2 min), whereas the aerobic system contributes to exercise at moderate intensity for a longer duration. This aerobic system generates ATP though the degradation of fatty acids and/or carbohydrates using oxygen.

**Energy demands of walking**

The energy demands of walking are determined by measuring the VO\textsubscript{2} and carbon dioxide output (VCO\textsubscript{2}) when a person walks at a self-selected speed. As the aerobic system needs time to start the oxygen delivery to the muscles and generate ATP, an individual needs to walk for at least two to three minutes before a steady-state is reached where there is an equilibrium between the oxygen demands and oxygen supply. The steady state is visually inspected and defined as two minutes of the whole test in which fluctuations in walking speed, VO\textsubscript{2} and VCO\textsubscript{2} showed the least change and RER was below 1.0. The RER is the ratio between the amount of VCO\textsubscript{2} produced in metabolism and the amount of VO\textsubscript{2} used and calculated as VCO\textsubscript{2} divided by VO\textsubscript{2}. The mean VO\textsubscript{2} (in ml·kg\textsuperscript{-1}·min\textsuperscript{-1}) and RER’s are computed over these steady state periods and used to calculate the average steady state resting and gross energy consumption (ECS\textsubscript{rest} and ECS\textsubscript{gross}, both in J·kg\textsuperscript{-1}·min\textsuperscript{-1}), calculated by \((4.960 \times \text{RER} + 16.040) \times \text{VO}_2\text{ (ml·kg}^{-1}·\text{min}^{-1})\) (Figure 1.1). The net energy consumption (ECS\textsubscript{net}) was calculated by ECS\textsubscript{gross} - ECS\textsubscript{rest}. Gross energy cost (EC) and net EC are than calculated by dividing the ECS\textsubscript{gross} and ECS\textsubscript{net} by walking speed (m·min\textsuperscript{-1}), expressed in J·kg\textsuperscript{-1} per meter (J·kg\textsuperscript{-1}·m\textsuperscript{-1}). The gross EC is defined as the total energy used per unit of distance covered. When normalization for resting energy consumption is required, for example to control for the effects of growth and development, the net EC is calculated. By doing so, the net EC gives a more direct indication of the actual EC of walking because it is independent of resting energy consumption. A normalization procedure for the net EC is the net nondimensional (NN) scheme, described by Schwartz et al. It is assumed that the NN EC is an even better variable for longitudinal evaluations, because this outcome is essentially independent of body height, weight and mass.

For children with CP, the energy demands of walking are approximately 17% (GMFCS level I) to 263% (GMFCS level III) higher compared to TD peers. Small studies for children with SB show that their energy demands of walking are approximately 89% to 100% higher compared to TD peers. The energy demands increase with larger motor involvement (higher GMFCS level) for children with CP. For TD children and...
adolescents, the gross EC declines with aging, while the net EC shows a more gradual decline with increasing age until adulthood. How the gross, net and NN EC develop with growth for individuals with CP is not completely understood yet. Differences between the development for individuals with CP compared to TD peers have not yet been described, while this information is necessary to select the most appropriate EC outcome to evaluate a treatment.

**Physical fitness**

Both the aerobic and anaerobic fitness are defined as components of the physical fitness in this thesis (Figure 1.2). While the anaerobic fitness is not a separate component according to the ACSM, the anaerobic fitness is an important determinant for physical activity in children, because they have mostly short, intermittent activity patterns. The outcomes of aerobic and anaerobic fitness tests can be defined in capacity and performance outcomes (Figure 1.2), both measuring different constructs. Capacity measures are a direct measure of the physiologic status, an example is the VO\textsubscript{peak}. Whereas performance measures express what the body is able to perform during aerobic or anaerobic exercise, for example time and power output.
Aerobic fitness

