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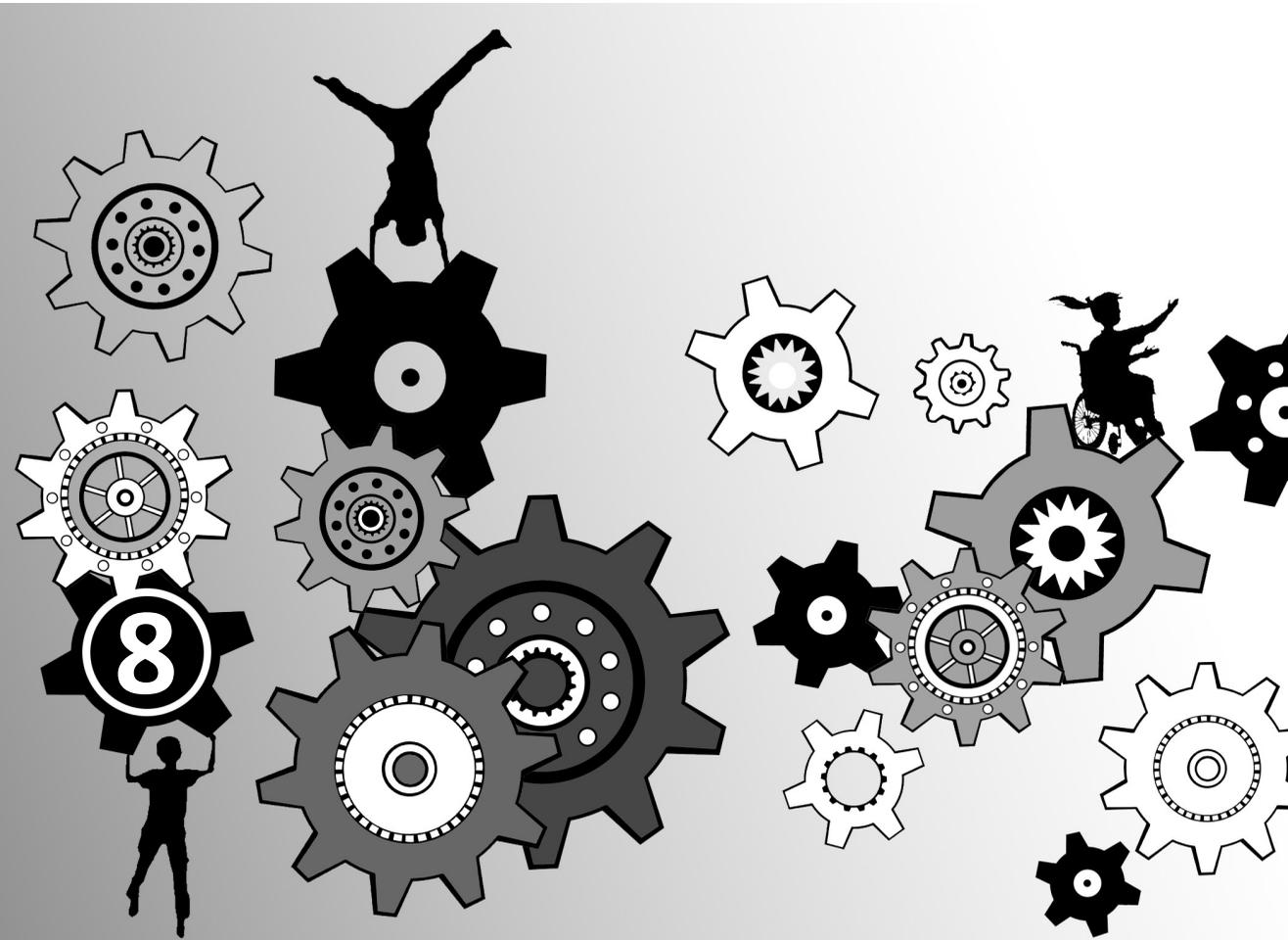
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# CHAPTER 8

General Discussion

Astrid CJ Balemans



The main aims of the studies described in this thesis were to investigate the level of physical fitness and physical activity across the different levels of gross motor function in walking children with cerebral palsy (CP) and to determine the relations between physical fitness and physical activity in this group.

