PROMOTING A HEALTHY LIFESTYLE

EFFECTIVENESS OF AN INTERVENTION ON PHYSICAL BEHAVIOUR AND PHYSICAL FITNESS AMONG ADOLESCENTS AND YOUNG ADULTS WITH SPASTIC CEREBRAL PALSY

JORRIT SLAMAN

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Promoting a Healthy Lifestyle

Effectiveness of an intervention on physical behaviour and physical fitness among adolescents and young adults with spastic cerebral palsy

Het stimuleren van een gezonde leefstijl

De effectiviteit van een interventie op het beweeggedrag en de fysieke fitheid onder jongeren en jongvolwassenen met spastische cerebrale parese

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Chapter 1

General introduction

CEREBRAL PALSY

Cerebral palsy (CP) is a frequently occurring condition with a prevalence of about 2 per 1000 live births, a number which has remained fairly stable over the past decade.[1] Analysis of a large European dataset of 4500 term and preterm children with CP showed that the incidence of CP was 30% higher among males compared to females.[2] CP describes a group of permanent disorders of the development of movement and posture, which limit activity and are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems.[3] While in certain cases there is no identifiable cause, typical causes of CP include problems in intrauterine development (e.g. exposure to radiation, infection), asphyxia before birth, hypoxia of the brain, birth trauma during labour and delivery, and complications in the perinatal period or during the first year of childhood.[4]

CP is categorised into three predominant types of motor impairments: spastic, ataxic and athetoid/dyskinetic; these types may also occur in combination. This thesis focused on persons with spastic CP, the most common type of the disorder, which accounts for nearly 90% of all cases.[5] Spastic CP is characterised by abnormal patterns of posture or movement, increased muscle tone, and pathological reflexes. The spastic CP type can be further categorised as unilateral if the involved limbs are limited to one side of the body or bilateral if the involved limbs are on both sides of the body. In addition to categorisation based on motor impairments, CP may be classified by the affected person's functional ability. The most commonly used classification system in persons with CP is the Gross Motor Function Classification System (GMFCS).[6] This system uses five classification levels to describe gross motor function based on self-initiated movement, with particular emphasis on walking, sitting and wheeled mobility. Persons classified as level I do not use assistive devices for mobility, whereas those classified as level V have no self-mobility and impaired head and trunk control.

LIFESTYLE OF PERSONS WITH CP

Due to increasing life expectancies for persons with CP, lifestyle-related diseases are of increasing concern. Similar to persons with other chronic conditions, primary disability treatment is combined with prevention of secondary conditions.[7] In the general population, physical activity (PA), defined as any bodily movement produced by the muscles that results in increased energy expenditure,[8] serves as primary and secondary prevention against several chronic diseases, and is associated with a reduced risk of premature death.[9] Independent of PA level, prolonged periods of sedentary behaviour, defined as a distinct class of activities that requires low levels of energy expenditure,[10] negatively affects the metabolic and cardiovascular systems.[11, 12] Consequently, favourable physical behaviour,[13] consisting

of sufficient PA with little sedentary time, is recommended for optimal health. For persons with CP, optimal physical behaviour may be even more important because physical inactivity can additionally contribute to functional deterioration.[14] Nevertheless, research shows that children, adolescents and bilaterally affected adults with CP have low PA levels compared to able-bodied persons of the same age.[15-19] In addition; average sedentary time is twice the recommended level among adolescents with CP.[19]

In contrast to PA, which refers to a behaviour related to the movements that people perform, physical fitness is a set of attributes that people have or achieve.[8] Sufficient physical fitness is considered a major contributor to a healthy lifestyle[20] because of its inverse relationships to total mortality and cardiovascular mortality.[21] Physical fitness is believed to be prerequisite to optimising and maintaining activity performance in daily life[7] and prevention of secondary health problems later in life[22] in persons with CP. However, research has consistently shown that people with CP have low physical fitness levels.[23-26]

Unfavourable physical behaviour levels and low physical fitness levels may also increase experienced fatigue. Durstine et al. hypothesised that these factors interact with each other, leading to a vicious cycle of deconditioning in persons with chronic disabilities.[27] This rationale could explain the high levels of fatigue commonly found among persons with CP.[28, 29] Recent support for this deconditioning cycle has been shown in a longitudinal study demonstrating decreased fatigue following an exercise training programme in ambulatory adults with CP.[30]

Apart from direct negative health consequences, unfavourable physical behaviour and subnormal physical fitness levels may also impact participation in life areas and perceived health-related quality of life (HRQoL). For adolescents and adults with CP, and particularly those with bilateral CP, restrictions in participation have been reported in several areas, including outdoor mobility, recreation, self-care and employment.[31, 32] Furthermore, studies in adults[29, 33-35] and adolescents[36-38] with CP have shown that perceived HRQoL is lower in persons with CP compared to the general population, especially in the physical domain. Several studies show that physical behaviour and physical fitness parameters are related to participation and HRQoL levels among persons with CP.[35, 39, 40]

Currently, most children with CP make the transition to adulthood, a developmental phase in which young people become independent in many life areas. During this transition, life changes substantially impact the development of the adult lifestyle.[41, 42] Achieving more favourable physical behaviour and improving physical fitness seem particularly important at this age, because of the associated lifelong health benefits. Despite the unfavourable physical behaviour profile and low physical fitness levels typical among persons with CP, little attention has been given to this issue.[7]

LEARN 2 MOVE

LEARN 2 MOVE is a Dutch national research programme that started in 2008. The research programme consists of four projects, each evaluating the effects and working mechanisms of an age-specific intervention to encourage movement in children, adolescents and young adults with CP. The present thesis is a result of the LEARN 2 MOVE 16-24 project, which evaluated effects and working mechanisms of a lifestyle intervention, the Active Lifestyle and Sports Participation (ALSP), in adolescents and young adults, aged 16 to 24 years, with spastic CP. The ALSP intervention is a six-month programme developed for adolescents and young adults with physical disabilities.[43] This intervention aimed to permanently improve physical behaviour and increase physical fitness by promoting behavioural changes toward a more active and less sedentary lifestyle and is offered in outpatient rehabilitation departments for young adults in The Netherlands. The intervention consisted of three parts: 1) individual counselling about daily PA and sedentary behaviour, which was guided by a personal coach to discuss barriers and facilitators of physical behaviour using motivational interviewing;[44] 2) physical fitness training, which consisted of supervised centre- and home-based training, and focused on increasing cardiopulmonary fitness and muscle strength; and 3) counselling about sports participation to find suitable, accessible and appropriate sports and sports facilities in participants' living environments.

OUTLINE OF THIS THESIS

The main objective of this thesis was to study the effectiveness of the ALSP lifestyle intervention on physical behaviour and physical fitness, on both the short and long term, among adolescents and adults with spastic CP. **Chapter 2** provides background for the study rationale and outlines the study protocol applied in the LEARN 2 MOVE 16-24 project. **Chapter 3** describes the determination regarding the 6-minute walk test (6MWT) as a predictor of peak oxygen uptake and its use as a clinically applicable alternative to cardio-pulmonary exercise testing among adolescents and young adults with CP. **Chapters 4** and **5** describe baseline values of movement behaviour and physical fitness for study participants. Knowledge of these values can help us optimise recommendations and treatments to increase PA and physical fitness among adolescents and young adults with spastic CP. Furthermore, by comparing baseline values to those of a non-disabled population of the same age, we gain insight into the magnitude of the deficit of movement behaviour and physical fitness in adolescents and young adults with spastic CP. **Chapter 6** provides insight into the underlying mechanisms of unfavourable physical behaviour of persons with CP by exploring cross-sectional relationships between aerobic capacity, oxygen uptake during walking and physical strain during walking on the one hand and total daily walking time on the other hand. **Chapter 7** describes the prevalence of fatigue among adolescents and young adults with spastic CP. Furthermore, analyses

were performed to explore which subgroups of young persons with CP are at risk for high fatigue levels and to explore the cross-sectional relationships between fatigue and movement behaviour and physical fitness. Short-term and long-term longitudinal effects of the ALSP lifestyle intervention are described in chapters 8 to 10. Chapter 8 and 9 report intervention effects on the primary outcome measures of the present study. **Chapter 8** focuses on objectively measured and self-reported movement behaviour, and **Chapter 9** focuses on measures of physical fitness. In addition to the direct effects of the ALSP intervention on movement behaviour and physical fitness, ALSP participation can also alter levels of fatigue, participation and HRQoL. These secondary outcomes are described in **Chapter 10**. Furthermore, in the case of significant effects of the ALSP lifestyle intervention on any of these latter outcome measures, the mediating effects of physical behaviour and physical fitness were explored in this chapter as well. A cost-utility analysis of the ALSP intervention is described in **Chapter 11** to determine whether intervention effects outweigh the costs involved. The thesis concludes with a general discussion (**Chapter 12**) describing the main findings, clinical implications, unanswered questions, and methodological considerations. Subsequently, directions for future research are proposed.

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Chapter 2

LEARN 2 MOVE 16-24: Effectiveness of an intervention to stimulate physical activity and improve physical fitness of adolescents and young adults with spastic cerebral palsy; a randomised controlled trial

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ABSTRACT

Background

Persons with cerebral palsy (CP) are at risk for developing an inactive lifestyle and often have poor fitness levels, which may lead to secondary health complications and diminished participation and quality of life. However, persons with CP also tend not to receive structural treatment to improve physical activity and fitness in adolescence, which is precisely the period when adult physical activity patterns are established.

Methods

We aim to include 60 adolescents and young adults (16-24 years) with spastic CP. Participants will be randomly assigned to an intervention group or a control group (no treatment; current policy). The intervention will last 6 months and consist of three parts; 1) counselling on daily physical activity; 2) physical fitness training; and 3) sports advice. To evaluate the effectiveness of the intervention, all participants will be measured before, during, directly after, and at 6 months following the intervention period. Primary outcome measures will be: 1) physical activity level, which will be measured objectively with an accelerometry-based activity monitor during 72h and subjectively with the Physical Activity Scale for Individuals with Physical Disabilities; 2) aerobic fitness, which will be measured with a maximal ramp test on a bicycle or armcrank ergometer and a 6-minute walking or wheelchair test; 3) neuromuscular fitness, which will be measured with handheld dynamometry; and 4 body composition, which will be determined by measuring body mass, height, waist circumference, fat mass and lipid profile.

Conclusions

This paper outlines the design, methodology and intervention of a multi-centre randomised controlled trial (LEARN 2 MOVE 16-24) aimed at examining the effectiveness of an intervention that is intended to permanently increase physical activity levels and improve fitness levels of adolescents and young adults with CP by achieving a behavioural change toward a more active lifestyle.

BACKGROUND

Cerebral palsy (CP) occurs in 1.5 to 3.0 of 1000 live births and is the most common cause of physical disability in paediatric rehabilitation medicine.[1] Representing a group of permanent disorders of the development of movement and posture, it causes activity limitation that is attributed to non progressive disturbances that occurred in the developing foetal or infant brain[2] which can lead to diminished quality of life, participation and health in adulthood.[3-5]

Participation in regular physical activity (PA) provides psychological and physiological benefits in adolescents.[6] In addition, it reduces both the deterioration of mobility-related activities[7] and the development of secondary health problems later in life.[8] However, performing physical activities is often burdensome in adolescents and adults with CP due to reduced muscle mass and inefficient locomotion.[9] This might, together with the distinctly subnormal fitness levels of persons with CP,[10] explain why they are at risk of developing an inactive lifestyle. Such an inactive lifestyle has been found in several studies of bilateral spastic CP populations[11-13], but it contrasts with the more active lifestyle of individuals with unilateral spastic CP.[14]

Persons develop their adult PA lifestyle in adolescence.[15, 16] Therefore, encouraging an active lifestyle and improving physical fitness at this age seems important. Nevertheless, in adolescence and young adulthood, persons with CP tend not to receive structural treatment to improve PA and fitness.[17] A recent review shows that children and adolescents with CP may benefit from exercise programmes to improve physical fitness.[18] However, higher fitness levels do not automatically lead to a more active lifestyle.[19, 20] Some evidence exists for the effectiveness of interventions aimed at stimulating an active lifestyle through individual counselling in adult populations with physical disabilities in both the short term[21] and long term.[22] It can be speculated that an intervention which combines individual counselling on daily PA with fitness training is ideal to increase PA and improve physical fitness in persons with CP. However, the effectiveness of such an intervention has, to our knowledge, never been evaluated in an adolescent or young adult population with CP.

The LEARN 2 MOVE 16-24 research project aims to evaluate the effectiveness and underlying working mechanisms on the short and long term of the Active Lifestyle and Sports Participation (ALSP) intervention. It is hypothesised that persons following the ALSP intervention will experience increased PA and improved physical fitness in both the short term and the long term (maintenance of effects) as the primary goal of the intervention is to achieve a behavioural change toward a more active lifestyle. The present paper describes the research design, methodology and intervention of the LEARN 2 MOVE 16-24 research project.[23-25]

METHODS / DESIGN

Ethical approval

Multi-centre approval was granted by the Erasmus MC Medical Ethics Committee, The Netherlands. Local approval was granted by all participating centres.

Study design

The study has a multi-centre randomised controlled design. The experimental group will receive the ALSP intervention. The control group will receive no intervention to improve PA and fitness, which is current policy. Erasmus MC (Rotterdam), Rijndam Rehabilitation Centre (Rotterdam), VU Medical Centre (Amsterdam), Rehabilitation Centre Amsterdam (Amsterdam), Rehabilitation Centre De Hoogstraat (Utrecht) and Sophia Rehabilitation (Den Haag / Delft) will participate in this study.

Blinding

This study has a single-blind research design; all measurements will be performed by assessors who are blind for group allocation and who have no involvement in the recruitment, randomisation procedure or intervention.

Setting

The ALSP intervention and the research measurements will be performed at each participant's house and at two university medical centres and four rehabilitation centres from which all participants will be recruited.

Sample size

At least 50 participants are required to detect a difference of 30 minutes a day in PA level between the control and experimental group, with a power of 0.8 and an alpha of 0.05. To allow for dropouts, we aim to recruit 60 participants. This calculation is based on data from previous research conducted by our research group.[13, 14]

Participants

Adolescents and young adults with spastic unilateral or bilateral CP are eligible for inclusion if they meet each of the following criteria:

- Age 16 - 24 years
- Gross Motor Functioning Classification System (GMFCS)[26] level I-IV

Individuals will be excluded if they meet any of the following criteria:

- Disabilities other than CP that affect PA or fitness level
- Contraindication for (maximal) exercise

- Severe cognitive disorders and insufficient comprehension of the Dutch language that preclude understanding the purpose of the project and its testing methods
- PA level at baseline exceeds the mean PA level + 2 SD of a CP population

Recruitment

Each participating centre will compile a list of its patients aged 16 – 24 years and diagnosed with CP. All patients will be checked on inclusion and exclusion criteria by their rehabilitation physician. An information letter and invitation to participate was sent to eligible participants. A second letter was sent 3 weeks later to non-responders.

Randomisation

After baseline measurement, participants will be stratified according to their GMFCS level to obtain an equal distribution of gross motor functioning between the two groups. Within each stratum and for each participating centre, participants will be randomly allocated (1:1) to the experimental or control group.

Intervention: Active Lifestyle and Sports Participation

The ALSP intervention lasts 6 months and was developed for adolescents and young adults with physical disabilities.[27] It aims to permanently increase PA and fitness levels by promoting behavioural changes toward a more active lifestyle (EMGO Institute VUmc, Amsterdam, The Netherlands; Health Partners & Io Solutions, Minneapolis, Minnesota, USA) and consists of three parts:

1. Counselling on daily PA
2. Physical fitness training
3. Sports advice

Counselling on daily PA

Counselling on daily PA is the main component of the intervention and consists of six individual counselling sessions over a period of 6 months with a PA counsellor (e.g. physical therapist, movement therapist) who serves as a 'personal coach'. During these counselling sessions, participants will receive individual PA advice which primarily focuses on PA in daily life, and not necessarily on sports. The counselling sessions on daily PA are based on Motivational Interviewing (MI) which is defined as a directive, client-centred counselling style for eliciting behavioural changes by helping clients to explore and resolve ambivalence.[28] Techniques that will be applied in the ALSP intervention to invoke the spirit of MI are reflective listening, rolling with resistance, asking open-ended questions, summarising during a conversation, and showing empathy for the participant. The stages of behavioural change of the Trans Theoretical Model[29] describe the stages a person experiences when changing his or her health behaviour. This model structures the clinical role of MI during the counselling sessions.[30] The first counselling session will last 45 minutes. The five subsequent 20- to 30- minute sessions will be

planned monthly. All counselling sessions for a participant will be supervised by the same counsellor. Each participating centre will have its own counsellor and all involved counsellors will undertake two days of training to learn the basic principles of MI. The counsellors will also participate in a 1-day follow-up workshop to discuss their initial experiences and refresh their MI knowledge and skills. The first and last counselling session will be sound-recorded for latter analysis to ensure that MI had been applied correctly.