The ‘gold standard’ outcome of the aerobic capacity is the VO₂peak, the maximal amount of oxygen that an individual can use for physical activities. Children and young adults with physical disabilities have low VO₂peak values compared to TD peers. VO₂peak is approximately 14 – 29% lower in children with CP and 32 – 54% lower in children and adults with SB. There are in general three physiological systems that can cause lower VO₂peak values: the muscular system, the cardiovascular system and the ventilatory system. Children with CP have impaired muscle function mostly due to a reduced muscle volume and this reduction may result in lower numbers of available mitochondria for aerobic oxidation. The cardiovascular system seems not directly influenced by the motor impairments in individuals with CP. However, GMFCS level I and II children show a lower oxygen pulse in comparison with TD peers. This may reflect a reduced oxygen extraction in the muscles (muscular system) and/or a lower stroke volume (cardiovascular system). While reduced muscle volume is expected to cause a lower oxygen pulse, lower levels of physical activities and consequently deconditioning may also result in lower stroke volumes and consequently in lower oxygen pulses. Inconclusive outcomes are reported for the role of the ventilatory system. It is suggested that the spastic paresis affects the respiratory muscles. However, two recent studies did not support this hypothesis for ambulant children with CP. So, a reduced VO₂peak in individuals with CP seems mostly influenced by impaired muscle function in combination with deconditioning.
Figure 1.2  Diagram of the components of physical fitness.
SRT-I, 10-meter Shuttle Run test GMFCS level I; SRT-II, 10-meter Shuttle Run test GMFCS level II; MPST, muscle power sprint test.
The anaerobic threshold is also an aerobic capacity outcome (Figure 1.2) and defined as the point above which energy production by aerobic oxidation is supplemented by anaerobic glycolysis. Walking in daily life is a light or moderate exercise activity for TD children and young adults. When walking at intensities near the anaerobic threshold one may become exhausted and muscles may become sore and painful because of intracellular accumulation of lactate and acidosis. Children with CP have increased VO$_{2\text{walk}}$ values and lower anaerobic threshold values compared to TD, therefore their VO$_{2\text{walk}}$ might be close to or even above their anaerobic threshold. While this might explain their complaints about walking-induced fatigue, it is not known yet how many individuals walk around or above their anaerobic threshold.

**Physical strain**

The combination of increased VO$_{2\text{walk}}$ (and consequently increased energy consumption) and reduced VO$_{2\text{peak}}$ values lead to higher levels of physical strain of walking and other daily activities. The physical strain (Figure 1.3) is expressed as the VO$_{2\text{walk}}$ (ml·kg$^{-1}$·min$^{-1}$) as a percentage of the VO$_{2\text{peak}}$ (ml·kg$^{-1}$·min$^{-1}$). Only two studies reported physical strain values for children. For TD children the physical strain shows values around 26% whereas higher values are reported for children with CP and SB; 52% in children with mild CP (mostly GMFCS level I and some GMFCS level II children) and 63% in ambulatory children with SB. Physical strain values for children with CP who are walking with hand-held devices are yet unknown.

![Figure 1.3 Visual representation of the physical strain.](image-url)

In this figure, 4 cases are presented with each a different physical strain. Case 1 and 2 both have normal VO$_{2\text{peak}}$ values (45 ml·kg$^{-1}$·min$^{-1}$), however their physical strain differs because their VO$_{2\text{walk}}$ differs. For case 1 the physical strain is 33% (15 ml·kg$^{-1}$·min$^{-1}$ / 45 ml·kg$^{-1}$·min$^{-1}$ * 100%). The physical strain for case 2 is 76% (35 ml·kg$^{-1}$·min$^{-1}$ / 45 ml·kg$^{-1}$·min$^{-1}$ * 100%). Case 3 and 4 both have a reduced VO$_{2\text{peak}}$ (25 ml·kg$^{-1}$·min$^{-1}$), because their VO$_{2\text{walk}}$ differs their physical strain is not identical (case 3 is 60%; case 4 is 100%). * PS, physical strain; VO$_{2\text{walk}}$, oxygen uptake during walking; VO$_{2\text{peak}}$, peak oxygen uptake.
Anaerobic fitness

Anaerobic capacity is the maximal amount of ATP resynthesized via anaerobic metabolism during short bursts of high-intensity exercise. Because it is not possible to measure the anaerobic capacity non-invasively, often the anaerobic performance is measured while cycling or running (Figure 1.2). The mean and peak anaerobic power are anaerobic performance outcomes [expressed in Watt per kilogram (W·kg⁻¹)]. Children with CP between the ages of 7 and 12 years show, compared to TD peers, 39 – 72% lower values for the mean anaerobic power and these values decrease with a higher GMFCS level. Lower values are probably associated with 1) decreased muscle volumes and therefore lower strength levels, 2) reduction in fast type II muscle fibers, and 3) muscle coordination problems.

CLINICAL EXERCISE TESTS

We can measure the energy demands of walking when children and young adults walk for 6 minutes at a self-selected speed on an oval track when they wear a portable gas-analysis system (Figure 1.4). When using this protocol, the EC can be determined reliable in children with CP and SB. The aerobic capacity is often measured with a maximal exercise test on a cycle ergometer. The test used in this thesis starts with a 2- to 4-minute warming-up, followed by a 3- to 5-minute submaximal exercise phase. After 1-minute rest, the maximal phase starts with 1-minute incremental exercise bouts until exhaustion. The test-retest reliability of this protocol is excellent for children with CP. A 20-second Wingate sprint capacity test is used to estimate the anaerobic performance in children with CP. The test starts with three warming-up sprints of 5 seconds after which the 20-second Wingate test is performed against a constant breaking torque. The test-retest reliability of the mean anaerobic power is excellent for children with CP, while the peak anaerobic power shows a lower reliability.