## MAIN FINDINGS

### *Part I: Clinimetric properties of physical fitness measurement*

- 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 Gross Motor Function Classification System (GMFCS) levels.
- In children with CP classified as GMFCS levels I and II, the reliability of  $VO_2$  peak, as assessed by a progressive maximal cycle ergometer test, is excellent and is expected to detect change in cardiorespiratory fitness over time.

### *Part II: Physical fitness*

- Children with CP have decreased aerobic and anaerobic exercise responses, although decreases in aerobic exercise responses were not as severe as expected based on motor impairment.
- Relationships between various physical fitness components and between physical fitness components and mobility capacity were found to differ in children with unilateral CP compared to those with bilateral CP. In children with unilateral CP, no relationships were found between physical fitness components. In children with bilateral CP, aerobic fitness was strongly related to anaerobic fitness, while aerobic fitness showed only a weak relationship to muscle strength. Anaerobic fitness was not related to muscle strength. Anaerobic fitness and muscle strength were determinants for gross motor function and walking capacity (mobility capacity) in children with bilateral CP but not in children with unilateral CP.

### *Part III: Daily physical activity and the relationship with physical fitness*

- Children classified as GMFCS levels I and II showed similar effort (% heart rate reserve) when walking with the same stride rate as typically developing children, while children classified as GMFCS level III showed a higher effort. Children with CP have a lower daily stride rate activity than typically developing children, while daily exercise intensity (also expressed as % HRR) seems comparable.
- In children with bilateral CP, all physical fitness components showed a positive, significant relationship to physical activity level, whereas no relationship between physical fitness and physical activity level was seen in children with unilateral CP. Physical fitness was statistically significantly related to fatigue in all children with CP, but was not clinically relevant.

The results of this thesis indicate that children with CP have decreased levels of physical fitness and physical activity. Greater physical fitness was longitudinally related to an improved mobility capacity and to a higher level of daily physical activity in children with bilateral CP. Therefore, increasing physical fitness through training interventions might have a dual benefit: if children with bilateral CP increase their maximum physical fitness level, limitations in mobility might be lowered and levels of daily physical activity might be increased. This is not the case for children with unilateral CP. Explanations for these findings will be discussed in this chapter.

### **Methodological considerations for measuring physical fitness in cerebral palsy**

The results of the study reported in chapter 4 showed that children with CP have lower levels of physical fitness compared to children showing typical development, and that among the children with CP there are major differences in physical fitness levels. A great deal of variation among children with different limitations in gross motor function was observed, but children with a comparable limitation in gross motor function also showed considerable variation. The large observed variation in physical fitness levels suggests that a low level of physical fitness is not present in all children with CP and that there are possibilities for improvement. This finding points to the need for objective fitness measurements in children with CP with which to guide interventions.

In order to measure physical fitness accurately, measurements that adequately reflect the level of physical fitness in individuals with CP are required.<sup>41</sup> In spastic CP, impaired muscle function, impaired muscle activation and impaired biomechanical muscle properties all influence the ability of the child to perform physical fitness assessments, and can affect the physical fitness outcome measures.<sup>17</sup> For example, impaired muscle activation can affect maximal exercise cycling performance, resulting in a lower peak load. This effect was confirmed by the results described in chapter 4, in which a decreased peak power output was found in children with CP, with a further decrease with higher GMFCS levels. The  $VO_2$ peak, however, is independent of the limitations imposed by impaired coordination, and is thus considered the single best indicator for aerobic fitness in children.<sup>4;24;47</sup>  $VO_2$ peak therefore provides the best reflection of the child's cardiorespiratory fitness level.