Physical fitness training

Physical fitness training will consist of 12 weekly supervised sessions and 12 home sessions. These training sessions of approximately one hour consist of aerobic endurance, aerobic interval and strength training. Over these 12 weeks, aerobic exercise duration and aerobic intensity (as determined by the Karvonen formula)[31] are gradually increased. The peak heart rate (HR), which is required for the Karvonen formula, will be determined during a maximal ramp protocol. The required resting HR will be determined after 5 minutes of rest in a sitting position. During training, HR will be recorded using a Garmin Forerunner 60 heart rate monitor (Garmin Ltd., Olathe, KS, USA). The exercise programme starts at a HR of 40% of the heart rate reserve (HRR) on a treadmill, cycle or armcrank ergometer. This will increase to a HR of 80% of the HRR at week 12.[32] Also; strength exercises of the large muscle groups are included. The training load will be based on a percentage of the baseline 1 repetition maximum (1RM), which is the maximum load that a person can lift once. The training load will begin with one set of 10 to 15 repetitions at 30% of 1RM during week 1 and will increase toward three sets of 15 to 20 repetitions at 75% of 1RM during week 12.[32] Slight adaptations to these guidelines will be allowed to ensure that the training is both feasible and challenging for each participant. Fitness equipment is available for upper extremities, lower extremities and abdominal muscles. For the training at home, participants will be instructed to perform aerobic exercises (walking/running, cycling, hand-cycling, wheelchair-driving, or swimming) and strength exercises (using Thera-Bands; Hygenic Corporation, Akron, OH, USA) of similar duration and intensity as the supervised training session. HR will also be recorded during home training sessions to evaluate whether participants accomplish the exercise instructions in terms of duration and intensity. After 12 weeks of supervised fitness training the possibilities will be explored to continue the fitness training in the day-to-day environment of each individual.

Sports Advice

Sports advice includes sports counselling and sport-specific training. Sports counselling is based on the Rehabilitation & Sports Programme.[21, 22] During 2 to 4 sessions of approximately 30 minutes, sports history, preferences, possibilities, barriers and facilitators will be identified. This will result in an individualised sports advice, including information on available, accessible and appropriate sports facilities in the person's day-to-day environment. Aspects as transportation, finances, and supervision are also taken into account to ensure long-term benefits. Sport-specific training includes practicing

the required skills to perform the sport and ensuring practice opportunities to match sports to each participant's interests and abilities. Examples of the sports to be included in the sport specific training are swimming, soccer, rowing, basketball, climbing, golf, hockey and racket sports. Participation in the sport-specific training sessions will depend on the interests and physical abilities of the participant.

International Classification of Functioning, Disability and Health.

The International Classification of Functioning, Disability and Health (ICF) model provides a unified language and framework for the description of health and health-related states.[33] This model identifies how a health condition, such as CP, can interact with features of the person and the environment to produce three levels of potential disablement: 1) impairments which occur at the level of body structures and functions; 2) activity limitations which occur at the level of performance of tasks or actions by the person; and 3) participation restrictions which occur at the level of participants in their social context. An overview of the ICF model with the parameters to be measured in the present study is shown in Figure 1. The primary outcome measures of this study are the objectively measured PA level, self-reported PA level and physical fitness. All outcome measures will be assessed: at baseline (T0); immediately after completion of the total intervention (6 months, T6) to establish the effectiveness of the ALSP intervention; and at 6 months following the intervention period (12 months, T12) to determine long-term effects. A limited set of outcome measures (physical fitness, health-related quality of life and fatigue) will be assessed after 3 months (T3) to establish the effectiveness of the fitness training of the ALSP intervention. A time schedule of the ALSP intervention and measurements is presented in Table 1. Comparable research equipment will be used in all participating centres.

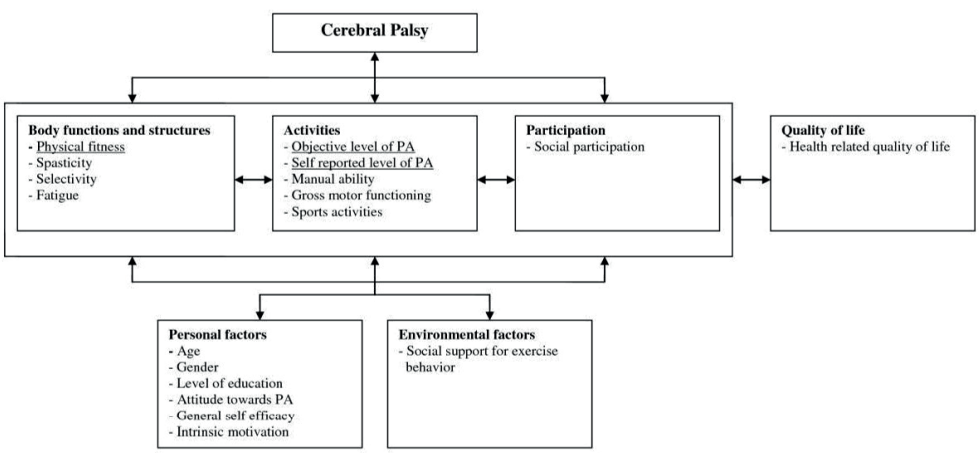

Figure 1. ICF model showing the outcome measures that will be assessed in this study. Primary outcome measures are underlined.

Table 1. Time schedule of the Active Lifestyle and Sports Participation intervention.

Week	Measurements	Counselling on daily PA	Fitness training		Sports advice
			Supervised	Home-based	
Week 1	Pre-test (T0)	PA session 1			
Week 2			Training 1	Training 2	
Week 3			Training 3	Training 4	Sports session 1
Week 4			Training 5	Training 6	
Week 5		PA session 2	Training 7	Training 8	
Week 6			Training 9	Training 10	
Week 7			Training 11	Training 12	
Week 8			Training 13	Training 14	
Week 9			Training 15	Training 16	
Week 10		PA session 3	Training 17	Training 18	Sports session 2
Week 11			Training 19	Training 20	
Week 12			Training 21	Training 22	
Week 13			Training 23	Training 24	
Week 14	Post-test 1 (T3)				
Week 15		PA session 4			
Week 16					
Week 17					(Sports session 3)
Week 18					
Week 19					
Week 20		PA session 5			
Week 21					
Week 22					
Week 23					
Week 24					(Sports session 4)
Week 25		PA session 6			
Week 26	Post-test 2 (T6)				
Week 52	Follow-up test (T12)				

Note: After 13 weeks the possibility of continuing fitness training in the day-tot-day situation will be explored for each participant

Primary outcome measures

Objectively measured level of daily physical activity

To objectively measure the level of daily PA the VitaMove (VM) system (2M Engineering, Veldhoven, The Netherlands) will be applied. This system is based on long-term ambulatory monitoring of signals from body-fixed accelerometers. This system consists of 3 to 5 recorders (Figure 2), each with its own accelerometer (Freescale MMA7260Q, Denver, USA), storage capacity and power supply. The recorders are wirelessly connected and synchronised every 10 seconds. Accelerometer signals will be stored digitally with a 128 Hz sampling frequency on a micro Secure Digital (SD) memory card with two gigabytes of storage. Measurements will be uploaded to a computer for kinematic analysis using Vitascore Software (Vitascore BV, Gemert, The Netherlands). A detailed description of the activity

Figure 2. VitaMove recorder

detection procedure has been described elsewhere.[34] From the accelerometer signals, the duration, rate, and moment of occurrence of stationary activities (e.g. lying, sitting and standing), dynamic activities (e.g. walking [including climbing/descending stairs], running, cycling, manual wheelchair-driving [including hand-cycling], and general non-cyclic movement) and transitions between postures can be automatically and separately detected with a 1-second resolution. Furthermore, from each measured signal, information on the variability of the acceleration signal (motility, which is related to the intensity of body-segment movements) will be obtained. The VM system is valid to quantify mobility-associated activities and to detect inter-group differences in levels of daily PA.[34, 35]

For ambulatory participants 3 recorders will be used. One recorder will be attached to each thigh to detect acceleration in anterior-posterior direction while standing and a third recorder will be attached to the sternum to detect acceleration in the anterior–posterior direction and in the longitudinal direction. For participants who use wheelchairs, one additional recorder will be attached to each wrist to detect acceleration in the longitudinal direction while seated with the forearm horizontal in the mid-pronation/supination position. Participants will wear the VM system for 72 hours on randomly selected weekdays while performing their ordinary activities with the exception of swimming and bathing. In addition, the VM system will not be worn during periods of sleep. The recorders will be attached to the body by using elastic belts. The VM system will be set up at each participant's home to minimise influencing the normal PA pattern. To avoid measurement bias, we will instruct the participants to continue their ordinary daily life activities. The principles of the activity monitor will be explained to the participants after all measurements have been made.

The following data will be analysed from these measurements: (*1*) duration of dynamic activities as a percentage of a 24-hour period; (*2*) number of transitions (includes all transitions except lying transitions between the prone and supine positions); (*3*) intensity of activities: (*3*a) mean motility (in gravitational acceleration (g)); (*3*b) motility during walking; (*3*c) motility during wheelchair-driving; and (*4*) distribution of continuous dynamic activity periods (5–10 sec; 10–30 sec; 30–60 sec; 1–2 min; 2–5 min; 5–10 min; or > 10 min).

Self-reported level of physical activity

To measure the self-reported level of PA the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD)[36] will be administered. The PASIPD is a 7-day recall questionnaire developed for people with a physical disability and consists of questions on leisure time, and household- and work-related PA. The questionnaire is translated into Dutch and question 10 (lawn work or yard care) and 11 (outdoor gardening) are combined into a single question, which better represents the Dutch situation. The total score of the PASIPD is created by multiplying the average hours per day for each item by a metabolic equivalent (MET) value associated with the intensity of the activity. The test-retest reliability of the PASIPD is good and its validity is comparable to well-established self-report PA questionnaires for the general population.[37]

Physical fitness: Aerobic capacity

The aerobic capacity will be measured during a maximal ramp protocol. This test will be performed on an electronically braked cycle ergometer or electronically braked armcrank ergometer depending on the main mode of ambulation during daily life, as this elicits the highest oxygen uptake.[38] The test will be preceded by a 3-minute warm-up without resistance. The resistance will be increased every 12 seconds during the test. The magnitude of this increase in resistance depends on the GMFCS level and gender of the participant and ranges from 1 to 6 watts, ensuring that total exercise time will range from 8 to 12 minutes. The target pedal rate during the test is 70 rpm. Strong verbal encouragement will be given throughout the test. The test will be terminated when the participant voluntarily stops due to exhaustion, or when the participant is unable to maintain the initial pedal/crank rate. Gas exchange and heart rate (HR) will be measured continuously using a breath-by-breath analysing system, which will be calibrated prior to each measurement. Aerobic capacity is defined as the highest mean oxygen uptake during 30 seconds of exercise (VO_{2peak} in $ml \cdot min^{-1}$). Subjective strain will be measured immediately after the final stage by the Borg Scale for Rating of Perceived Exertion.[39] Determining a participant's contra-indications for PA will be assessed prior to the test by use of the Physical Activity Readiness Questionnaire.[40]

Physical fitness: sub-maximal aerobic capacity

The 6 minute walking test[41] will be employed as a measure of sub-maximal aerobic capacity. Patients will be instructed to walk, not run, as far as they can along a 30-meter marked track during a 6-minute

period. Non-ambulant participants will perform the test in their wheelchair. Patients are allowed to stop and rest during the test, but will be instructed to resume walking / wheelchair driving as soon as they feel able to do so. The average HR during the test and the covered distance will be registered.

Physical fitness: Muscle strength

Muscle strength will be measured with a hand-held dynamometer (MicroFet, Hoggan Health Industries Inc, West Jordan, UT, USA) using the "break" testing method. The strength of the hip flexors, hip abductors and knee extensors will be measured in individuals whose main mode of ambulation is walking. The strength of shoulder abductors and elbow extensors will be measured in non-ambulant individuals. The applicator of the dynamometer is held against the distal part of the limb segment, and participants will be asked to build up their maximum force against it. When maximum is reached the examiner applies sufficient resistance to overcome the force exerted by the participant. Both the left and right side will be measured. The lever arm from the joint to the dynamometer will be kept constant by marking the position of the dynamometer on each participant's leg. Each trial lasts approximately 4 seconds, and three repetitions will be performed with 1 minute of rest in between. The average value of the three repetitions will be analysed.

Physical fitness: Body composition

Height will be measured barefoot in a standing position. In case of joint contractures, measurements will be performed from joint to joint in a lying position. Body mass of ambulatory participants will be obtained while standing barefoot on a scale and of non-ambulatory participants while sitting on an electronic scale. Body mass index (BMI, $kg \cdot m^{-2}$) will be calculated from height and body mass. Waist circumference (cm) will be measured mid-way between the lowest rib and the iliac crest while standing. Waist circumference will be measured in a sitting position in persons using a wheelchair. Thickness of four skin folds (biceps, triceps, subscapular and suprailiac) will be measured twice on the left side of the body with a Harpenden calliper (Burgess Hill, UK). The mean of the two measurements will be used as representative. Percentage body fat will be predicted from skin fold thickness according to the method of Durnin and Womersley.[42] Non-fasting blood samples of approximately 10ml will be drawn from the vena antecubiti with a Vacutainer needle and collected into an evacuated serum separator tune II (SST II tube) while the participants are seated. Total serum cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol will be determined from this blood sample.

Secondary outcome measures:

The secondary outcome measures will be assessed for descriptive reasons and to get insight into the working mechanisms of the ALSP intervention. These secondary outcome measures will not be fully described, but will only be mentioned here; spasticity (Ashworth Scale),[43] selectivity,[44] fatigue (Fatigue Severity Scale,[45] Checklist Individual Strength,[46] Visual Analog Scale[47]), manual ability (MACS),[48] sports

activities, social participation (Life-H 3.0),[49] health related quality of life (Short-Form-36),[50] age, gender, level of education, attitude towards PA, general self efficacy (Generalised Self Efficacy scale),[51] intrinsic motivation (Intrinsic Motivation Inventory),[52] gross motor functioning (GMFM),[53] and social support for exercise behaviour (Social support for exercise behaviour Scale)[54].

Statistics

To evaluate the change in PA level and physical fitness, as well as the secondary outcome measures, multilevel regression analyses will be applied, because these analyses allow for missing values. Another advantage of these analyses is that patient data can be clustered within the participating centres. For all multilevel analyses, MLwiN (Version 1.1, Institute of Education, London, UK) software will be used.

DISCUSSION

This paper outlines the design, methodology and intervention of a multi-centre randomised controlled trial that examines the effectiveness of an intervention that aims to achieve a permanent increase in PA level and improve the fitness level of adolescents and young adults with CP by promoting a behavioural change toward a more active lifestyle. The results of this trial are expected to be presented in 2012.

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Chapter 5

The six minute walk test cannot predict peak cardiopulmonary fitness in ambulatory adolescents and young adults with cerebral palsy

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ABSTRACT

Objective

To determine whether the 6-minute walk test predicts peak oxygen uptake and whether the 6-minute walk test is a clinically applicable alternative to cardiopulmonary exercise testing in ambulatory adolescents and young adults with cerebral palsy.

Design

Cross-sectional.

Setting

University hospital and rehabilitation centres.

Participants

Forty-one adolescents and young adults with cerebral palsy classified in GMFCS level I or II.

Interventions

Not applicable.

Main Outcome Measures

The covered distance during 6 minutes was measured with a 6-minute walk test. Peak oxygen uptake was obtained with cardiopulmonary exercise testing on a cycle ergometer.

Results

Univariate linear regression analysis was used to study the relationship between the outcomes of both tests. A multiple linear regression analysis was performed to determine whether peak oxygen uptake could be predicted by the 6-minute walk test, sex, body mass and GMFCS level. A significant relationship ($p<0.01$) was found between the outcomes of the 6-minute walk test and cardiopulmonary exercise test with an explained variance of 21%. The multiple linear regression analysis showed an explained variance of 58% and a standard error of estimate corresponding to 18% of the mean peak oxygen uptake.

Conclusions

The 6-minute walk test is poorly related to peak oxygen uptake in ambulatory adolescents and young adults with CP. Due to a high standard error of estimate, the multiple regression model did not allow for prediction of peak oxygen uptake from the 6-minute walk test in ambulatory adolescents and young adults with cerebral palsy.

INTRODUCTION

Physical fitness contributes to a healthy lifestyle in the general population,[1] but is even more important in persons with cerebral palsy (CP) to optimise and maintain performance in daily life.[2] Nevertheless, physical fitness, among which cardiopulmonary fitness is a key component, is low in persons with CP[2-4] and deserves attention in rehabilitation medicine.

The gold standard for measuring cardiopulmonary fitness is the peak oxygen uptake (VO_{2peak}) with cardiopulmonary exercise testing (CPET).[5] However, CPET is time consuming and requires relatively expensive equipment and trained staff. Therefore, CPET measurements are not suitable for use in clinical practice[6] and consequently, CPET is likely to be limited to specialised centres for research purposes. Therefore, simple, inexpensive and sub-maximal exercise tests are advised to assess peak cardiopulmonary fitness in clinical practice.