RACERUNNER

While laboratory tests, such as the maximal exercise test on a cycle ergometer, are indicated for research purposes and clinical decision making, field tests are easier to perform in a clinical environment. For children with CP classified as GMFCS levels I and II there is a set of valid field tests that are used to measure the aerobic performance (shuttle run test) and anaerobic performance (muscle power sprint test). However, only
a few tests are available for children classified as GMFCS level III and especially GMFCS level IV. A review stated that further clinimetric studies of field tests for children who are classified as GMFCS levels III to V are required. This review also concluded that adaptation to the equipment might be necessary for existing measurements in order to develop adequate tests for this population.

Therefore, a novel field test was developed, based on the 6 minute walking test, to measure the walking distance with the racerunner in children with CP classified as GMFCS levels III and IV: the 6-Minute RaceRunner Test (6MRRT). The racerunner is an alternative-walking device for individuals with limited walking abilities. This device consists of a 3-wheeled frame, with handlebars, saddle and a trunk support, like a tricycle. Rather than using a pedaling system, participants propel themselves forward by stepping their feet on the ground (Figure 1.5). An advantage of the racerunner is that participants reach higher levels of speed because the racerunner is light and has a more aerodynamic shape in comparison with existing gait trainer devices. Consequently, we assume that individuals who use the racerunner achieve high heart rates during an intervention and
therefore, the racerunner might be suitable for variable training programs. Whether the 6MRRT is a reliable and valid test to measure improvements in the walking distance with the racerunner on individual and group level needs to be determined.

AIMS AND OUTLINE OF THIS THESIS

The studies presented in this thesis focus on assessing the usefulness of clinical exercise tests for children and young adults with physical disabilities. While many studies reported group mean values for the energy demands of walking and aerobic capacity, there is no information about the occurrence of increased energy demands or decreased aerobic capacity for individuals with physical disabilities. In order to describe how many individuals have deviated values, cut-off values are needed to define whether the gross EC are within normal ranges or increased and whether the VO\text{peak} values are within normal ranges or decreased. Chapter 2 describes these cut-offs for the gross EC and VO\text{peak} and, based on these cut-offs, this chapter describes the occurrence of increased gross...
EC and decreased VO\textsubscript{peak} values in children and young adults with physical disabilities and walking problems. Measuring all individuals with walking problems is a time and money consuming issue and therefore this chapter furthermore investigates whether patient characteristics can be used to select those individuals most likely to require clinical exercise testing.

**Chapter 3** describes the average physical strain of walking in children and adolescents with CP classified as GMFCS levels I, II and III, and compares these values with the physical strain in TD peers. Furthermore, this chapter describes how many children and adolescents with CP, and who are typically developing, walk above their anaerobic threshold.

**Chapter 4** determines whether walking-induced fatigue and general fatigue are related to energy demands of walking and physical fitness in children and young adults with physical disabilities who experience problems with walking. Since measuring fatigue immediately after walking is a more direct measure of fatigue compared to general fatigue measured with a questionnaire, we hypothesized that the relation with the energy demands of walking and physical fitness will be stronger for walking-induced fatigue compared to general fatigue.

When energy demands of walking are used to evaluate treatment in CP children, the process of more efficient walking, observed in TD children, needs to be considered. In TD children, the energy demands of walking decrease as they get older, even until adult age, and it is assumed that this is similar for individuals with CP. **Chapter 5**, therefore, cross-sectionally assessed the association between the energy demands of walking with age and body height for children and young adults with CP, compared to TD peers. Three outcomes for the energy demands of walking were used: 1) the gross EC, 2) the net EC, and 3) the NN EC.

Because the 6 minute walking test is a valid and reliable test for measuring walking distance in children with CP classified as GMFCS levels I, II, and III\textsuperscript{85-87} we assume that the 6MRRT test is also a valid and reliable test for children with CP classified as GMFCS levels I, II and III to determine the distance covered with the racerunner. **Chapter 6**, therefore, investigates whether the 6MRRT is a valid and reliable test for children and young adults with CP classified as GMFCS levels II, III and IV. Finally, **Chapter 7** discusses findings, clinical implications and directions for future research.
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