The results in chapter 2 show that physical fitness can be assessed with a laboratory-based test (cycle ergometer, arm crank ergometer, treadmill) or a field-based (running) test. The usefulness of these different measurement methods was acknowledged in a previous Delphi study.<sup>41</sup> The selection of the measurement tool - either a laboratory-based or field-based test - is essentially determined by the goal of the assessment. In the studies described in this thesis, a laboratory-based test was used to measure  $VO_2$ peak and to obtain more information on exercise responses (chapter 4). In children who were able to walk, the preferred activity-specific mode of exercise testing was walking or running. However, a cycle ergometer test was used to enable testing of children with disturbances in balance and of children dependent on assistive devices for walking. The results in chapter 3 showed an excellent

reliability of  $\text{VO}_2$ peak as assessed on a cycle ergometer. Although laboratory-based tests are acknowledged to be appropriate standardized testing modes, these tests also have disadvantages such as expense and the availability of equipment. When a more practical field test is performed, the same influence of impaired coordination on test performance applies as described earlier in this chapter. Impaired coordination affects walking ability and consequently influences the outcome measure (maximal time).<sup>30</sup> Therefore, when an estimate of aerobic fitness is required, peak power output on a cycle ergometer and maximal time for a walking test are appropriate measures,<sup>36;38</sup> unless the influence of coordination is taken into account when interpreting test outcomes. Therefore, a field-based test is especially useful for evaluation over time within one individual. However, in clinical decision making evaluation of the physical strain may be required. The physical strain is the oxygen consumption during walking expressed as a percentage of the  $\text{VO}_2$ peak. For this purpose, an objective standardized laboratory-based test with measurement of gas exchange, enabling measurement of  $\text{VO}_2$ peak, is recommended.

Another advantage of assessing aerobic fitness by measurement of gas exchange is the possibility to monitor the respiratory exchange ratio (RER). The RER can serve as a criterion to estimate whether an individual has reached his or her maximal cardiorespiratory capacity.<sup>3</sup> We observed that not all children with CP achieved maximal cardiorespiratory capacity. This was indicated by heart rates (HR) lower than 180 and/or RER values beneath 1.00, with no signs of subjective exhaustion. There are several possible explanations for an inability to achieve maximal exercise. Firstly, a lack of motivation to make sufficient effort to achieve maximal exercise may have played a role. Secondly, some children appeared to be unable to keep up with the pedaling rate when the load was increased. A reason for this might be impaired coordination.<sup>12;28</sup> The inability of continuing pedaling with increasing load may also be due to low muscle strength.<sup>45</sup> It is difficult to distinguish between insufficient effort and peripheral limitations, such as impaired coordination and low muscle strength, when seeking an explanation for a failure to achieve maximal cardiorespiratory exercise. For this reason, we used objective criteria (HR and RER) described in the literature to determine whether the test was successful in achieving maximal aerobic exercise.<sup>3;42</sup> Test performances of some children seemed to be limited by peripheral limitations. For example, one child completed an exercise test with a HR value lower than 180 and an RER below 1.0 but with subjective exhaustion. Despite maximal effort, this test outcome might not reflect the child's maximal aerobic fitness as represented by the total amount of oxygen that the body can use during exercise, but might actually reflect the child's aerobic cycling capacity. We observed that some children, after following physical fitness training that included muscle strength exercises, achieved higher HR's and RER's at test termination, with a concomitant increase in  $\text{VO}_2$ , than during the baseline exercise test. In these cases it is possible that a child was able to put more stress on the cardiorespiratory system, resulting in a higher aerobic cycling capacity. In addition to a better cycling capacity, a larger muscle mass may have resulted in a higher oxygen extraction during exercise, resulting in higher  $\text{VO}_2$ . Therefore, and as

acknowledged in chapter 2 and 3, more research into aerobic fitness is required in the more severely impaired - those prevented by peripheral restrictions from achieving maximal cardiorespiratory exercise.

### Insights into exercise responses

The results described in chapter 4 show that physical fitness is lower in children with CP compared to children who show typical development. These results were comparable with earlier studies on physical fitness in CP.<sup>10;16;31;31;35</sup> Chapter 4 also describes investigations of the aerobic and anaerobic exercise responses, differentiated by GMFCS level. 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.

