SUMMARY

Applied exercise physiology in rehabilitation of children with cerebral palsy

Cerebral palsy (CP) is the most common cause of physical disability in childhood. 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”. Persons with spastic CP can be involved unilateral or bilateral and have an impaired muscle function: an impaired muscle activation, muscle stiffness and impaired muscle length. The severity of the motor impairment with regard to gross motor function can be classified according to the Gross Motor Function Classification System (GMFCS), which identifies five levels: 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 level IV and V are not able to walk.

Children with CP are at risk for an inactive lifestyle and low levels of physical fitness, which can lead to increased health risks later in life. This reduction in physical fitness and physical activity may increase the impact of the disorder on daily functioning. Although previous studies have reported decreased values of aerobic and anaerobic fitness in walking children with CP, few researchers have investigated how different physical fitness components are influenced by the severity of the motor disorder, and in which way the level of physical fitness affects daily physical activity. 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. The main aims of the studies described in this thesis are therefore to investigate the level of physical fitness and physical activity in walking children with spastic cerebral palsy across the different levels of gross motor function I-III and to determine the relations between physical fitness and physical activity.

In order to measure physical fitness, we have primarily assessed aerobic fitness, anaerobic fitness and secondarily, muscle strength. These fitness components are considered to be important determinants for physical activity and exercise in children who have short, intermittent activity patterns. The maximum amount of oxygen consumed during exercise (VO_2peak) reflects the aerobic fitness and 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. Anaerobic fitness is the maximal amount of adenosine triphosphate (ATP) that is resynthesized via anaerobic metabolism during short bursts (30-45 s) of high intensity exercise. In order to estimate anaerobic fitness, mean power output can be measured during a short sprint test (20-30 s) on a cycle ergometer, i.e. a Wingate test. Muscle strength is the amount of force generated by muscle contraction. In this thesis, measurement of muscle strength is limited to isometric muscle strength of the knee extensors and hip abductors.

In order to properly measure these physical fitness components in children with CP, exercise tests appropriate for children with CP are required. **Chapter 2** presents a systematic review of studies investigating clinimetric properties of aerobic and anaerobic fitness tests in children with CP. The systematic search identified twenty-four studies that used a laboratory-based or field-based test to measure maximal aerobic or anaerobic fitness. Five studies reported clinimetric properties for 5 tests (2 aerobic and 3 anaerobic measures). The level of evidence is strong for good validity and reliability of the field-based tests and, the level of evidence is unknown for validity and low to moderate for good reliability of laboratory-based tests. The results show that there is a paucity of reliable and valid measurement instruments with which to assess aerobic and anaerobic fitness in children with CP. Of particular note, we detected a lack of clinimetric studies of laboratory-based measures in children with CP at all GMFCS levels.

The study in **chapter 3** evaluates the reliability of VO_2peak assessed with a progressive maximal cycle ergometer test in children classified as GMFCS level I, II or III. Each participant performed a progressive maximal cycle ergometer test on two separate days, with the workload increasing every minute in steps of 3-11 W, dependent on height and GMFCS level. Sixteen participants performed two successful tests. Reliability for VO_2peak, using the intraclass correlation coefficient (ICC) was excellent (ICC: 0.94; 95% CI: 0.83-0.97). The smallest detectable change was 5.72 $mL \cdot kg^{-1} \cdot min^{-1}$, reflecting 14.6% of the mean. These results show that in children with CP classified as GMFCS levels I and II, the reliability of VO_2peak, as assessed by a progressive maximal cycle ergometer test, is excellent and is expected to detect change in cardiorespiratory fitness over time. More research is required to establish the reliability of VO_2peak in children classified as GMFCS level III.

Chapter 4 describes the level of physical fitness in walking children with CP compared with children who show a typical development (TD). Seventy children with CP, classified as GMFCS level I, II or III, and 31 TD children participated in fitness measurements. Analysis revealed a lower VO_2peak for children with CP (I: 35.5 ± 1.2 (SE); II: 33.9 ± 1.6; III: 29.3 ± 2.5 $mL \cdot kg^{-1} \cdot min^{-1}$, $p < 0.001$) compared with TD children (41.0 ± 1.3, $p < 0.001$) and similar differences for the anaerobic threshold ($p < 0.001$). In addition, peak ventilation (VEpeak) and peak O_2 pulse were lower in children with CP, whereas the peak ventilatory coefficient of CO_2 (VE/VCO_2) was higher in children with CP compared with TD children ($p < 0.05$) and the peak ventilatory coefficient of O_2 (VE/VO_2) was similar between groups. All these aerobic variables showed no differences between GMFCS levels. Peak aerobic power output was lower for children with CP versus TD children ($p < 0.001$) and decreased significantly with increasing motor impairment. Anaerobic fitness (P20mean) was also lower in children with CP (I: 4.6 ± 0.2; II: 3.3 ± 0.2; III: 2.5 ± 0.4 $W \cdot kg^{-1}$) versus TD children (6.4 ± 0.2, $p < 0.001$) and showed a further decrease with increasing motor impairment. Interestingly, these results show that differences between the different GMFCS levels are less pronounced for aerobic fitness, while anaerobic fitness decreases with increasing GMFCS level. Future research should aim to uncover the role of inactivity and the effects of training interventions on exercise responses in children with CP.