The 6-minute walk test (6MWT) is a simple and sub-maximal exercise test in which the distance walked in 6 minutes under controlled conditions is measured.[7] Moderate to strong relationships between 6MWT distance and VO_{2peak} have been shown in persons with cardiopulmonary disease,[8] heart failure,[9, 10] and traumatic brain injury,[11] with correlation coefficients ranging from 0.58 to 0.73. Estimation of VO_{2peak} is possible from 6MWT distance for persons with cardiopulmonary disease or heart failure with a relatively small standard error of estimate (SEE).[12] The authors concluded that the 6MWT is an inexpensive and suitable alternative to CPET for these clinical populations.

The 6MWT has also been employed as a surrogate measure of cardiopulmonary fitness in persons with CP.[13-15] In addition, a Delphi study, which proposed a core set of exercise tests for children and adolescents with CP, advised using the 6MWT as a sub-maximal exercise test because the test seems to correspond to functional activities performed in daily life.[16] To our knowledge, only one study assessed the relationship between the 6MWT and VO_{2peak} in persons with CP. The authors concluded that the 6MWT is a valid test for estimating peak oxygen uptake.[15] However, given the low peak heart rates during CPET in that study, it is unlikely that (near) maximal exercise was achieved. Their results indicate that both the 6MWT and cycle ergometry were performed at sub-maximal exercise levels, which does not support the conclusion that the 6MWT is a valid test for estimating peak oxygen uptake.[17]

In a CP population, several factors may influence the 6MWT distance; decreased walking capacity due to gait abnormalities[18, 19] caused by spasticity, impaired balance and reduced muscle strength.[19-22] These factors may decrease walking speed[23] during the 6MWT. In a study on the relation between VO_{2peak} and 6MWT outcome in patients with stroke, the authors concluded that the 6MWT outcome appeared to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary

fitness.[24] Due to walking disabilities this might also be the case in persons with CP and, therefore, it is unclear whether the 6MWT can be employed as a surrogate measure of cardiopulmonary fitness in persons with CP.

As exercise training becomes recognised as an integral component of rehabilitation programmes for persons with CP, the aim of this study was to explore whether the 6MWT is a suitable alternative to CPET. Specifically, the study was designed to examine 1) whether 6MWT distance is related to VO_{2peak}, and 2) whether 6MWT distance predicts VO_{2peak} in ambulatory adolescents and young adults with CP.

METHODS

Subjects

Eligible participants were recruited from six rehabilitation centres and rehabilitation departments at university hospitals throughout the western and central regions of The Netherlands, and by the Association of Physically Disabled Persons and their Parents. Adolescents and young adults with unilateral or bilateral CP were eligible if they met each of the following inclusion criteria: 1) age 16 to 24 years; 2) Gross Motor Function Classification System (GMFCS)[25] level I to II; and 3) had a spastic type of CP as measured with the Modified Ashworth Scale.[26] Persons were excluded if they had any of the following: 1) disabilities other than CP that affected physical activity or peak cardiopulmonary fitness; 2) contraindication to (maximal) exercise; or 3) severe cognitive disorders or insufficient comprehension of the Dutch language to preclude understanding of the purpose of the project and its testing methods. Patient records were screened in the participating centres and an informational letter and invitation to participate was sent to eligible persons. A reminder letter was sent three weeks later to non-responders. All participants provided written informed consent. The study was approved by the Medical Ethics Committee of the Erasmus Medical Centre and local approval was granted by all participating centres.

Procedure

This study is part of a longitudinal multi-centre intervention study to encourage daily physical activity and improve peak cardiopulmonary fitness among adolescents and young adults with spastic CP.[13] The data were collected at three different collaborating centres using consistent testing protocols. Baseline measurements from the longitudinal study were used to perform analyses of the current study.

The 6MWT and CPET were performed sequentially in this order, separated by at least two hours of rest. All participants reported that they had sufficient rest before starting CPET. Additional to screening

for exercise contraindications by a rehabilitation physician, all participants completed the Physical Activity Readiness Questionnaire,[27] to assure that there were no contraindications to CPET.

Six minute walk test

Participants performed the 6MWT according to the method described by Gyatt et al.[7] Patients were instructed to walk, not run, as far as they could along a 30-meter level surface track during a 6-minute period. At the end of each minute, participants were told the elapsed time and standardised encouragement was provided using the following phrases: "you are doing well" and "keep up the good work", as recommended by the American Thoracic Society 6MWT guidelines.[28] Patients were allowed to stop and rest during the test, but were instructed to resume walking as soon as they felt able to do so. The 6MWT distance (in meters) was registered. Measured 6MWT distance was compared with healthy norm-values using the formula of Gibbons et al.,[29] which includes participant characteristics (sex and age). Mean heart rate during the 6MWT was measured using a Polar S810 heart rate monitor[a]. Gas exchange was not measured during the 6MWT because this does not correspond to the execution of the 6MWT in clinical practice. The 6MWT has been found a reliable test in young adults and adults with CP.[30]

Cardiopulmonary exercise testing (CPET)

VO_{2peak} was measured during a progressive ramp protocol on electronically braked cycle ergometers (Jaeger ER800[b] and Corival V2 Lode[c]), which has been found a reliable method in children[31] and adults with CP.[32] The test was preceded by a 3-minute warm-up without resistance. Following warm-up, the resistance was increased every 12 seconds. The magnitude of this increase varied by GMFCS level and gender, and ranged from 2 to 6 Watts, to ensure that total exercise time ranged from 8 to 12 minutes. The target pedal rate during the test was 70 rpm. Strong verbal encouragement was given throughout the test. The test was terminated when the participant voluntarily stopped due to exhaustion, or when the participant was unable to maintain the initial pedal/crank rate. During testing, gas exchange and heart rate were measured continuously by oximetry. Two comparable breath by breath analysing systems were used (Oxycon Pro[d] and Quark CPET[e]), which were calibrated prior to each measurement using reference gases of a known mixture. VO_{2peak} was defined as the highest absolute mean oxygen uptake during 30 seconds of exercise ($mL \cdot min^{-1}$). As objective criteria for maximal exercise, we used the peak heart rate of at least 90% of the predicted maximum heart rate of 194 beats per minute[33] or a respiratory exchange ratio greater than or equal to 1.1.[34] Measured VO_{2peak} was compared to healthy VO_{2peak} norm-values using the formula of Jones et al.,[35] which includes participant characteristics (e.g., sex, height and age). CPET has been found reliable in both children[36-38] and adults[39] with CP in previous studies.

Statistical analyses

All data are presented as means ± SD. Outcomes of VO_{2peak} and 6MWT distance were compared with healthy norm-values using paired t-tests. Independent sample t-tests were performed to test for differences on 6MWT and CPET outcomes between GMFCS groups and between the study sample and dropouts.

Univariate linear regression analysis was performed, using VO_{2peak} as the dependent variable and 6MWT distance as the independent variable. Multiple linear regression analysis was performed to determine whether prediction can be improved by adding patient characteristics, such as sex (coded 0 for males and 1 for females), body mass (in kg) and GMFCS level (coded 0 for level I and 1 for level II). These characteristics were added to the model in a second regression block by the Enter method. The alpha level was set at 0.05. All analyses were performed using PASW statistics for Windows, version 17.0[f].

RESULTS

Descriptive results

In total, 50 adolescents and young adults with CP met inclusion criteria. All participants were classified as spastic as they reached at least a score of 1 on the Modified Ashworth Scale on at least one of the measured muscle groups (hip-adductors, hip-flexors, knee-flexors, ankle-plantar-flexors, elbow-flexors and wrist-plantar-flexors). Nine did not meet the objective criteria for maximal exercise and were excluded, leaving a study sample of 41 participants. Clinical characteristics of the study sample are presented in Table 1.

The nine excluded persons (3 males and 6 females) had a mean peak maximum heart rate of 165 ± 6 beats per minute and respiratory exchange ratio of 1.04 ± 0.04 during CPET. Independent sample t-tests showed that both of these values were significantly lower than those of persons who met

Table 1. Clinical characteristics of the study sample

Characteristic	Value
n	41
Age (years)	20.2 ± 2.5
Body mass (kg)	71.6 ± 18.6
Height (cm)	172.0 ± 10.1
Sex (M / F)	23 / 18
CP distribution (unilateral / bilateral)	24 / 17
GMFCS* distribution (level I / level II)	24 / 17

* Gross Motor Function Classification System

objective criteria for maximal exercise (p<0.01). The mean age of those excluded was 19 ± 3 years and the mean body mass was 59 ± 9 kg; neither value differed significantly from those of participants (p=0.42 and p=0.16, respectively). Six excluded persons were classified at GMFCS level I and three at level II.

No participant required a test stop during the 6MWT and all performed the test without complications. The mean 6MWT distance of 522 ± 88 meters was 32% lower than the mean healthy norm-value of 772 ± 37 meters (p<0.01).[29] The mean heart rate during the 6MWT was 145 ± 21 beats per minute. Table 2 shows that 6MWT distances and 6MWT heart rates did not significantly differ by GMFCS level.

Table 2. Results of the 6-minute walk test and cardiopulmonary exercise testing

	All	GMFCS* I	GMFCS II	p-value for differences between GMFCS I & II
n	41	24	17	
6MWT distance (m) †	522 ± 88	528 ± 75	515 ± 107	0.65
HR_{6MWT} (bpm) ‡	145 ± 21	143 ± 20	148 ± 23	0.50
VO_{2peak} ($mL \cdot min^{-1}$) §	2459 ± 769	2570 ± 694	2302 ± 861	0.28
Maximum heart rate (bpm)	189 ± 12	189 ± 12	188 ± 13	0.66
Maximum RER ||	1.16 ± 0.09	1.18 ± 0.09	1.14 ± 0.07	0.14
Maximum VE (L/min) ¶	98 ± 33	101 ± 33	93 ± 33	0.43
Maximum load (Watts)	180 ± 66	195 ± 56	159 ± 76	0.09

* Gross Motor Function Classification System
† Six minute walk test
‡ Heart rate during six minute walk test
§ Peak oxygen uptake
|| Respiratory exchange ratio
¶ Minute ventilation

Table 3. Univariate linear regression analysis between 6-minute walk test distance (m) and VO_{2peak} ($mL \cdot min^{-1}$)

Variable	B *	ß (95% CI)†	p-value	R^2	SEE ‡	(SEE/mean)*100 §
Constant	387.83			0.21	694	24%
6MWT distance ||	3.97	0.46 (0.18, 0.74)	< 0.01			

* Unstandardised coefficient
† Standardised coefficient
‡ Standard error of estimate
§ Standard error of estimate expressed as percentage of the mean $VO_{2peak.}$
|| 6-minute walk test distance

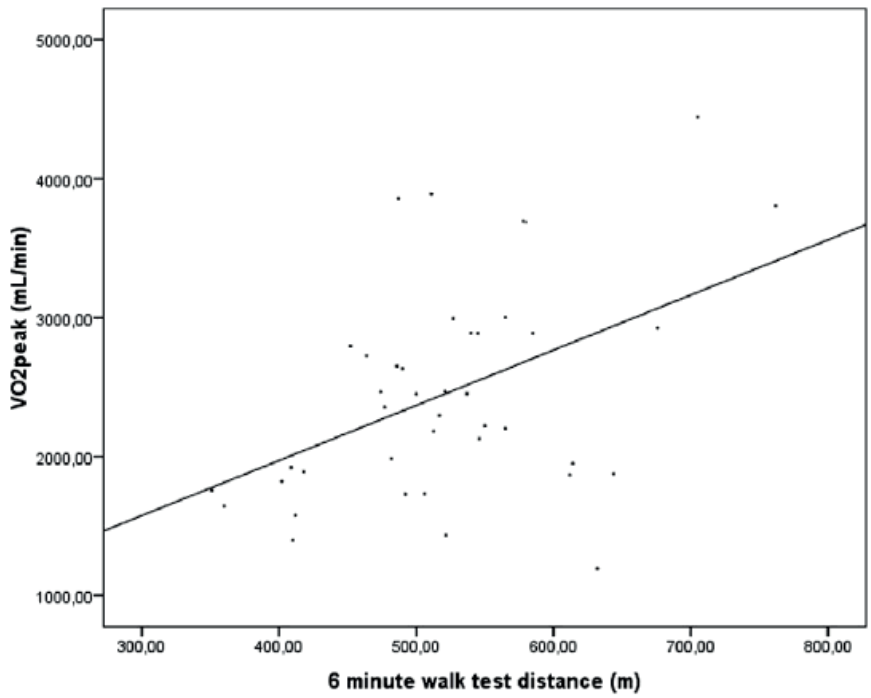

Figure 1. Univariate linear regression line defining the relationship between 6-minute walk test distance and VO_{2peak}

CPET showed a mean VO_{2peak} of 2459 ± 769 mL·min^{-1}, which was 14% lower than the mean healthy norm-value of 2845 ± 712 mL·min^{-1} ($p<0.01$).[35] Table 2 shows that CPET outcomes (presented for all participants and stratified by GMFCS level) did not differ significantly by GMFCS level.

Regression analyses

Table 3 shows outcomes from the univariate linear regression model of 6MWT distance and VO_{2peak}, which is graphically depicted in Figure 1. A significant positive relationship was found between 6MWT and VO_{2peak} ($p<0.01$), with a β of 0.46 and an explained variance of 21%. The SEE of the model was 694 mL•min^{-1}, representing 24% of the mean VO_{2peak}.

The multiple linear regression model was significant, with an explained variance of 58% and a SEE of 523 mL•min^{-1} (Table 4). This SEE represents 18% of the mean VO_{2peak}. The 6MWT distance (ß = 0.38), body mass (ß = 0.37) and sex (ß = -0.38) all significantly contributed to the prediction of VO_{2peak} in the regression model ($p<0.01$). GMFCS level did not contribute significantly to the model (ß = -0.14, p = 0.23).

Table 4. Multiple linear regression analysis of 6-minute walk test distance (m), body mass (kg), sex and Gross Motor Function Classification System level to predict VO_{2peak} ($mL \cdot min^{-1}$). Sex was coded 0 for males and 1 for females. GMFCS level 1 was set as the reference dummy level.

Variables	B *	ß (95% CI) †	p-value	R^2	SEE ‡	(SEE/mean)*100 §
Constant	-2.23			0.58	523	18%
6MWT distance ‖	3.29	0.38 (0.17, 0.59)	<0.01			
Body mass	15.14	0.37 (0.14, 0.60)	<0.01			
Sex	-578.96	-0.38 (-0.61, -0.15)	<0.01			
GMFCS 2 ¶	-210.62	-0.14 (-0.37, 0.09)	0.23			

* Unstandardised coefficients
† Standardised coefficients
‡ Standard error of estimate
§ Standard error of estimate expressed as percentage of the mean $VO_{2peak.}$
‖ 6-minute walk test distance
¶ Gross Motor Function Classification System

DISCUSSION

The current study investigated whether the 6MWT could be used as a simple, inexpensive and sub-maximal alternative to CPET in ambulatory adolescents and young adults with CP. A significant, but weak, positive relationship was found between 6MWT distance and VO_{2peak}. Ross et al. recently published a review in which results from 11 groups studying diverse pulmonary diseases and heart failure were merged to develop a formula to predict VO_{2peak} from 6MWT distance.[12] In that review, 6MWT distance explained 35% of the variance in VO_{2peak}, meaning that they have also found a weak relationship between these two variables.

Compared to able-bodied persons, 6MWT distance is probably decreased among persons with CP due to a common decreased walking capacity[18, 19] caused by spasticity, impaired balance and reduced muscle strength.[19-22] The severity of the walking disability can vary greatly among persons with CP. We expect that this wide variation may explain the weak relationship between VO_{2peak} and 6MWT distance in persons with CP and, therefore, conclude that the 6MWT is inadequate to measure peak cardiopulmonary fitness in adolescents and young adults with CP classified at GMFCS level I and II. Our conclusion contrasts with the recommendation presented in a recent Delphi study.[16] Despite the lack of difference in 6MWT distance between GMFCS groups in the current study, we believe that the 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in persons with CP. This opinion is supported by results of another recent study in which the authors concluded that mean VO_2 uptake during the 6MWT is a valid measure of walking capacity.[40] Furthermore, our conclusion is in accordance with a similar study on patients with stroke where the authors concluded that the 6MWT outcome appeared to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness.[24]

The addition of sex, body mass and GMFCS level to the regression model using 6MWT distance substantially improves the ability to predict VO_{2peak}, as demonstrated by an explained variance of 58%. The extended model shows a SEE of 523 mL•min^{-1}, which represents 18% of the mean VO_{2peak} found in this study. Because of the magnitude of the SEE, the predictive equation is, like other prediction equations for persons with pulmonary disease[8, 12] or heart failure,[10] of limited value for predicting VO_{2peak} in individual patients. This conclusion contrasts with that of a recent study of Leunkeu et al. reporting that the 6MWT is a valid tool to assess peak aerobic power in children with CP.[15] However, in their study, measured VO_{2peak} and heart rate were lower during CPET than during the 6MWT. This indicates that both tests were performed at a sub-maximal level, which weakens their conclusion substantially as reported by Slaman et al. in a letter to the editor.[17] In reaction to this letter, the authors of the study by Leunkeu et al. state that the 6MWT provides a simple and useful indicator of functional exercise capacity,[41] with which we agree. However, in line with our conclusion, we do not agree with them that the 6MWT can be used for evaluating aerobic training in persons with CP because it is likely that improvements in aerobic capacity are masked by walking disabilities.