For aerobic fitness, no differences were detected between children classified as GMFCS level I or II and there was only a tendency to lower  $VO_2$  peak values in GMFCS level III compared to levels I and II. The impaired muscle function in CP influences the whole chain of ventilatory and cardiovascular coupling to muscle respiration during exercise.<sup>7;44</sup> The systems in this chain determine  $VO_2$  peak, which reflects cardiorespiratory fitness (i.e. aerobic fitness).<sup>44</sup> Generally, it is believed that it is not the availability of mitochondria and oxidative enzymes that is the major limiter of  $VO_2$  peak in healthy individuals but rather the oxygen supply to the exercising muscle.<sup>46</sup> However, the smaller muscle mass in CP might result in a lower number of available mitochondria for aerobic oxidation.<sup>6</sup> In children with CP,  $VO_2$  peak might therefore be primarily limited by impaired muscle respiration. This would also explain the finding of a lower anaerobic threshold in children with CP compared to typically developing children. While it has been shown that muscle fibers of children with CP can increase in volume after training,<sup>19</sup> whether an increase in muscle volume in CP leads to an increase in  $VO_2$  peak has not yet been investigated. Because children with CP are suggested to have proportionally more type I muscle fibers, this would suggest that the fiber type distribution favors  $VO_2$  peak.<sup>8;11</sup> Chapter 4 also includes the finding that children classified as GMFCS level I show a lower oxygen pulse in comparison to typically developing children. As oxygen pulse is a measure that reflects both oxygen extraction in the muscle and stroke volume, this might indicate that the limited oxygen pulse could also be a result of lower stroke volumes. Stroke volume is determined by cardiac output and heart rate. As cardiac output was found to increase with training, oxygen pulse in children with CP might increase following physical fitness training.<sup>46</sup> The decreases in aerobic fitness seem to be a result of the impact of the disorder on the whole chain that determines aerobic fitness. However, as several factors in this chain seem to be subject to improvement, opportunities for training are available.

In agreement with previous studies, the results described in chapter 4 show that anaerobic fitness is decreased to a larger extent than aerobic fitness in children with CP. An explanation for this might be that anaerobic mean power, as representative of anaerobic fitness, is strongly dependent on muscle coordination. Impaired muscle coordination results in a lower mechanical efficiency, which in turn influences power output. In addition, the

previously mentioned predominance of type I fibers might also affect anaerobic fitness.<sup>8</sup> The larger differences in anaerobic fitness by level of gross motor function compared to aerobic fitness indicates that anaerobic fitness is more strongly influenced by the motor disorder than aerobic fitness, a conclusion supported by the absence of a correlation between aerobic fitness and gross motor function and the presence of a moderate correlation between anaerobic fitness and gross motor function.<sup>39</sup> As children have activity patterns with short bursts of exercise, the decrease in anaerobic fitness might limit their daily physical activity.<sup>5</sup> Since studies that investigated the effect of training on anaerobic fitness are few in numbers, it is important to investigate further the effect of physical fitness programs on anaerobic fitness in this population.<sup>33;40</sup>

### **Intensity of exercise**

In all individuals, maintaining and improving one or more components of physical fitness requires regular exercise.<sup>2</sup> Exercise has been 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”,<sup>2;9</sup> Exercise consisting of intensive activities is especially important in improving physical fitness.<sup>13</sup> Guidelines for exercise aimed at increasing physical fitness state that the intensity of training should be moderate (40-60% of heart rate reserve) to vigorous (60-85% of heart rate reserve).<sup>13</sup> When improving physical fitness levels in deconditioned individuals, training programs should consist of exercises with a low intensity, i.e., 40-50% of heart rate reserve, which should be progressively increased throughout the training period to ensure an overload.<sup>1</sup> It is especially recommended to train at an exercise intensity relative to the individual’s maximum.<sup>13</sup> In addition to exercises as part of a training program, daily activities of sufficient intensity might contribute to maintaining and enhancing physical fitness. In children with CP who show lower levels of physical fitness, the intensity of normal exercise during the day might be sufficient to contribute to physical fitness. Therefore, in order to investigate levels of exercise intensity in children with CP, in chapter 6 the exercise intensity as determined by heart rate reserve during a normal day was determined in walking children with CP.