The aim of the study described in **chapter 5** was to investigate the longitudinal relationship among changes in the previously described fitness components in children with CP, and between changes in fitness and mobility capacity. Forty-six children with bilateral (N = 24) or unilateral (N = 22) CP participated in fitness measurements. Mobility capacity was assessed with the gross motor function measure (GMFM) and a walking capacity test. It appeared that in children with bilateral CP fitness components were related to each other, and that physical fitness showed a relationship with mobility capacity, while no relationships were found in children with unilateral CP. In children with bilateral CP, aerobic fitness was strongly related to anaerobic fitness ($p < 0.001$), while aerobic fitness showed only a weak relationship with muscle strength ($p < 0.05$). Anaerobic fitness was not related to muscle strength. Anaerobic fitness and muscle strength were determinants for mobility capacity in children with bilateral CP but not in children with unilateral CP. The strong longitudinal relationships in children with bilateral CP indicate that increasing anaerobic fitness is likely to have a positive effect on aerobic fitness and might have some positive influence on mobility capacity. In children with unilateral CP, alternative approaches should be the subject of future research.

The study presented in **chapter 6** compares the walking-related physical activity of children with CP and TD children. Physical activity was determined by stride rate activity measured with an activity monitor. Exercise intensity was measured by heart rate, expressed as percentage of heart rate reserve (%HRR). In addition, the %HRR of stride rate activity levels (0 strides/min, 1-15 strides/min, 16-30 strides/min, 31-60 strides/min and > 60 strides/min) was determined. Forty-three children with CP (GMFCS I, II or III) and 27 TD children wore a StepWatch™ activity monitor for 1 week and a heart rate monitor for 3 days. The results showed that the levels of daily stride rate activity in children with CP were lower than those of TD children ($p < 0.05$). Improving stride rate appears to be a priority, as children with CP are less able to cover the same distance and are therefore hindered when participating in peer activities. Mean %HRR at all stride rate activity levels was not different between TD, GMFCS I and II, while mean %HRR was higher for GFMCS level III at stride rates ≤ 30 strides/min ($p < 0.05$). The StepWatch™ monitor can be used to compare stride rate activity in TD children and children with CP classified as GMFCS level I or II, as they show a similar effort when walking with the same stride rate, while children classified as GMFCS level III show a higher effort. This should be taken into account when interpreting results of stride rate activity levels. However, a physiological measure, such as the heart rate monitor, is recommended to measure daily exercise intensity. Exercise intensity over the day was comparable between children with CP and TD children. This result is remarkable as physical fitness and stride rate activity are lower in children with CP than in TD children. Apparently, exercise intensity over the day does not make a major contribution to adequate levels of physical fitness in children with CP. Future studies should investigate the relation between daily exercise intensity and whether a different distribution of exercise intensity leads to better physical fitness in CP.

The study described in **chapter 7** investigates the longitudinal relations between physical fitness and daily walking-related physical activity and fatigue. Twenty-four children with bilateral CP and 22 children with unilateral CP performed fitness and physical activity (stride rate) measurements. Fatigue was determined with the PedsQL multidimensional fatigue scale. All physical fitness parameters showed a positive, significant relationship to the level of walking-related physical activity in children with bilateral CP, whereas no relationship was seen in children with unilateral CP. Although not clinically relevant, a significant relationship between functional muscle strength and fatigue was found in children with a unilateral CP. Children with bilateral CP might benefit from improved physical fitness to increase their physical activity level or vice versa. Interventions aimed at improving physical activity levels should be differently targeted in children with either bilateral or unilateral CP**.**

In conclusion, children with CP have lower levels of physical fitness and walking-related physical activity compared with children showing typical development, indicating this is an important issue to consider in rehabilitation treatment. **Chapter 8** presents an extensive discussion of our studies and their clinical implications. The main findings indicate that the differences between each of the GMFCS levels are less pronounced for aerobic fitness, while anaerobic fitness decreases with increasing GMFCS level. The major differences in physical fitness levels among the children with CP point to the need for objective fitness measurements in children with CP with which to guide interventions. Children with bilateral CP might benefit from increasing their anaerobic fitness for improving the capacity of activities, while increasing aerobic fitness relates to better performance of physical activities in daily life. Interventions aimed at improving physical activity levels should be differently targeted in children with either bilateral or unilateral CP**.**