In our sample of adolescents and young adults with spastic CP, the mean peak cardiopulmonary fitness was 17% lower ($p<0.01$) compared to calculated healthy norm-values for peak cardiopulmonary fitness, using the formula of Jones et al.[35] This finding is consistent with previous results of decreased peak cardiopulmonary fitness in persons with CP.[3, 42] The mean 6MWT distance in our study was 522 ± 88 meters, which is slightly higher compared to a study using the 6MWT in adults with CP.[43] However, our measured 6MWT distance is 32% lower ($p<0.01$) compared to healthy norm-values for 6MWT distance, as calculated using the formula of Gibbons et al.[29]

Study limitations

The American Thoracic Society states that a practice test of the 6MWT is not needed in most clinical settings, but should be considered.[28] In CP populations, the use of an additional 6MWT is inconclusive. Maher et al. showed that practicing the 6MWT is not required in adolescents with CP where the majority of the sample was classified as GMFCS level I or II,[37] whereas Andersson et al. found that 6MWT distance increased during subsequent 6MWTs in adults with CP where the majority of the sample was classified as GMFCS level II-III.[39] As the study sample of Maher et al. corresponds most closely to the study group of the current study, we decided to perform one 6MWT.

Ideally, the 6MWT and CPET should be performed on separate days to ensure sufficient rest between the tests. Unfortunately, this was not practically achievable within the current study. Both tests were separated with at least two hours of rest. However, for persons with GMFCS level I and II we feel that 2 hours of rest should be enough to recover from a sub-maximal exercise as the 6MWT.

The use of cycle ergometers to obtain VO_{2peak} might be considered a limitation as treadmill testing corresponds more with the execution of the 6MWT. However, current treadmill protocols used in clinical practice (Bruce protocol[44] and Balke protocol[45]) are not appropriate for children with CP.[46] From studies on children with CP we know that raising the workload during treadmill testing by substantially increasing walking speed is often not feasible in persons with CP due to problems with coordination.[47] Furthermore, raising workload by increasing the inclination of the treadmill can be a substantial drawback for participants with spastic legs.[16] Therefore, we chose to obtain VO_{2peak} on cycle ergometers.

The current study is a multi-centre study in which two different types of breath-by-breath analysers and cycle ergometers were used to determine VO_{2peak}. However, these analysing systems were calibrated with reference gases before each measurement. Furthermore, both systems have been validated against the Douglas bag method[48, 49] and therefore give similar output.

Nine persons did not meet one of the two objective criteria for maximal exercise. Their mean age and weight did not differ significantly from those of the participants. Furthermore, GMFCS distribution was comparable between those included and those excluded. Therefore, the included sample does not seem to be affected by selection bias, and thus does not affect generalisability of the results.

Conclusions

In conclusion, the current study indicates that the 6MWT is unsuitable to measure peak cardiopulmonary fitness in ambulatory adolescents and young adults with CP. We believe that the 6MWT is more suitable as a measure of walking capacity than of physical fitness in persons with CP. Furthermore, the regression model to predict VO_{2peak} from 6MWT distance and personal characteristics had a high SEE. Therefore the 6MWT seems a poor alternative to CPET in ambulatory adolescents and young adults with CP.

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SUPPLIERS LIST

[a] Polar S810 heart rate monitor. Polar Electro, Oy. Professorintie 5 ,Kempele, Finland.
[b] Jaeger ER800, Jaeger Toennies, Nikkelstraat 2, 4823AB Breda, The Netherlands
[c] Corival Lode, ViaSys Healthcare, De Molen 8-10, 3994DB, Houten, The Netherlands
[d] Oxycon Pro, ViaSys Healthcare, de Molen 8-10, 3994DB, Houten, The Netherlands
[e] Quark CPET system, Cosmed, Via dei Piani di Monte Savello 37, Albano Laziale, Rome, Italy
[f] PASW statistics for Windows, version 17.0. IBM Corporation, 1 New Orchard Road, Armonk, New York, United States.

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Chapter 4

Inactive and sedentary lifestyles amongst ambulatory adolescents and young adults with cerebral palsy

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ABSTRACT

Background

To assess physical behaviour, including physical activity and sedentary behaviour, of ambulatory adolescents and young adults with cerebral palsy (CP). We compared participant physical behaviour to that of able-bodied persons and assessed differences related to Gross Motor Functioning Classification System (GMFCS) level and CP distribution (unilateral/bilateral).

Methods

In 48 ambulatory persons aged 16 to 24 years with spastic CP and in 32 able-bodied controls, physical behaviour was objectively determined with an accelerometer-based activity monitor. Total duration, intensity and type of physical activity were assessed and sedentary time was determined (lying and sitting). Furthermore, distribution of walking bouts and sitting bouts was specified.

Results

Adolescents and young adults with CP spent 8.6% of 24 hours physically active and 79.5% sedentary, corresponding with respectively 123 minutes and 1147 minutes per 24 hours. Compared to able-bodied controls, persons with CP participated 48 minutes less in physical activities ($p<0.01$) and spent 80 minutes more sedentary per 24 hours ($p<0.01$). Physical behaviour was not different between persons with GMFCS level I and II and only number of short sitting bouts were significantly more prevalent in persons with bilateral CP compared to unilateral CP ($p<0.05$).

Conclusions

Ambulatory adolescents and young adults with CP are less physically active and spend more time sedentary compared to able-bodied persons, suggesting that this group may be at increased risk for health problems related to less favourable physical behaviour.

BACKGROUND

Physical activity has been defined as "any bodily movement that results in energy expenditure."[1] Physical activity contributes to the primary and secondary prevention of several chronic diseases, including cardiovascular disease, cancer, diabetes mellitus, hypertension and obesity, and is associated with a reduced risk of premature death in the general population.[2] Sedentary behaviour, defined as a distinct class of activities that require low levels of energy expenditure and involve sitting and lying,[3] also negatively impacts metabolism and cardiovascular health.[4] Physical activity and sedentary behaviour are distinct aspects of physical behaviour.[5] Independent of physical activity, a person with a large amount of sedentary time may still be at risk of poor health outcomes.[4] Consequently, besides meeting physical activity guidelines it is also recommended to limit the amount of sedentary time.[4]

Persons with cerebral palsy (CP) experience problems with movement and posture, including difficulty with balance and walking, gross and fine motor control, and muscle spasticity. Therefore, they are at risk of reduced physical activity and increased sedentary behaviour.[6] Previously, it has been indicated that children and adults with CP participate substantially less in physical activities compared to reference populations, and less than recommended by guidelines.[7-9] With regard to sedentary behaviour, children aged 5 to 17 years with CP fail to achieve recommended activity levels.[7] To our knowledge, sedentary behaviour has not been studied previously in persons with CP after childhood.

Transition to adulthood is thought to be an important time for interventions that promote physical activity and limit sedentary time because at this age many changes in life may influence the adult lifestyle.[10, 11] However, to our knowledge, physical behaviour for 16 to 24 year-olds has not yet been studied in persons with CP. Knowledge of physical behaviour at this age can help optimise recommendations and treatments to increase physical activity and limit sedentary behaviour in persons with CP across the lifespan. Furthermore, by comparing physical behaviour of subgroups based on CP characteristics, recommendations and treatments can be further optimised and tailored for disorder severity.

Therefore, the aim of the current study was to assess physical behaviour of ambulatory adolescents and young adults, aged 16 to 24 years, with spastic CP. Physical behaviour variables included objectively measured physical activity and objectively measured sedentary behaviour. Total duration, intensity and types of physical activities (walking, running, cycling, and non-cyclic movement) were assessed, and distribution of walking bouts was described. Total sedentary time was determined (sitting and lying) and specified with regard to total duration of sitting and distribution of sitting bouts. Furthermore, self-reported physical activity was assessed. Objective data were compared with data of able-bodied controls, and differences within the CP group related to Gross Motor Functioning Classification System (GMFCS) and distribution of CP (unilateral/bilateral) were explored.

METHODS

This study is part of the longitudinal, multi-centre, randomised controlled trial LEARN 2 MOVE 16-24, which evaluates an intervention to promote daily physical activity and sports participation, reduce sedentary behaviour, and improve physical fitness amongst adolescents and young adults with spastic CP.[12] In the current study, baseline data from the longitudinal study were used.

Participants

Adolescents and young adults with spastic unilateral or bilateral CP, aged 16 to 24 years, were recruited from six rehabilitation centres and rehabilitation departments at university hospitals in west-central Netherlands, and by the Association of Physically Disabled Persons and their Parents.

Exclusion criteria were: 1) disabilities other than CP that affect physical activity or physical fitness; 2) contraindications to (maximal) exercise; 3) severe cognitive disorders or insufficient comprehension of Dutch; 4) partly dependent or fully dependent on a manual wheelchair; 5) physical activity level higher than 15.6% of 24 hours (mean physical activity level + 2 standard deviations (SD) of an adult CP population).[9] No one was excluded by this latter criterion.

All participants provided written informed consent. The study was approved by the Medical Ethics Committee of the Erasmus Medical Centre. Local approval was granted by all participating centres.

Physical behaviour

To objectively measure physical behaviour, we used the ambulatory monitoring system VitaMove (2M Engineering, Veldhoven, The Netherlands), with body-fixed accelerometers (Freescale MMA7260Q, Denver, USA) (Figure 1). This activity monitor has demonstrated validity to quantify mobility-related activities and postures and to detect intergroup differences in physical behaviour.[13, 14] The system consists of three recorders that are wirelessly connected and synchronised every ten seconds. One recorder was attached to each thigh and a third recorder was attached to the sternum. The recorders were worn on the body using elastic belts. The measurements were started at participants' homes and activity monitors were worn continuously on consecutive weekdays, except during swimming, bathing and sleeping. Participants kept activity diaries that allowed for correction for periods of non-wearing time of the activity monitor. The intended duration of measurement was 72 hours with a minimum duration of 24 hours. This minimum duration was previously established as adequate for determining activities and postures.[15] To avoid measurement bias, we instructed participants to continue their ordinary daily life and the principles of the activity monitor were only explained after study completion.

Figure 1. VitaMove activity monitor

Accelerometer signals for each recorder were sampled and stored digitally on a micro Secure Digital memory card. Measurements were uploaded to a computer for kinematic analysis using VitaScore Software (VitaScore BV, Gemert, The Netherlands). The duration, rate, and moment of occurrence of physical activity, sedentary behaviour, and transitions between postures were automatically and separately detected with a 1-second resolution. Furthermore, motility was determined, which provides information on the variability of the acceleration signal and is related to the intensity of body-segment movements. A detailed description of the configuration and analysis has been described elsewhere.[13]

The following data were obtained:

1. Total duration of physical activities, including walking, running, cycling, and non-cyclic movement and separate duration of each of these activities. All physical activity measures were expressed as a percentage of a 24-hour period.

2. Total duration of sedentary behaviour, including sitting and lying, and separate duration of sitting and standing, all expressed as a percentage of a 24-hour period.
3. Mean motility of the total of physical activities and mean motility of walking, expressed as gravitational force (g).
4. Distribution of continuous walking and sitting bouts with pre-defined durations: 0-10 sec; 10-60 sec; 1-10 min; 10- 30 min; or > 30 min.

For reference, we used activity monitor data of 32 able-bodied persons aged 14 to 29 years available from previous studies at our department (mean age 22 years (SD=5), 14 males). All able-bodied persons wore the activity monitor for two consecutive weekdays. Measurements were performed with a non-wireless version of the activity monitor and analysed with a previous software version. However, the underlying technique of the activity monitor is the same as that of the monitors worn by the participants with CP, and the algorithms of data analysis are comparable between software versions. Data for participants with CP were expressed as a percentage of reference data.

Self-reported physical activity levels were measured with the Dutch version of the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD),[16] a 13-item, 7-day recall questionnaire developed for people with a physical disability. The scale consists of questions regarding leisure time, and household-related and work-related physical activity. The total PASIPD score was calculated by multiplying the average hours per day for each item by a given metabolic equivalent (MET) value associated with the intensity of the activity. Because the PASIPD was developed for persons with physical disabilities, there are no reference data for able-bodied persons.

Statistical analysis

An independent t-test was used to test for differences in age and a Chi-Square test to test for difference in gender between the total group of participants with CP and able-bodied persons. Regression analyses, correcting for age and gender, were used to assess differences in physical activity and sedentary time between participants with CP and able-bodied persons. Regression analyses correcting for age and gender were used to test for differences in physical behaviour between subgroups on basis of GMFCS level and CP distribution. Statistical analyses were preformed using SPSS 20 (SPSS Inc, Chicago, IL). The significance level was set at $p<0.05$.

RESULTS

In total, 48 ambulatory adolescents and young adults with CP completed the physical behaviour measurements. Due to technological challenges with the activity monitor, data were not available for

the intended three days for all participants. Measurement duration was 72 hours for 37%, 48 hours for 51% and 24 hours for 12% of participants.

Characteristics of participants with CP and able-bodied persons are described in Table 1. No significant differences were found in age (p=0.1) and gender (p=0.5) between these groups. Furthermore, Table 1 shows data on physical activity, sedentary time and self-reported physical activity, and the comparison with able-bodied persons. Compared to able-bodied persons, persons with CP were significantly less physically active (p<0.01) and spent more time sedentary (p<0.01). On average, persons with CP participated 48 minutes per 24 hours less in physical activities compared to able-bodied controls (123 vs. 171 minutes/24h). Sedentary time was 80 minutes per 24 hours more in the group with CP compared to able-bodied controls (1147 vs. 1077 minutes/24h). Self-reported physical activity level in participants with CP was on average 13.0 (8.6) MET-hr./day.

Between participants with GMFCS levels I and II, no significant differences were found in physical activity, sedentary behaviour, and self-reported physical activity level. Since the sample size of the subgroup with GMFCS level III was limited to four persons, statistics were not performed for this subgroup. When comparing unilateral and bilateral participants, only the number of sitting bouts 0-10 sec (p=0.04) and 10-60 sec (p=0.02) were significantly higher for participants with bilateral CP.

DISCUSSION

This was the first study to assess both physical activity and sedentary behaviour in a sample of ambulatory persons with spastic CP after childhood. Persons with CP participated 48 minutes less in physical activities and spent 80 minutes more sedentary per 24 hours, compared to able-bodied controls. A comparison between the present data and guidelines for healthy physical behaviour is difficult. The latter are primarily based on self-report using questionnaires to estimate overall physical behaviour, whereas our data are objective and based on continuous registrations.[17] Future studies defining guidelines based on objectively measured data are necessary.

Consistent with previously published studies, physical behaviour did not differ between participants with GMFCS levels I and II.[8, 18, 19] However, studies that included GMFCS level III and IV have shown significant associations between GMFCS level and physical activity.[8, 20, 21] Although we did not test for significance, physical activities seemed to be lower in persons with GMFCS level III (5.1%) compared to GMFCS levels I and II (8.9%), and sedentary times were higher as well (87.4% vs. 78.8%). Therefore, the subgroup of GMFCS III seems to have even less favourable physical behaviour. Since this subgroup was only small, further research is necessary.