### **Daily exercise intensity**

The findings described in chapter 6 suggest that the intensity of normal exercise during the day for children with CP was comparable to that of typically developing children. This was remarkable considering that the levels of physical fitness and the levels of stride rate activity are lower in children with CP compared with typically developing children (see chapter 4). These findings indicate that exercise intensity over the day does not make a major contribution to adequate levels of physical fitness in children with CP. An explanation for the lack of difference in exercise intensity, despite lower physical fitness levels in CP, might be found in the distribution of intensity of activities over the day. It could be that several periods of short, highly intensive activity accumulated to a total exercise intensity. Equally,

longer periods of moderate intensity may account for the total intensity over the whole day. It is thus possible that it is more important for children with CP to perform activities with an anaerobic character in order to maintain and enhance both aerobic and anaerobic fitness. Therefore, training programs aimed at improving physical fitness through high intensity exercises might contribute to a larger extent to the level of physical fitness than normal daily exercise. A previous study that included anaerobic exercises reported increases in both aerobic and anaerobic fitness.<sup>40</sup> Moreover, focusing on anaerobic activities has additional benefits in terms of a better representation of the physical activity pattern of children in general, which is characterized by short bursts of high intensity activities. In addition, anaerobic activities might be more feasible in children who have a shorter attention span.<sup>5</sup>

### **The relation of physical fitness to daily physical activity**

As shown in chapter 7,  $VO_{2peak}$  was positively related to the level of daily walking activity in children with bilateral CP, as measured by the stride rate. This is an interesting and promising finding since the results of chapter 6 showed that the levels of daily stride rate activity in children with CP were lower than those of typically developing children. 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. The intervention program 'Learn 2 Move' was developed with the aim of stimulating the level of physical activity in daily living. This multi-component program included physical fitness training and physical activity stimulation through counseling and home-based physiotherapy.<sup>34</sup> However, the program showed no effects on physical fitness and physical activity as measured by stride rate.<sup>33</sup> The results of the *Learn 2 Move* study showed that there is large inter-individual variation in changes in physical fitness and daily physical activity.<sup>33</sup> Some participants improved on physical fitness and physical activity, while others deteriorated despite their group allocation. Interestingly, the results of chapter 7 showed that a change in aerobic fitness was related to a change in daily stride rate activity in children with bilateral CP. This relationship indicated that physical fitness training might be a suitable approach to improving the level of physical activity in children with bilateral CP. This relationship was not found in children with unilateral involvement. The *Learn 2 Move* intervention program included both unilateral and bilateral involved children<sup>33</sup>. The lack of a relationship between physical fitness and physical activity in children with unilateral CP indicated that physical fitness training might not be a suitable approach to improving the level of physical activity in unilateral children. Despite this, the lower levels of physical fitness and physical activity in children with unilateral CP, as described in chapter 7, indicate that these issues are important and should be considered in rehabilitation treatment. The decrease in physical fitness and physical activity is less pronounced in children with unilateral CP than in children with bilateral CP. Other factors, such as cognition and environmental factors, may have a greater impact on the level of physical activity in children with unilateral CP.<sup>43</sup>

*Capacity vs. performance of activities*

There is a discrepancy between what a child can do (capacity) and what a child actually does in his or her own environment (performance).<sup>29</sup> In this thesis we determined capacity as mobility capacity (gross motor function and walking ability) and performance as physical activities in daily living (stride rate activity).<sup>29</sup> It was shown in chapter 5 that anaerobic fitness is strongly associated with the capacity for activities, while the results in chapter 7 showed that aerobic fitness is more strongly associated with the performance of physical activities (the level of physical activity in daily life).

It was suggested in earlier reports that aerobic fitness is seldom a limiting factor in a child's ability to perform activities of daily living.<sup>2</sup> However, the relation between aerobic fitness and daily physical activity described in chapter 7 indicates that aerobic fitness does show a relationship with performance of activities in children with bilateral CP. It appears that aerobic fitness shows a stronger association with the performance of activities, while anaerobic fitness has a stronger relation with the capacity for activities. An explanation for this might be the higher physical strain of walking in CP.<sup>10;27</sup> This higher physical strain is a result of the increased energy expenditure during walking in children with CP and/or low  $\text{VO}_2\text{peak}$ . As physical strain is related to daily physical activity,<sup>18;27</sup> low  $\text{VO}_2\text{peak}$  may serve as an aggravating factor in limitations in the ability to walk for longer distances due to high physical strain. This may be less of a limiting factor for mobility capacity. As shown in chapter 5, anaerobic capacity is an important determinant of mobility capacity. Anaerobic training might therefore have, in addition to a positive effect on aerobic fitness, some positive influence on mobility capacity.