Table 1. Characteristics, physical activity, sedentary time and self-reported physical activity

	CP	Able-bodied[4]				GMFCS level[7]			CP distribution[8]	
Characteristics			Mean dif.[5]	p[6]	95% CI	I	II	III	unilateral	bilateral
Number of participants	48	32				29	15	4	27	21
Age, mean (SD)	20 (3)	22 (5)		0.10		19 (2)	21 (3)	19 (2)	19 (2)	21 (3)
Gender, number of males/females	23/25	18/14		0.50		13/16	8/7	2/2	11/16	12/9
Physical activity Mean (SD)										
% Physical activities[1]	8.6 (3.0)	12.0 (3.9)	-3.4	<0.01*	-5.2 – -2.1	9.2 (3.2)	8.3 (2.4)	5.1 (1.0)	8.8 (2.9)	8.2 (3.2)
% Walking	4.3 (2.3)	8.5 (3.5)	-4.2	<0.01*	-5.6 – -3.0	4.9 (2.3)	4.0 (2.0)	1.5 (1.4)	4.7 (2.2)	3.8 (2.5)
% Running	0 (0.1)	0.1 (0.5)	-0.08	0.18	-0.3 – 0.1	0 (0.1)	0 (0)	0.1 (0.1)	0 (0.1)	0 (0.1)
% Cycling	1.1 (1.2)	1.4 (1.8)	-0.3	0.10	-1.2 – 0.1	1.2 (1.2)	0.9 (1.1)	0.9 (1.4)	1.2 (1.2)	0.9 (1.1)
% Non-cyclic movement	3.2 (1.7)	1.8 (1.1)	1.4	<0.01*	0.7 – 2.1	3.2 (1.7)	3.4 (1.9)	2.6 (1.7)	2.9 (1.6)	3.5 (1.9)
Motility physical activities (g^2)	43.9 (8.1)					45.5 (5.5)	41.9 (11.0)	40.3 (10.2)	45.8 (5.7)	41.5 (9.9)
Motility walking (g^2)	52.6 (8.9)					52.9 (6.9)	52.1 (9.5)	52.3 (16.3)	53.8 (7.5)	50.9 (9.9)
0-10 sec walking bouts	124.6 (45.4)					137.0 (41.1)	117.0 (41.9)	63.6 (40.1)	132.0 (39.9)	115.2 (51.0)
10-60 sec walking bouts	88.8 (48.3)					100.8 (50.1)	79.5 (37.5)	36.2 (32.8)	96.1 (45.2)	79.4 (51.6)
1-10 min walking bouts	7.1 (6.0)					7.7 (5.8)	7.7 (6.3)	0.8 (1.5)	7.5 (4.9)	6.6 (7.2)
10-30 min walking bouts	0.1 (0.3)					0.1 (0.3)	0.1 (0.3)	0	0.1 (0.3)	0.02 (0.1)
>30 min walking bouts	0					0	0	0	0	0
Sedentary time Mean (SD)										
% Sedentary time (sitting + lying)[3]	79.5 (7.1)	74.0 (7.5)	5.5	<0.01*	1.6 – 8.3	77.9 (7.0)	80.6 (5.8)	87.4 (7.6)	78.7 (6.8)	80.6 (7.5)
% Sitting	36.8 (8.1)	36.7 (7.0)	0.1	0.79	-3.1 – 4.1	36.6 (7.6)	35.7 (8.8)	42.3 (8.0)	36.9 (8.6)	36.7 (7.5)
0-10sec sitting bouts	18.0 (12.2)					15.6 (7.8)	22.0 (17.4)	19.8 (15.2)	14.8 (7.4)	22.0 (15.8)
10-60sec sitting bouts	34.7 (19.3)					31.7 (14.7)	38.5 (22.8)	41.7 (33.9)	29.6 (15.0)	41.2 (22.7)
1-10min sitting bouts	40.2 (19.2)					39.7 (18.2)	40.0 (18.2)	44.5 (33.6)	38.1 (18.3)	42.9 (20.4)
10-30min sitting bouts	11.4 (3.3)					11.8 (3.0)	10.9 (3.3)	10.4 (6.0)	11.8 (3.2)	10.9 (3.5)
>30min sitting bouts	3.5 (1.9)					3.3 (1.9)	3.3 (1.5)	5.0 (3.0)	3.5 (2.0)	3.4 (1.9)
% Standing	11.9 (5.4)	13.2 (5.3)	-1.3	0.54	-3.2 – 1.7	12.9 (5.3)	11.1 (4.9)	7.6 (6.7)	12.5 (5.5)	11.2 (5.4)
Self-reported physical activity										
PASIPD (MET-hr/day), Mean(SD)	13.0 (8.6)					15.3 (9.5)	9.8 (6.0)	7.8 (2.4)	14.6 (8.5)	10.9 (8.5)

[1] Physical activities is total duration of walking, running, cycling, and non-cyclic movement, as a % of 24 hours
[2] g=gravitational forces*100
[3] Sedentary time is total duration of lying and sitting, as % of 24 hours
[4] Note that data on motility, bouts and self-reported physical activity were not available for able-bodied controls.
[5] Mean difference between all participants with CP and able-bodied persons.
[6] Difference in characteristics between all persons with CP and able-bodied persons was tested. Difference in physical activity and sedentary time was analysed with regression analyses corrected for age and gender.
[7] Corrected for age and gender, no significant differences were found in physical behaviour between participants with GMFCS level I and II ($p>0.05$). Differences with the subgroup GMFCS level III were not assessed because sample size was limited.
[8] Corrected for age and gender, participants with bilateral CP had a significantly higher number of sitting bouts 0-10 sec ($p=0.04$) and 10-60 sec ($p=0.02$) compared to unilateral CP. No other significant differences were found in physical behaviour between participants with bilateral and unilateral CP ($p>0.05$)
* indicates significant difference $p<0.05$
GMFCS=Gross Motor Functioning Classification System
PASIPD=Physical Activity Scale for Individuals with Physical Disabilities
CI= confidence interval

Compared to persons with unilateral CP, persons with bilateral CP had significantly more short sitting bouts of 0-10 seconds and 10-60 seconds. Previous studies suggest that these short sitting bouts are favourable behaviour in terms of reducing cardiovascular risk because they break up sedentary time.[22] If these short sitting bouts break up sedentary time, this would also lead to less sittings bouts of more than 30 minutes.[23] However, the numbers of these long sitting bouts were comparable in both subgroups. Since the number of short sitting bouts was the only difference between persons with unilateral CP and bilateral CP, we can conclude that these subgroups are comparable with regard to movement behaviour and health problems.

Although physical behaviour was found to be less favourable in adolescents and young adults with CP, physical strain may be comparable or higher compared to able-bodied persons. Previously, it had been reported that physical strain during walking is higher in persons with CP compared to reference groups,[19] and that the physical strain of walking is inversely related to the total time of daily walking.[19, 24] Because of higher physical strain, persons with CP may be less active in daily life to conserve energy or prevent fatigue.[19, 24] Unfortunately, physical strain during the objective measurement of physical activities was not assessed in the present study. It is unknown how this higher strain in persons with CP relates to the risk of cardiovascular disease and other chronic diseases related to physical behaviour.

Self-reported physical activity was relatively high in the present sample of ambulatory adolescents and young adults with CP (13.0 MET-hour/day, SD=8.6), as compared to previously published self-reported physical activity in ambulatory persons with CP and meningomyelocele (11.3 MET-hour/day (SD=8.6)).[17] However, objectively measured physical activity was also reported to be lower in those groups: 8.1% in adults with bilateral CP and 7.8% in ambulatory persons with meningomyelocele, compared to 8.6% in the current sample.[25]

Limitations

Although a large number of persons with varying GMFCS levels were invited to participate, our sample included only four persons with GMFCS level III. Further research is required in persons with lower functioning GMFCS levels, including GMFCS level III and IV and wheelchair-bound persons. Wearing the activity monitor may have influenced activities in daily life, despite participants' reports that they were able to perform their regular activities. Although all measurements took place on weekdays and no significant differences were found between days, measurement duration in participants with CP was one to three days while measurement duration in able-bodied persons was two days. Furthermore, comparisons between persons with CP and able-bodied persons have to be interpreted with some caution since in able-bodied persons a previous version of the activity monitor and software was used. However, the underlying technique and analysis procedures were comparable between versions and therefore no differences between systems versions are expected.

Our study may overestimate physical activity because of selection bias; persons with CP interested in physical activity and sports may have been more likely to participate in the study. Despite of that, this group was less physical active and had more sedentary time compared to reference.

Conclusions

Objective measurements show that ambulatory adolescents and young adults with CP are less physically active and spend more time sedentary compared to able-bodied persons, suggesting that this group may be at increased risk for health problems related to less favourable physical behaviour.

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Chapter 5

Health-related physical fitness of ambulatory adolescents and young adults with spastic cerebral palsy

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ABSTRACT

Objective

To extensively describe health-related physical fitness of adolescents and young adults with cerebral palsy (CP), compare with able-bodied reference, and assess differences related to Gross Motor Functioning Classification System (GMFCS) level and distribution of CP.

Design

Cross-sectional.

Subjects

Fifty ambulatory persons with spastic CP, GMFCS level I or II, aged 16-24 years.

Methods

Physical fitness measures were: (1) cardiopulmonary fitness by maximal cycle ergometry, (2) muscle strength, (3) Body Mass Index (BMI) and waist circumference, (4) skinfolds, (5) lipid profile.

Results

Regression analyses, corrected for age and gender, showed that persons with bilateral CP had lower cardiopulmonary fitness and lower hip abduction muscle strength than persons with unilateral CP. Comparison between persons with GMFCS level I and II showed only a difference on peak power during cycle ergometry. Measures marked as considerably lower (<75%) in persons with CP compared to reference were: cardiopulmonary fitness, hip flexion and knee extension strength.

Conclusion

Distribution of CP seems to affect fitness more than GMFCS level. Furthermore, adolescents and young adults with CP seem to have reduced health-related physical fitness compared to able-bodied persons. Because this phase in life has great influence on adult lifestyle, it can be an important period for intervention.

INTRODUCTION

Cerebral Palsy (CP) describes a group of disorders of movement and posture that are attributed to non-progressive disturbances in the developing brain.[1] Movement and posture problems in CP include walking and balance, gross and fine motor control, and muscle spasticity.[2] These movement and posture problems might impair physical fitness and physical activity levels in persons with CP.[3, 4] Reduced physical fitness and physical activity possibly interact to cause a cycle of de-conditioning: low physical fitness might result in high physical strain during activities in daily life,[5, 6] possibly leading to a reduction in activity, and consequently further decreasing physical fitness. Moreover, physical fitness is known to contribute to health and quality of life of persons with chronic conditions.[7]

Improving physical fitness during adolescence seems important, because at this age many changes in life may influence the adult lifestyle.[8] Moreover, it is known that childhood fitness and habitual activity participation track into adulthood.[9] Knowledge of health-related physical fitness at this age can help in optimising recommendations and treatments to improve physical fitness in adolescents and young adults with CP. Furthermore, by comparing physical fitness between subgroups with specific CP characteristics, recommendations and treatments to improve physical fitness can be further optimised and tailored to a person's characteristics.

Caspersen et al. defined several health-related components of physical fitness, including cardiopulmonary fitness, muscle strength and body composition.[10] In addition, lipid profile has been found to be an important objective indicator for the risk of cardiovascular disease.[11] We found seven previous studies describing health-related physical fitness components in adolescents and young adults with CP.[12-18] Most of these studies focused on only one component, e.g. cardiopulmonary fitness,[12-15] muscle strength,[16] or body composition.[17] One study assessed both cardiopulmonary fitness and body composition.[18] To our knowledge there has been no study reporting on lipid profile in adolescents and young adults with CP. Furthermore, the sample sizes of the previous studies were small (range N=5-19), and the study groups were heterogeneous with regard to level of motor functioning.[19] Moreover, most of the studies are old (range 1976-2003),[12, 13, 15, 17, 18] with four of the seven older than 20 years. Because the approach to paediatric rehabilitation has changed and developed over the years, this might have influenced current physical fitness levels in adolescents and young adults with CP.[2] Therefore, the goal of the present study was to extensively describe health-related physical fitness of adolescents and young adults with spastic CP aged 16-24 years. Multiple components of health-related fitness were assessed, including cardiopulmonary fitness, muscle strength, anthropometric measures, skinfolds, and lipid profile. Data were compared with reference values of able-bodied persons, and differences were explored within the CP group related to Gross Motor Functioning Classification System (GMFCS),[20] and distribution of CP.

METHODS

Participants

Ambulatory adolescents and young adults with spastic unilateral or bilateral CP, aged 16 to 24 years, were recruited from six rehabilitation centres and rehabilitation departments at university hospitals throughout the western and central regions of The Netherlands, and by the Association of Physically Disabled Persons and their Parents.

This study is a retrospective cross-sectional analysis, as part of the longitudinal, multi-centre, randomised controlled trial LEARN 2 MOVE, which evaluates an intervention that aims to promote daily physical activity and sports participation, reduce sedentary behaviour, and improve physical fitness among adolescents and young adults with spastic CP.[21] Exclusion criteria were: 1) disabilities other than CP that affect physical activity or cardiopulmonary fitness; 2) contraindications to (maximal) exercise; or 3) severe cognitive disorders or insufficient comprehension of the Dutch language. All participants provided written informed consent. The study was approved by the Medical Ethics Committee of the Erasmus Medical Centre and local approval was granted by all participating centres.

Procedures

Data collection took place at three different centres using consistent testing protocols. In the present study, baseline data of the longitudinal study were analysed. All tests were performed on the same day, and sufficient rest periods were provided between the different tests. A rehabilitation physician screened on contraindications for exercise and all participants completed the Physical Activity Readiness Questionnaire.[22]

Outcome measures

The health related physical fitness outcome measures were: (1) cardiopulmonary fitness (2) muscle strength (3) anthropometric measures including Body Mass Index (BMI) and waist circumference, (4) skinfolds, and (5) blood lipid profile.

Cardiopulmonary fitness

All participants performed a maximal exercise test consisting of a progressive ramp protocol[23] on electronically braked cycle ergometers (Jaeger ER800, Jaeger Toennies, Breda, The Netherlands or Corival V2 Lode B.V., Groningen, The Netherlands). The test started with a 3-minute warm-up without resistance. After this warm-up period, the resistance was increased every 12 seconds with steps of 2 to 6 Watt, depending on GMFCS level and gender. The target pedal rate during the test was 70 rpm. Participants were verbally encouraged to continue as long as possible. The test ended when the participant stopped voluntarily due to exhaustion or when the participant was unable to maintain the target pedal rate. During the test, gas exchange and heart rate (HR) were measured continuously. In the

different centres, two comparable breath-by-breath analysing systems were used (Oxycon Pro, ViaSys Healthcare, Houten, The Netherlands; Quark CPET system, Cosmed, Rome, Italy). The highest mean oxygen uptake during 30 seconds was defined as VO_{2peak}. VO_{2peak} was expressed in $L \cdot min^{-1}$ and in mL/[kg•min] and as a percentage of the reference values of Jones et al., taking into account gender, age, height and body mass.[24] Furthermore, peak ventilation (VE_{peak}), ventilatory equivalent ratio for oxygen (VE_{peak}/VO_{2peak}), and highest power output (PO_{peak}) during 30 seconds were determined. In addition, the ventilatory anaerobic threshold (VAT, in $L \cdot min^{-1}$ and $\%VO_{2peak}$) was estimated by the ventilatory equivalent method:[25] when VE/VO_2 and the end tidal O_2 partial pressure ($PETO_2$) increased while the ventilatory equivalent for CO_2 (VE/VCO_2) and end-tidal CO_2 partial pressure ($PETCO_2$) remained stable. Also HR_{peak} and peak respiratory exchange ratio (RER_{peak}) were determined and used as objective criteria for maximal exercise. Criteria were $HR_{peak} \geq 175$ bpm (90% of predicted maximum HR)[26] or $RER_{peak} \geq 1.1$.[27] When criteria were not met, results of the maximal exercise test were excluded.

Muscle strength

Muscle strength of the hip flexors, hip abductors and knee extensors was measured with a hand-held dynamometer (MicroFet, Hoggan Health Industries Inc, West Jordan, UT, USA) using the "break" method.[28] The applicator of the dynamometer was held against the distal part of the limb segment, and participants were asked to build up their maximum force against it. When maximum was reached the examiner applied sufficient resistance to overcome the force exerted by the participant. Both the left and right side were measured three times, with one minute of rest in between. The average value of the three repetitions was determined. The leg with the highest muscle strength was categorised as the stronger leg, and the other leg as the weaker leg. The mean of both legs was compared to able-bodied Dutch reference values for muscle strength measured with the break testing method in a group of 16 year olds.[29]

Anthropometric measures

Height (cm) and body mass (kg) were measured, and Body Mass Index (BMI, $kg \cdot m^{-2}$) was determined. Waist circumference (cm) was measured mid-way between the lowest rib and the iliac crest while standing. For BMI and waist circumference, Dutch reference values for persons aged 30-39 years from the project "NLdeMaat 2009-2010" were used.[30] Similar to the general population, we considered a BMI <18.5 underweight, ≥18.5 and <25 normal weight, a BMI ≥25 and <30 overweight, and a BMI ≥30 obese. In males, waist circumference was categorised as: <79 cm underweight, ≥79 and <94 cm normal weight, ≥94 and <102 cm normal weight, ≥102 cm obese. In females: <68 cm underweight, ≥68 and <80 cm normal weight, ≥80 and <88 cm normal weight, ≥88 cm obese

Skinfolds

The thickness of four skinfolds (biceps, triceps, subscapular and suprailiac) was measured twice on the left side of the body with a Harpenden calliper (Burgess Hill, UK), and mean values were determined.[31]

Lipid profile

Non-fasting blood samples were taken, and total serum cholesterol (TC), high density lipoprotein cholesterol (HDL) and TC/HDL ratio were determined. TC and HDL are known to be minimally altered when measured in fasting or non-fasting blood samples.[32, 33] Dutch reference values for persons aged 30-39 years were used.[30] TC was considered unfavourable when ≥6.5 mmol/l and HDL unfavourable when ≤0.9 mmol/l.

Statistical analyses

Participants' characteristics and the components of health-related fitness are presented as means (SD). Furthermore, mean values (SD) for subgroups regarding GMFCS level and distribution of CP were determined. Regression analyses were performed to test whether there were differences in age and gender between the subgroups regarding GMFCS level and distribution of CP. To test for differences in health-related fitness between subgroups, separate linear regression models were made, all corrected for age and gender. Statistical analyses were performed using SPSS 20 (SPSS Inc, Chicago, IL). The significance level was set at $p \leq 0.05$.

Percentages of reference values were determined for VO_{2peak}, mean muscle strength of both legs for hip flexion, hip abduction and knee extension, BMI, waist circumference, TC and HDL. VO_{2peak} was predicted per person[24] and the measured VO_{2peak} was expressed as a percentage of the predicted VO_{2peak}. A paired t-test was used to test for differences between the measured VO_{2peak} and the predicted VO_{2peak}. For muscle strength, BMI, waist circumference, TC and HDL, the mean value of the participants with CP was expressed as a percentage of the reference mean. When values were found to be less than 75% of reference they were marked considerably lower. For VO_{2peak}, and mean muscle strength of both legs we described the number of participants with an outcome <50% of reference and <%75 of reference. For BMI and waist circumference we described the number of participants in the categories: underweight, normal weight, overweight and obese. For lipid profile, we described the number of participants with a favourable and an unfavourable outcome.

RESULTS

In total, 55 adolescents and young adults with CP were measured for attributes of health-related physical fitness. Of these 55, only five were GMFCS level III. Since this subgroup was small, we excluded these persons from further analyses. We included 50 participants with GMFCS level I or II.

In Table 1 participants' characteristics and their cardiopulmonary fitness and muscle strength are described. The distribution of CP was unknown in 1 participant. Participants with bilateral CP were significantly older than the participants with unilateral CP (p=0.03).

Table 1. Participants' characteristics, cardiopulmonary fitness & muscle strength, and differences related to GMFCS level and distribution of CP

		GMFCS			Distribution		
	All	*I*	*II*	*p†*	*Unilateral*	*Bilateral*	*p†*
Participants' characteristics							
Number of participants	50	30	20		28	21	
Age, mean (SD)	20 (3)	20 (3)	21 (3)	0.35	19 (2)	21(3)	0.03*
Gender, number of males/females	25/25	14/16	11/9	0.57	13/15	12/9	0.47
Cardiopulmonary, mean (SD)							
number of participants	41	24	17		23	17	
VO_{2peak} ($L \cdot min^{-1}$)	2.46 (0.77)	2.57 (0.69)	2.30 (0.86)	0.06	2.66 (0.16)	2.20 (0.17)	<0.01*
VO_{2peak} (mL/[kg•min])	35.08 (9.37)	35.85 (9.37)	34.00 (9.56)	0.35	37.01 (1.93)	32.15 (2.25)	0.05*
VE_{peak} ($L \cdot min^{-1}$)	97.71 (32.68)	101.17 (32.61)	92.82 (33.13)	0.15	106.00 (30.46)	87.94 (33.98)	0.01*
VE_{peak}/VO_{2peak} (Vo2 $L \cdot min^{-1}$)	40.04 (7.13)	39.47 (7.65)	40.84 (6.48)	0.55	40.27 (6.42)	40.11 (8.22)	0.92
VAT ($L \cdot min^{-1}$)	1.62 (0.60)	1.65 (0.13)	1.58 (0.15)	0.34	1.69 (0.15)	1.54 (0.13)	0.14
VAT (%VO_{2peak})	65.23 (13.24)	64.12 (2.54)	67.86 (4.27)	0.53	63.38 (2.88)	68.33 (3.52)	0.36
PO_{peak} (Watt)	180.37 (66.14)	195.21 (55.57)	159.41 (75.51)	0.02*	204.00 (14.35)	149.82 (12.34)	<0.01*
HR_{peak}	188.62 (12.34)	189.43 (11.90)	187.56 (13.22)	0.47	191.85 (8.55)	184.82 (15.08)	0.05*
HR_{peak} % of predicted max	94.49 (6.55)	94.71 (6.19)	94.19 (7.20)	0.48	96.00 (4.82)	92.71 (7.92)	0.04*
VO_{2peak}/HR_{peak}	13.14 (3.88)	13.79 (3.62)	12.29 (4.15)	0.07	14.32 (4.06)	11.77 (3.23)	<0.01*
RER_{peak} (VCO_2/VO_2)	1.16 (0.09)	1.18 (0.09)	1.14 (0.07)	0.12	1.18 (0.10)	1.14 (0.07)	0.13
Muscle strength, mean (SD)							
number of participants	46	27	19		24	21	
Hip flexion, strongest leg (N)	238.79 (93.66)	249.23 (88.06)	233.95 (101.65)	0.19	246.12 (107.30)	229.77 (79.61)	0.29
Hip flexion, weakest leg (N)	211.15 (88.73)	215.73 (79.81)	204.65 (102.01)	0.37	213.91 (97.69)	206.75 (81.70)	0.36
Hip abduction, strongest leg (N)	246.50 (107.12)	252.10 (94.83)	238.54 (124.84)	0.53	282.05 (122.74)	209.41 (72.50)	<0.01*
Hip abduction, weakest leg (N)	224.17 (95.68)	227.45 (87.59)	219.53 (108.48)	0.68	257.43 (104.72)	188.76 (72.09)	<0.01*
Knee extension, strongest leg (N)	263.75 (105.06)	262.26 (102.86)	265.86 (110.93)	0.69	275.29 (131.09)	254.54 (66.87)	0.16
Knee extension, weakest leg (N)	233.92 (101.88)	233.69 (81.83)	234.25 (127.58)	0.65	248.54 (129.22)	215.98 (59.37)	0.08

*significant difference $p \leq 0.05$, VO_2=oxygen uptake, VE_{peak}=ventilation, VAT=ventilatory anaerobic threshold, PO=power output, HR=heart rate, RER=respiratory exchange ratio

† regression analyses studying differences in cardiopulmonary fitness and muscle strength between GMFCS level I and II and between unilateral and bilateral CP were corrected for age and gender

Results of the maximal exercise test are given for 41 participants. Nine participants were excluded because they did not meet objective criteria due to lack of motivation. Muscle strength data of 46 participants were available. Data of four participants were missing either because a participant could not perform the test or for logistical reasons.

Corrected for age and gender, persons with GMFCS level II had significantly lower PO_{peak} compared to persons with GMFCS level I (p=0.02). When comparing persons with unilateral and bilateral CP, corrected for age and gender, we found significant differences between groups for VO_{2peak}, VE_{peak}, PO_{peak}, HR_{peak}, and VO_{2peak}/HR_{peak}. Furthermore, participants with unilateral CP had significantly higher hip abduction muscle strength compared to persons with bilateral CP (p<0.01).

Table 2 shows the comparison to reference on cardiopulmonary fitness and muscle strength. Mean VO_{2peak} was 62% of reference which was found to be a significant difference (p<0.01). Hip flexion and knee extension strength were marked to be considerably lower than reference (both 65% of reference). The nine persons who did not reach maximal exertion due to lack of motivation (three males/six females, six GMFCS level I/three GMFCS level II) had a mean HR_{peak} of 165 ± 6 beats per minute, RER_{peak} of 1.04 ± 0.04, and VO_{2peak} of 1.69 ± 0.45 $L \cdot min^{-1}$. Independent t-tests showed that these three measures were significantly lower than those of persons who met objective criteria for maximal exercise (p<0.01). The excluded persons did no differ significantly in terms of age (mean 19 years, SD=3) and body mass (mean 59, SD=9).

Table 3 shows results regarding anthropometric measures, skinfolds and lipid profile and results of the subgroup analysis. No significant differences on these outcomes were found between subgroups with different CP characteristics.

Table 4 presents comparisons of anthropometric measures and lipid profile with reference values. Mean BMI and mean waist circumference were comparable to reference. BMI indicating underweight

Table 2. Cardiopulmonary fitness and muscle strength compared to reference

	% Reference	P[3]	<75% reference[4]	<50% reference[4]
VO_{2peak}[1]	62	<0.01*	30/41	16/41
Hip flexion[2]	65		33/46	16/46
Hip Abduction[2]	85		19/46	6/46
Knee extension[2]	65		33/46	13/46

[1] Per person the VO_{2peak} was predicted according to Jones (24). The measured VO_{2peak} was expressed as % of the predicted VO_{2peak}

[2] The mean of both legs was used for comparison with reference. Reference values of 16 year olds.

[3] A paired sample t-test was used to test for differences between measured VO_{2peak} and predicted VO_{2peak}

[4] Number of participants in this category/ number of participant's data available

*Significant difference p≤0.05

Table 3. Anthropometric measures, skinfolds & lipid profile, and differences related to GMFCS level and distribution of CP

		GMFCS			Distribution		
	All	*I*	*II*	*p†*	*Unilateral*	*Bilateral*	*p†*
Anthropometric measures, mean (SD)							
number of participants	50	30	20		28	21	
Body mass (kg)	69.60 (17.88)	71.35 (20.08)	66.99 (14.05)	0.25	71.92 (18.35)	67.25 (17.41)	0.16
Body Mass Index (kg·m^{-2})	23.71 (4.85)	24.33 (5.46)	22.78 (3.71)	0.27	24.42 (5.19)	23.00 (4.34)	0.33
Waist circumference (cm)	84.30 (14.04)	84.17 (14.67)	84.50 (13.42)	0.98	84.54 (14.29)	84.57 (14.12)	0.91
Sum of skinfolds, mean (SD)	68.58 (28.80)	69.98 (31.28)	66.48 (25.24)	0.75	72.97 (29.70)	63.88 (27.60)	0.34
Lipid profile, mean (SD)							
number of participants	23	16	7		11	12	
Total cholesterol (mmol/l)	4.29 (0.62)	4.25 (0.60)	4.39 (0.71)	0.74	4.39 (0.67)	4.20 (0.58)	0.44
HDL (mmol/l)	1.37 (0.31)	1.41 (0.32)	1.27 (0.26)	0.68	1.46 (0.29)	1.28 (0.31)	0.11
TC/HDL ratio	3.29 (0.85)	3.18 (0.93)	3.53 (0.63)	0.83	3.12 (0.78)	3.44 (0.92)	0.33

*Significant difference p≤0.05

† Regression analyses were corrected for age and gender

Table 4. Anthropometric measures and lipid profile compared to reference

	% Reference*	Underweight†	Normal weight†	Overweight†	Obese†
BMI	96	3/50	33/50	8/50	6/50
Waist circumference	97	11/50	22/50	5/50	12/50

	% Reference*	Favourable†	Unfavourable†
Total cholesterol	87	23/23	0/23
HDL	85	21/23	2/23

* Reference values of persons aged 30-39 years

† Number of participants in this category/ number of participants data available

was found in 6% of participants (3 out of 50) compared to 0.9% of the reference sample. Overweight was found in 16% of participants (8 out of 50), compared to 21% in the reference sample. Furthermore, 12% (6 out of 50) had a BMI indicating obesity, compared to 10% in the reference sample. Waist circumference indicated obesity in 24% of males (6 out of 25), compared to 12% of the reference sample, and in 24% of females (6 out of 25), compared to 26% of the reference sample. None of the 23 persons had unfavourable TC, compared to 8.5% in the reference sample. Two out of 23 participants (8.7%) had unfavourable HDL compared to 7.9% in the reference sample. Twenty-one blood samples were missing.

DISCUSSION

This is the first study describing multiple aspects of health-related physical fitness in a substantial sample of ambulatory adolescents and young adults with spastic CP (GMFCS level I and II). Distribution of CP (unilateral vs. bilateral) seems to affect physical fitness more than GMFCS level (I vs. II). Persons with bilateral CP had lower cardiopulmonary fitness and lower hip abduction muscle strength compared to persons with unilateral CP. Persons with GMFCS level I and II had almost comparable outcomes, except on peak power output. Compared to able-bodied reference, cardiopulmonary fitness, hip flexion strength, and knee extension strength seemed to be considerably lower (<75%) in adolescents and young adults with CP (GMFCS level I and II). Proportions of participants with overweight and obesity were found to be comparable to reference, except for the larger waist circumference found in males. Almost all outcomes on lipid profile were found to be favourable with respect to norm values.

Although the approach to paediatric rehabilitation has evolved over the past decades, cardiopulmonary fitness results in the present study were comparable to those in studies performed 30 years ago.[12, 13, 15] This suggests that there is a need to change the approach or that there should be even more attention for physical fitness in young persons with CP. Adolescence and young adulthood is a critical phase in life with great influence on adult lifestyle, and therefore might be an important period of intervention. Previous research in children with CP has shown that exercise programmes focusing

on lower extremity muscle strength, cardiovascular fitness, or a combination leads to increases in cardiopulmonary fitness and muscle strength.[34, 35] In order to maintain a favourable physical fitness level, there is initial evidence for behavioural interventions to be of added value.[36] Further longitudinal studies on the effects of such interventions on health-related physical fitness are necessary.

Hip flexion and knee extension strength were considerably lower (<75%) in participants with CP compared to reference values. Mean hip abduction was 85% of reference. However, persons in the bilateral subgroup had significantly lower hip abduction strength than persons with unilateral CP. Therefore, hip abduction muscle strength should be a point of attention in persons with bilateral CP.

Comparison with reference has to be done with caution since values were only available for 16-years old, possibly leading to an overestimation of the percentage of reference values[29] since it is known that muscle strength is still developing at that age. However, no reference values for these three muscle groups were available for ages 16 to 24 years measured with the break testing method. The results from a previous study in adolescents with CP are difficult to compare because that study used a totally different method: electromyography while seated in an adjustable chair, strapped in a fixed position.[16]

Based on BMI, the number of participants in the categories 'overweight' and 'obesity' were comparable to reference. However, regarding waist circumference, 6 out of 25 males had a waist circumference indicating obesity, which is a propensity twice as high as reference. There were also 6 out of 25 females with a waist circumference indicating obesity. However, the propensity in the reference female population was comparable. Comparisons with reference values should be interpreted with caution since the reference population was somewhat older (age 30-39 years). Further research should compare persons with CP to sex- and age matched able-bodied controls. Anthropometric measures of the participants were on average found to be comparable to that of previous studies in adolescents and young adults with CP.[17, 18] A BMI indicating underweight was found in two persons with GMFCS level I and in one person with GMFCS level II. Three out of fifty is a higher propensity for underweight compared to reference. However, although the propensity was higher, it only considered three persons and therefore further research is necessary. BMI has to be interpreted with caution since BMI in persons with CP has been reported to be less valid than in able-bodied persons.[37, 38]

This is one of the first studies to assess lipid profiles in a group of high-functioning adolescents and young adults with CP. Our results indicate that, both at the group and individual levels, there is no indication for increased cardiovascular risk based on lipid profile for persons with GMFCS level I and II at this age. This is in line with a previous study in adolescents (9-16 years) with CP, in which it was concluded that arterial health was not different from that of a control group.[39] In a recent study of adults with bilateral CP (aged 25-45 years) lipid profile was found to be slightly less desirable compared

to the present study.[40] There is a limitation in power when studying subgroup differences in lipid profile when correcting for both age and gender in the analyses, since data of only 23 persons was available. Furthermore, larger amounts of data of females were missing, partly explained by a larger proportion of females who did not give consent for taking a blood sample. Therefore, our sample is limited to data of only 6 females. More research, especially longitudinal studies, on this important indicator for cardiovascular disease, is necessary. Furthermore, it would be interesting to study the relation between lipid profile and other health-related physical fitness measures.

A significant difference was found in age between our subgroups of persons with unilateral CP and bilateral CP. However, the difference in mean age of persons with unilateral CP and bilateral CP was only two years (mean ages of 19 years and 21 years old). This difference of two years is not very likely to have a big influence on physical fitness. Moreover, we corrected for age in our regression analyses. Although this is a limitation of our study, we believe that this difference in characteristics did not influence our conclusions.

The present results are limited to the description of health-related physical fitness of ambulatory adolescents and young adults with GMFCS level I and II. Further research in persons with GMFCS level III and IV is necessary. Furthermore, criteria for maximal exercise were not met by nine participants. However, since their GMFCS level, age and weight were comparable to the group that did meet the criteria, their exclusion is supposed to have minimally influenced the generalisability of the results. Skin fold thickness was measured on the left side of the body. However, regarding the asymmetry of topography, it could be possible that an involved side would not have the same anthropometric features as a non-impaired side.

Ambulatory adolescents and young adults with CP have impaired cardiopulmonary fitness and hip flexion and knee extension strength. Fitness outcomes in persons with bilateral CP were found to be lower compared to persons with unilateral CP. This phase in life is of great influence on adult lifestyle, and therefore would seem an important interventional period for intervening on physical fitness.

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Chapter 9

Physical strain of walking relates to activity level in adults with cerebral palsy

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ABSTRACT

Objective

To gain insight into underlying mechanisms of inactive lifestyles among adults with spastic bilateral CP with a focus on aerobic capacity, oxygen consumption and physical strain during walking at preferred walking speed, as well as fatigue.

Design

Cross sectional.

Setting

University hospital.

Participants

Thirty-six adults, aged 25-45 years, with spastic bilateral cerebral palsy, walking with (n=6) or without (n=30) walking aids.

Main outcome measures

Physical strain during walking was defined as oxygen uptake during walking, expressed as percentage of peak aerobic capacity. Participants with spastic bilateral CP walked their preferred walking speed while oxygen uptake was measured using a portable gas analyser. Peak aerobic capacity was measured during maximal cycle ergometry. An accelerometry-based Activity Monitor measured total daily walking time. Regression analyses were performed to assess the relation between aerobic capacity, oxygen uptake and physical strain of walking on the one hand and total daily walking time on the other hand.