**Exercise is medicine**

Research has proven that exercise, at the correct intensity and duration, improves health. Regular exercise decreases the incidence of disease, chronic health conditions and obesity in children and adults.<sup>13</sup> In children with CP, exercise can have a variety of beneficial effects on health outcomes. As CP is a disorder that affects the function of muscles, exercise might contribute to a better muscular function. The impaired muscle activation in CP might also lead to a lower number of muscle fibers.<sup>6</sup> In addition, the muscle volume is lower in children with CP.<sup>6</sup> Exercise has the potential to increase muscle volume, which may lead to a higher number of mitochondria for aerobic oxidation.<sup>46</sup> In addition, muscle weakness, which is a major issue in children with CP, can be improved through exercise.<sup>26;37</sup> Therefore, exercise may decrease the impact of the disorder on muscle function.

Another important issue is that exercise decreases the incidence of chronic health conditions like diabetes, cardiovascular diseases, and osteoporosis.<sup>13</sup> Because persons with CP have lower levels of health-related physical fitness and reduced levels of physical activity, they are at higher risk for developing cardiovascular diseases. This was shown by increased cardiometabolic risk factors, including hypertension, cholesterol, HDL-C, waist circumference and obesity in young adults with CP.<sup>22;32</sup> Furthermore, children with CP, especially those

with moderate to severe impairment, showed a decreased bone mineral density.<sup>15</sup> It is yet unknown whether a higher level of physical fitness, as a result of regular exercise, prevents the development of chronic disease in persons with CP. Although it is not expected that the beneficial effects of exercise on health will differ in persons with CP, this should be confirmed in future research.

In order to avoid health issues at older ages and to prevent inactive lifestyles during adulthood,<sup>20;21</sup> it is important to encourage a healthy and active lifestyle during childhood. If this can be achieved, children with CP create a better starting position and have a greater chance of having adequate physical fitness at older ages.<sup>25</sup> As regular exercise also positively influences the development of the musculoskeletal system, the decline in mobility that is observed in children with CP might also be prevented.<sup>14</sup> An additional benefit could be that when children have positive experiences with exercise, they might increase their participation in sport clubs during childhood, which could translate to greater participation in sport clubs at older ages, thus contributing to an active lifestyle.<sup>23</sup> The benefits of regular exercise should be communicated to children with CP and their parents, as understanding the health benefits of exercise is an important factor in their decision to become physically active.<sup>43</sup>

## MAIN CONCLUSIONS AND FUTURE RESEARCH DIRECTIONS

- Children with CP have lower levels of physical fitness compared to children showing typical development, indicating that this is an important issue to consider in rehabilitation treatment. The major differences in physical fitness levels among children with CP point to the need to objectively measure the level of physical fitness in children with CP in order to guide interventions.
- The reliability of  $VO_2$ peak in children with CP classified as GMFCS levels I and II (assessed by a progressive maximal cycle ergometer test) is excellent. The potential to detect change in cardiorespiratory fitness over time should be confirmed in future research.
- In clinical decision making, an objective standardized laboratory-based test with measurement of  $VO_2$ peak is recommended, since this is considered the single best indicator for aerobic fitness in children with CP.
- While anaerobic fitness decreased with increasing GMFCS level, the differences between the different GMFCS levels were less pronounced for aerobic fitness. Future research should aim to uncover the effects of training interventions on exercise responses in children with CP.
- Increasing anaerobic fitness might contribute to improved aerobic fitness and might have a positive influence on mobility capacity in children with bilateral CP. In children with unilateral CP, alternative approaches should be the subject of future research. As children show activity patterns with short bursts of exercise, it is important that the potential for improving anaerobic fitness be investigated further.

- 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. 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 typically developing children. 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.
- Improving step rate appears to be a priority in children with CP, since they have lower stride rates over the day, impeding them from covering the same distance as their peers and potentially hindering participation in peer activities. Future research should confirm whether increased stride rates lead to better participation in daily life.
- Better anaerobic fitness relates to a higher capacity for activities, while better aerobic fitness relates to higher performance of physical activities in daily life in children with bilateral CP. Children with bilateral spastic 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.

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