Results

Neither aerobic capacity nor oxygen uptake during walking was related to total daily walking time (r^2=0.29, p=0.10 and r^2=0.27, p=0.16). Physical strain of walking at preferred walking speed was inversely related to total daily walking time (r^2=0.44, p<0.01).

Conclusion

Physical strain during walking is moderately related to total daily walking time, implying that people with high physical strain during walking at preferred walking speed are likely to walk less in daily life.

INTRODUCTION

Cerebral palsy (CP) affects 1.5 to 3.0 out of every 1000 live births and is the most common cause of physical disability in paediatric rehabilitation medicine.[1] Physical activity level (PAL) is low in persons with CP, regardless of age.[2-5] Studies in the general population show that low PAL may increase the risk for cardiovascular disease, diabetes and cancer[6, 7] and that it contributes to the decline of mobility-related activities.[8] Despite these detrimental effects, the working mechanisms of low PAL in persons with CP remain unclear. Knowledge of the underlying mechanisms of inactive lifestyles in persons with CP are prerequisite to improving interventions to increase PAL.

Although many determinants influence PAL, physical fitness and physiologic load receive the most attention. A review of the literature shows that persons with CP have low PAL, but that aerobic capacity is also affected.[9, 10] Low aerobic capacity may cause low PAL, while high levels of PAL may lead to improved fitness levels. Durstine et al.[11] described a circular process wherein aerobic capacity and PAL interact. However, a direct relationship between PAL and aerobic capacity, which would support this process, has not been identified in the small number of studies addressing this topic.[10, 12]

Another possible explanation for low PAL in persons with CP is their abnormal gait pattern, often leading to decreased walking efficiency and increased oxygen consumption of walking. Studies indicate that, at fixed walking speeds, oxygen consumption is up to three times higher in children with CP compared with able-bodied age mates,[13, 14] This indicates that walking in daily life is associated with a high oxygen consumption, presumably leading to lower daily walking duration or lower walking pace in daily life in order to reduce physical stress. However, results of studies on the relationship between oxygen consumption during walking and PAL in children with CP are conflicting.[12, 15]

Physical strain of walking is defined as the oxygen uptake of walking, expressed as a percentage of peak aerobic capacity. Because oxygen uptake of walking is high and aerobic capacity is low in persons with CP, physical strain during walking may be increased compared with able-bodied persons. Such a high physical strain could contribute to small metabolic reserves during walking in daily life in persons with CP.[13] High levels of physical strain can be regarded as a training stimulus, but Dallmeijer and Brehm hypothesised that this should rather be regarded as cause of physical inactivity.[13] Fatigue, a common problem in CP,[10, 16] is thought to play a role in this. Patients with high physical strain during walking could experience fatigue and may, as a consequence, walk less in daily life to conserve energy or prevent excessive fatigue.[12, 13, 17]

The purpose of this study was to gain insight into underlying mechanisms of inactive lifestyles among adults with spastic bilateral CP. We focused on aerobic capacity, oxygen consumption, and physical strain during walking at preferred walking speed, as well as fatigue. We hypothesised that

aerobic capacity, oxygen consumption during walking at preferred walking speed, and especially physical strain during walking at preferred walking speed inversely relate to total daily walking time. Furthermore, we hypothesised that fatigue plays an essential role in these relationships.

METHODS

Participants

This study is part of a larger study of functioning and physical fitness in adults with bilateral CP.[5] Eligible participants were recruited from 10 rehabilitation centres and rehabilitation departments from university hospitals and via the Association of Physically Disabled Persons and Their Parents.

Persons with CP were eligible for inclusion if they met each of the following criteria: 1) diagnosis of spastic bilateral CP; 2) Gross Motor Function Classification System[18] level I to III; and 3) aged 25 to 45 years. Individuals were excluded if they met any of the following criteria: 1) comorbidities impacting PAL; 2) contraindications to maximal ergometer testing, like hypertension or cardiovascular disease;[19] or 3) severe cognitive disorder or insufficient comprehension of the Dutch language precluding understanding of study instructions.

Although 52 participants were enrolled in this study, 16 had missing values for aerobic capacity or oxygen consumption of walking. These missing values were due to measurement problems or inability to perform the testing protocol due to motivational problems, coordination problems or recent injuries which were not regarded as contra indication on intake. Therefore, our sample consisted of 36 adults (23 males) which had a mean age of 36 ± 6 years. Twenty-one participants were diplegic and 15 were tetraplegic. Nine participants were classified at Gross Motor Function Classification System level I, 21 at level II, and 6 at level III. All participants provided written informed consent. The study was approved by the medical ethics committee of the Erasmus Medical Centre and local approval was granted by all participating centres.

Physical strain during walking

Participants walked their preferred walking speed in a laboratory setting for 3 minutes with (n=6) or without (n=30) walking aids. This was performed on a 12 meter trajectory, with smooth turns at the corners. Participants were asked to walk continuously and at a constant speed.

Oxygen uptake during walking (VO_{2walk}) was assessed by indirect calorimetry. Gas volume and concentrations were determined continuously using a valid[20] portable breath-by-breath gas analyser. This system was calibrated before each test using reference gases. VO_{2walk} at preferred walking speed was defined as the mean oxygen uptake during the last 30 seconds of walking in steady state,

expressed per kilogram of body mass. Steady state was defined as less than 10% variation in VO2 uptake or less than 5% variation in the respiratory exchange ratio. We divided the last 30 seconds of the walk test into two 15 second periods from which average values were calculated to check for steady state.

Peak oxygen uptake (VO_{2peak}) and heart rate (HR) were measured using a portable breath-by-breath gas analyser in combination with a HR belt[b], during progressive aerobic testing on an electronically braked cycle ergometer[c]. Additional to screening for contraindications by a physician, all participants completed the Physical Activity Readiness Questionnaire[21] to assure that there were no contraindications to perform this test. The test was preceded by a 3 minute warm-up with a resistance of 20W. During the test, resistance was increased every 2 minutes with a variable load, depending on the ability of the participant, and following the McMaster All-Out Progressive Continuous Protocol.[22] The target pedal rate was 60 rpm. The test was terminated when the participant voluntarily stopped due to exhaustion, or when the participant was unable to maintain the initial pedal rate. VO_{2peak} was defined as the highest mean oxygen uptake during 30 seconds of exercise (mL/kg/min). As objective criteria for maximal exercise, we used the peak HR of 95% or more of predicted HR (220 – age), or a respiratory exchange ratio greater than or equal to 1.1.[23] Physical strain during walking was defined as the oxygen uptake during walking (VO_{2walk}) at preferred speed as percentage of peak aerobic capacity (VO_{2peak}). All measurements were performed on the same day with approximately 1.5 hour of rest between the tests.

Total daily walking time

To measure total daily walking time, an Activity Monitor[d] (AM) was used to obtain long-term ambulatory monitoring of signals from body-fixed accelerometers. Participants wore the AM for 48 continuous hours on weekdays and were instructed to perform their ordinary activities. To avoid measurement bias, the AM instruments were fitted in the participants' own environments and the purpose of the AM measurement was explained to the participants after finishing the measurement.

The AM consisted of 4 accelerometers and a portable data recorder (15 × 9 × 4.5 cm). One accelerometer was attached to the skin of each thigh to detect anterior-posterior direction while standing, and two accelerometers were attached to the skin of the sternum: one to detect anterior-posterior direction, and one in longitudinal direction to detect up and downward movements in an upright position. Measurements were analysed using Vitagraph Software[e]. A detailed description of the activity detection procedure has been described elsewhere.[24] The AM system has been validated in the quantification of mobility-related activities.[24] For the present study, we calculated the duration of walking as percentage of a 24-hour period.

Severity of fatigue

Severity of fatigue was assessed using the Fatigue Severity Scale, a self-reported nine-item questionnaire.[25] 'Severe fatigue' was defined as a score of more than two standard deviations (SD) above the mean for healthy individuals (score ≥ 5.1) and 'fatigue' as a score of 1 SD above the mean for healthy individuals (score ≥ 4.0).[26]

Statistical analyses

All data are presented as means ± SD. Three multiple linear regression analyses were performed to study the relationships between total daily walking time as dependent variable with three independent variables; VO_{2peak}, VO_{2walk} at preferred walking speed, or physical strain during walking at preferred walking speed. All regression analyses were corrected for sex, age and classification on the Gross Motor Function Classification System, as these variables confounded the relationships (change in ß of more than 10%). These confounders were added to the model in a second regression block by the Enter method. The uncorrected regression analyses are showed to demonstrate the magnitude of confounding effects. When a significant relationship was found in an analysis corrected for confounders, an additional, confounder corrected, multiple linear regression analysis was performed with this independent variable to study its relationship with fatigue as dependent variable. The alpha level was set at 0.05. All analyses were performed using PASW statistics, version 17.0.

RESULTS

Descriptive results

Descriptive results for all participants and stratified per GMFCS level are given in Table 1. All participants reached steady state during walking at preferred walking speed: one person did not meet the criterion for VO2 uptake, but did meet the criterion for RER. All other participants have met both criteria for steady state. The mean variation during the last 30 seconds of the walk test was 5.1±3.2% for oxygen uptake and 2.2±1.4% for respiratory exchange ratio. Based on heart rate or respiratory exchange ratio, all participants reached maximal exercise performance during the progressive aerobic test. Participants had a mean walking duration of 5.8±3.0% of each 24-hour period. The mean score on the Fatigue Severity Scale was 4.1±1.3. Based on our study criteria, 18% of all participants were fatigued (score≥4.0 & <5.1) and another 30% were severely fatigued (score ≥5.1).

Regression analyses

Results of the regression analysis are shown in Table 2. No significant relationships were found between total daily walking time and VO_{2peak} ($p=0.10$) or VO_{2walk} ($p=0.16$). A significant inverse relationship was found between total daily walking time and physical strain during walking at preferred walking speed ($p<0.01$). This relationship is shown in Figure 1. Table 3 shows that no relations were found between

Table 1. Results of walk test, cycling test, PAL, and fatigue for all participants and stratified per GMFCS level

	All	GMFCS* I	GMFCS* II	GMFCS* III
	n=36	n=9	n=21	N=6
Walk test				
Walking speed (km/h)	2.8 ± 0.6	3.1 ± 0.4	2.8 ± 0.6	2.4 ± 0.5
$VO2_{walk}$ (ml/kg/min)	15.0 ± 4.4	11.6 ± 3.2	16.7 ± 3.9	15.7 ± 4.9
Physical strain (% of $VO2_{peak}$)	52 ± 17	37 ± 10	58 ±17	54 ± 14
Maximum RER	0.86 ± 0.08	0.83 ± 0.08	0.88 ± 0.07	0.86 ± 0.10
Cycling test				
Maximum HR (beats/min)	175 ± 18	182 ± 13	174 ± 19	171 ± 22
VO2peak (ml/kg/min)	30.3 ± 6.7	32.3 ± 7.4	29.6 ± 6.2	30.0 ± 7.7
Maximum RER	1.19 ± 0.12	1.21 ± 0.10	1.19 ± 0.13	1.17 ± 0.12
Physical activity level				
Total daily walking time (% of 24h period)	5.8 ± 3.0	7.4 ± 1.9	5.6 ± 3.0	4.3 ± 3.7
Fatigue				
FSS score	4.1 ± 1.3	4.2 ± 1.3	3.8 ± 1.3	4.9 ± 1.0

* = Gross Motor Classification System

Table 2. Linear regression analyses with total daily walking time as dependent variable and with VO_{2peak} (ml/kg/min), VO_{2walk}, and physical strain as independent variables. All results are both uncorrected and corrected for age, sex and GMFCS level. GMFCS level I was set as the reference dummy level

Variables	ß*	95% confidence interval for ß		p-value	R^2
		lower bound	upper bound		
VO_{2peak} uncorrected	0.16	-0.18	0.49	0.37	0.02
VO_{2peak} corrected	0.31	-0.04	0.66	0.10	0.29
Age	0.40	0.05	0.75	0.03	
Sex	0.21	-0.12	0.54	0.23	
GMFCS II †	-0.30	-0.67	0.07	0.12	
GMFCS III	-0.56	-0.95	-0.17	**<0.01**	
VO_{2walk} uncorrected	-0.38	-0.70	-0.06	**0.02**	0.14
VO_{2walk} corrected	-0.27	-0.64	0.10	0.16	0.27
Age	0.28	-0.05	0.61	0.11	
Sex	0.02	-0.28	0.32	0.90	
GMFCS II	-0.21	-0.64	0.21	0.34	
GMFCS III	-0.44	-0.86	-0.02	0.05	
Physical strain uncorrected	-0.48	-0.78	-0.19	**<0.01**	0.23
Physical strain corrected	-0.57	-0.89	-0.25	**<0.01**	0.44
Age	0.43	0.13	0.73	0.01	
Sex	0.09	-0.17	0.35	0.51	
GMFCS II	-0.03	-0.42	0.36	0.88	
GMFCS III	-0.40	-0.76	-0.05	0.04	

* = Standardised Beta coefficients.

† = Gross Motor Classification System

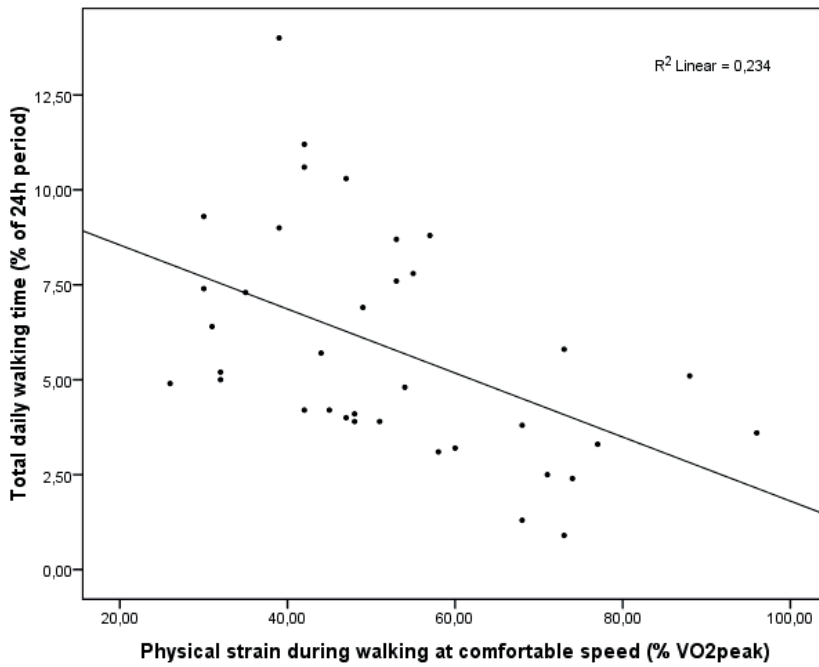

Figure 1. The relation between total daily walking time and physical strain during walking at comfortable walking speed.

Table 3. Linear regression analyses with severity of fatigue as dependent variable and physical strain during walking and total daily walking time as independent variables. All results are both uncorrected and corrected for age, sex and GMFCS level. GMFCS level I was set as the reference dummy level

Variables	ß*	95% confidence interval for ß		p-value	R^2
		lower bound	upper bound		
Physical strain uncorrected	0.11	-0.24	0.46	0.55	0.01
Physical strain corrected	0.22	-0.20	0.64	0.32	0.18
Age	0.20	-0.17	0.57	0.30	
Sex	-0.08	-0.45	0.29	0.67	
GMFCS II †	-0.36	-0.83	0.11	0.15	
GMFCS III	0.03	-0.47	0.53	0.91	
Total daily walking time uncorrected	0.02	-0,29	0,33	0.90	0.00
Total daily walking time corrected	-0.04	-0,43	0,36	0.85	0.14
Age	0.26	-0,13	0,65	0.21	
Sex	-0.07	-0,43	0,29	0.71	
GMFCS II	-0.25	-0,68	0,19	0.28	
GMFCS III	0.06	-0,41	0,52	0.82	

* = Standardised Beta coefficients.

† = Gross Motor Classification System

the severity of fatigue and physical strain during walking (p=0.32) or between the severity of fatigue and total daily walking time (p=0.85).

DISCUSSION

The purpose of the current study was to gain insight into underlying mechanisms of inactive lifestyles among adults with spastic bilateral CP with a focus on aerobic capacity, oxygen consumption, and physical strain during walking at preferred walking speed, as well as fatigue. We did not find relationships between VO_{2peak} or VO_{2walk} and total daily walking time. However, physical strain during walking at preferred walking speed was related to total daily walking time.

In this relatively young sample of adults with spastic bilateral CP, mean aerobic capacity was 30.3±6.7 mL/kg/min. Based on participant characteristics, we calculated norm-values for aerobic capacity, using the formula of Jones et al.,[27] to be 38.6±9.7 mL/kg/min. The measured aerobic capacity was 21% lower than these norm values (p<0.01), which is consistent with previous reports of decreased aerobic capacity in persons with CP.[9, 10]

The preferred walking speed of the participants was 2.8±0.6 km/h, which is 32% lower than the preferred walking speed of 3.7±0.8 km/h of able-bodied persons of similar age.[28] This lower walking speed affects oxygen consumption[28] and consequently physical strain. Therefore, we calculated physical strain during preferred walking speed instead of fixed walking speeds in the current study. Despite differences in GMFCS distribution and preferred walking speed, our results of physical strain at preferred walking speed of 52 ± 17% were consistent with findings of a study with children with spastic CP (52 ± 8%).[13] These levels of physical strain are considerably higher compared to that experienced by able-bodied adults walking at preferred walking speed (27 ± 6%).[28] The present results add to the evidence that persons with CP use a large proportion of their metabolic reserve for walking compared with able-bodied persons.[13]

Total daily walking time was 5.8 ± 3.0% over a 24-hour period, corresponding with 1 hour and 24 minutes of walking each day. This low PAL is consistent with findings among diplegic children[4] and adolescents[2, 3] who have lower PALs compared with able-bodied age-mates.

The lack of a significant relationship between total daily walking time and VO_{2peak} is in accordance with previous studies of adults[10] and children[12] with CP that did not find a relationship between VO_{2peak} and physical activity level. A significant relationship was found between total daily walking time and VO_{2walk} at preferred walking speed in the uncorrected regression model. However, this relationship lost significance when corrected for confounding variables. Physical strain was inversely related to total

daily walking time. Two previous studies investigated the relationship between VO_{2walk} and PAL in children with CP.[12, 15] Maltais et al. found that PAL and VO_{2walk} inversely correlated at 2 of 3 fixed walking speeds.[12] Furthermore, physical strain during walking correlated more strongly with PAL than VO_{2walk} at all 3 fixed walking speeds.[12] In children with CP, Bell and Davies found no relationship between PAL and VO_{2walk} at preferred walking speed.[15] In contrast to our study, which used accelerometry to measure total daily walking time, these two previous studies used the doubly labelled water technique to assess PAL.[29] While the outcome measure of these studies are not the same as that of the current study, the studies are comparable as walking is the main component of PAL in persons with CP.[5] These previously published results and the current study both suggest that, compared to VO_{2walk}, physical strain is more strongly related to PAL in persons with CP. This indicates that persons with CP with a high physical strain during walking are likely to walk less than persons with CP with a low physical strain during walking. Whether high physical strain during walking is caused by low PAL or vice versa needs to be confirmed in longitudinal research.

We found that physical strain is related to total daily walking time. As aerobic capacity is incorporated in physical strain, it seems likely that aerobic capacity is indirectly related to total daily walking time, despite the lack of statistical significance for a direct relationship in our study. Therefore, we support the recommendation of Dallmeijer and Brehm[13] that the practical implementation is that health professionals should not only focus on treatments to improve the efficiency of walking but should also consider training interventions to improve the maximal aerobic capacity to lower physical strain of walking. Although longitudinal research is required to confirm these cross sectional associations; we assume that decreasing physical strain has possible positive effects on total daily walking time.

It is speculated that persons with high physical strain during walking are less active in daily life to conserve energy or prevent fatigue.[12, 17] Fatigue was a serious problem in our study sample: nearly half of the participants were fatigued. However, no significant relationship was found between physical strain during walking at preferred walking speed and severity of fatigue. This means that adults with CP with a high level of physical strain during walking were not more fatigued compared to those with low levels of physical strain during walking. Furthermore, we did not find a relationship between level of fatigue and total daily walking time, which indicates that persons with high PALs do not experience more fatigue than persons with low PALs. Despite the high level of fatigue demonstrated, these results suggest that participants with high levels of physical strain during walking adapt their PAL downwards to reduce fatigue levels. In interpreting these results, one should consider that the Fatigue Severity Scale measures severity of fatigue in general and not fatigue that occurs in association with walking. Bearing in mind that other factors can also influence self reported fatigue, future studies should consider determining fatigue immediately after walking.

Study limitations

The measurement to determine VO_{2walk} was performed for only three minutes due to the large number of other measurements required for the study. Three minutes is a short timeframe to achieve steady state in oxygen uptake. Nevertheless, all participants reached steady state.

We measured the duration of walking over two days, but three to five days of monitoring may be necessary to characterize habitual PAL.[30] However, the AM used could not measure beyond 48 hours. Nevertheless, White et al. concluded that a 24-hour measurement with the applied AM was an adequate duration for reliable recording of activities.[31] Furthermore, this method has been applied successfully in studies focusing on activity levels in persons with CP.[5, 32]

The size and wires of the AM may have impeded activities in daily life. When asked, participants confirmed that they were able to perform their regular activities, so influence of the measurement equipment itself is considered to be little. This is supported by a study of Bussmann et al., which concluded that wearing the applied AM did not systematically influence the amount of daily manual wheelchair propulsion in a population with spinal cord injury.[33] However, such a study has not been performed in ambulatory populations.

Finally, we may have overestimated everyday PAL because of selection bias. Adults with CP who are interested in physical fitness (and may therefore have a higher baseline PAL) may have been more likely to participate.

Conclusions

Physical strain during walking is increased among adults with spastic bilateral CP. Furthermore, physical strain during walking is moderately related to total daily walking time, implying that people with high physical strain during walking at preferred walking speed are likely to walk less in daily life.

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Chapter 7

Focus on fatigue in adolescents and young adults with spastic cerebral palsy

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ABSTRACT

Objective

To estimate the prevalence of fatigue in adolescents and young adults with spastic cerebral palsy (CP), to explore subgroups at risk for fatigue and to explore the relations between fatigue and the level of daily physical activity and cardiopulmonary fitness.

Setting

University hospital.

Subjects

Adolescents and young adults with spastic CP, GMFCS level I-III, aged 16-24 years.

Methods

Fatigue (Fatigue Severity Scale) and self-reported daily physical activity (Physical Activity Scale for Individuals with Physical Disabilities) were assessed in 56 participants using questionnaires. Daily physical activity was also objectively measured with accelerometry (Vitamove system) during 72 hours. Progressive maximal aerobic cycle tests determined cardiopulmonary fitness.

Results

The average score on the Fatigue Severity Scale was 3.7 (SD 1.4). Forty percent of participants was fatigued, including 12,5% severely fatigued. Participants with bilateral CP (FSS=4.2 (SD 1.4)) are significantly ($p<0.01$) more fatigued than participants with unilateral CP (FSS=3.1 (SD 1.3)). Daily physical activity and cardiopulmonary fitness were both low; nevertheless this was not significantly related to fatigue.

Conclusions

The results indicate that fatigue is already present at a relatively young age in persons with CP. Subtype of CP is a determinant of fatigue. We did not find evidence for a physical origin for the fatigue.

INTRODUCTION

Cerebral palsy (CP) is a permanent disorder in the development of movement and posture, causing activity limitations, that is attributed to non-progressive disturbances that occurred in the developing foetal or infant brain.[1] The prevalence of CP is high, 1.5 to 3 per 1000 live births and it is the most common physical disability in paediatric rehabilitation medicine.[2] The most frequently occurring type of CP, the spastic form, is characterised by velocity-dependent resistance to passive stretching.[3]

In clinical practice, fatigue is a frequently reported symptom in children and adults with CP. Nevertheless, only few studies, and merely in adults, have focused on the magnitude of the problem in CP. One study indicated that 61% of the adults with bilateral CP were fatigued and 41% was severely fatigued.[4] Another study in adults with uni- and bilateral CP reported that 30% was substantially fatigued.[5] Thus at adult age; the prevalence of fatigue is higher than in the general population, of which 18% is fatigued.[4, 6, 7] Research on fatigue in children with CP is scarce, but it suggests that fatigue has a great impact on daily functioning.[8] Because of these high levels of fatigue in adults and children with CP,[4, 5, 8, 9] fatigue is likely to be present in adolescents and young adults with CP. However, systematic assessment of fatigue in adolescents or young adults with CP has, to our knowledge, not been performed. In addition, literature hardly addressed key factors to prevent or decrease fatigue in persons with CP.

Fatigue is a multifactorial symptom.[4] It may be hypothesised that fatigue in CP is related to personal characteristics (such as age and gender) and CP-related characteristics (such as level of gross motor function[10] and subtype of CP (unilateral or bilateral)). In the present study we focus on additional physical factors that may be related to fatigue, such as level of daily physical activity (PA) and cardiopulmonary fitness. Durstine et al. described a vicious circle of deconditioning[11] which hypothesised that fatigue, low levels of daily PA and low cardiopulmonary fitness influence each other. It is known that both children and adults with CP have decreased levels of objectively measured daily PA[12-15] and cardiopulmonary fitness[16-19] compared with able-bodied age mates. Cardiopulmonary fitness is known to be modifiable from a rehabilitation perspective[20] and studies on the effectiveness of improving daily PA with lifestyle interventions are ongoing.[21-23] However, previous studies found no evidence for the cycle of deconditioning in adults with CP,[5, 9, 16, 24] whereas no studies on these relationships are available for adolescents and young adults with CP. Knowledge on correlates of fatigue in CP may yield information on specific subgroups at risk and it provide starting points for optimising treatment. A recent study suggested that exercise therapy lowers fatigue in adults with CP.[25] Also in young adulthood, lifestyle interventions are expected to be appropriate to prepare for a healthy future. At this age, persons adapt to major changes in life occurring in their transition to adulthood and develop their adult lifestyle.[26, 27]

The aim of the current study was to estimate the prevalence of (severe) fatigue in adolescents and young adults with spastic CP. Furthermore, we investigated which subgroups are at increased risk for fatigue. Finally, we explored relations of fatigue with level of daily PA and cardiopulmonary fitness, factors that are amenable to change.

METHODS

Participants

Baseline data of the LEARN 2 MOVE 16-24 research project[21] were used for the current study. Eligible participants were recruited from 6 rehabilitation centres and rehabilitation departments from university hospitals in West-Central Netherlands and by the Association of Physically Disabled Persons and Their Parents (BOSK). Persons with CP were included when they were 16-24 years old, had a spastic type of CP and were classified in GMFCS level I (walks without restrictions) to III (walks with adaptive equipment assistance).[10] Exclusion criteria were: disorders other than CP influencing the level of daily PA, contra-indications for (maximal) exercise, severe cognitive disorders or insufficient comprehension of the Dutch language that precluded understanding the purpose of the project and its testing methods. An information letter and invitation to participate were sent to eligible participants. A reminder was sent 4 weeks later to non-responders. All participants provided written informed consent. The study was approved by the medical ethics committee of the Erasmus Medical Centre and local approval was granted by all participating centres.

Fatigue

Fatigue was measured with the Dutch version of the Fatigue Severity Scale (FSS).[28, 29] The FSS is a nine-item, self-administered questionnaire with scores ranging from 1 (strongly disagree) to 7 (strongly agree). The mean score of the nine items range from 1 (no signs of fatigue) to 7 (most disabling fatigue). Fatigue is defined as a FSS score more than 1 standard deviation (SD) above the mean score in Dutch healthy individuals (FSS≥4.0) and severe fatigue as a score of at least 2 SD above the mean score in Dutch healthy individuals (FSS≥5.1).[29] Internal consistency, reliability, validity and sensitivity of the FSS have been established in several patient groups.[28, 29]

Correlates of fatigue

Height was measured in standing position. Body mass was measured while standing on an electronic scale. Body Mass Index (BMI) (kg/m^2) was calculated from height and body mass and used in the analyses. Age, gender and CP subtype (unilateral or bilateral) were obtained from medical records. GMFCS level[10] was obtained from the baseline measurement by the assessor.

Daily physical activity

To objectively measure the level of daily PA, the Vitamove (VM) system (2M Engineering, Veldhoven, The Netherlands) was applied. This system consists of 3 recorders (trunk and thighs) for ambulant participants. The non-ambulant participants were able to walk with or without walking aids, but use a wheelchair in daily life for long distances (GMFCS level II/III). For these non-ambulant persons, we used 5 recorders (trunk, thighs and wrists) to measure their level of daily PA. The system is based on body fixed accelerometers which detects the acceleration of the trunk, thighs and wrists. The VM system is valid to quantify mobility-associated activities and to detect inter-group differences in levels of daily PA.[30, 31] Participants wore the system for 72 hours on randomly selected, consecutive, weekdays. Measurements were analysed using Vitascore software (Vitascore BV, Gemert, The Netherlands). A detailed description of the activity detection procedure has been given elsewhere.[30] Analysis yielded the duration of dynamic activities (composite measure consisting of walking, including climbing stairs and running; cycling; wheelchair propulsion, including hand cycling; and general noncyclical movement) and was expressed as a percentage of a 24-hour period. Due to system failure or incorrect use of the VitaMove system by some participants not all PA measurements had a duration of 72-hours. Therefore, measurements were analysed when they covered at least a 24 hour period, which was not achieved by eight participants. Of the remaining participants (n=48) 6 had at least a 24-hour measurement, 24 had a 48-hour measurement and 18 had a 72-hour measurement.

To determine self-reported PA, the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD)[32] was administered. This questionnaire consists of 12 items concerning leisure time, household activities, and work-related physical activities. We used the Dutch version of the PASIPD, which integrates lawn work and gardening into 1 item about gardening.[33] The total score of the PASIPD is created by multiplying the average hours per day for each item by a metabolic equivalent (MET) value associated with the intensity of the activity. The test-retest reliability of the PASIPD is good and the criterion validity is comparable with well-established, self-report PA questionnaires from the general population.[33]

Cardiopulmonary fitness

All participants were able to cycle, therefore aerobic capacity was measured using a maximal ramp protocol on a cycle ergometer (Jaeger ER800 and Jaeger ER800SH, Jaeger Toennies, Breda, The Netherlands). The test started with a 3-minute warm-up without resistance. The resistance was increased every 12 seconds during the test, depending on GMFCS level and gender of the participant. The target pedal rate during testing was 60-70 rpm. The test finished when the participant stopped due to exhaustion or when the participant was unable to maintain the initial pedal/crank rate. Gas exchange and heart rate (HR) was measured continuously during the test, using oximetry with different, but comparable breath by breath analysing systems (Oxycon Pro, ViaSys Healthcare, Houten, The Netherlands; Quark CPET system, Cosmed, Rome, Italy). These systems were calibrated prior to

each measurement with reference gases of a known mixture. Aerobic capacity was defined as the highest mean oxygen uptake during 30 seconds of exercise (VO2peak in L/min). Subjective strain was measured immediately after the final stage by the Borg Scale for Rating of Perceived Exercise.[34] Additional to screening by a rehabilitation physician, contra-indications for PA were assessed prior to the test by the Physical Activity Readiness Questionnaire (PARQ).[35] Forty-four persons met the objective criteria for maximal exercise; a peak heart rate of at least 90% of the predicted maximum heart rate of 194 beats per minute[36] or a respiratory exchange ratio greater than or equal to 1.1.[37] For these participants levels of aerobic capacity were compared with healthy norm-values using the formula of Jones et al, based on gender, height, age and weight.[38] Persons who performed a valid maximal exercise test did not differ from those excluded on this criterion (n=12) for age, gender, CP subtype, GMFCS-level and BMI ($p>0.05$), nor for mean FSS-scores (3.5 and 4.2 respectively, $p=0.14$).

Statistics

Descriptive statistics were applied to describe level of fatigue, proportion of (severely) fatigued participants, personal and CP specific characteristics, daily PA and cardiopulmonary fitness. Since data were merely normally distributed, we applied parametric statistical tests. Persons who performed a valid maximal exercise test (n=44) did not differ from those excluded on this criterion, using independent sample t-test (age), Chi-square test (gender, CP subtype, GMFCS level) or Mann-Whitney U test (BMI). VO2peak was compared with healthy norm values using paired samples T-tests.[38] Univariate linear regression analyses were applied to evaluate whether fatigue is related with personal or CP related characteristics or with the modifiable factors, daily PA or cardiopulmonary fitness. A multivariate linear regression model was performed to correct for age, gender, GMFCS-level, BMI and CP subtype, as these variables confounded the relations between fatigue and modifiable factors (change of more than 10% in β). GMFCS levels were included in the analyses as dichotome variables. Due to the low number of participants classified in GMFCS level III, participants with GMFCS level II and III were combined into one category. If a significant relation between fatigue and a modifiable factor is found, subgroup analyses were performed. Independent sample t-tests were used to test the difference in level of fatigue; Chi square-tests for differences in proportion of (severely) fatigued participants. For the analyses SPSS (Statistical Package of Social Sciences) version 17.0 was used. A P value of ≤ 0.05 was considered as significant.

RESULTS

Participants

Fifty-six adolescents and young adults, with a mean age of 20 (SD 2.8) years were included in this study. Five of them used a wheelchair in daily life for long distances, but were able to walk with or without walking aids (GMFCS level II/III). Characteristics of the participants are described in Table 1.

Table 1. Personal and CP-related characteristics, daily physical activity and cardiopulmonary fitness.

		Total *(n = 56)*
Personal and CP related factors	Age, years (SD)	20.0 (± 2.8)
	Gender, M/F	27/29
	GMFCS level, I/II/III	31/21/4
	BMI, kg/m^2 (SD)	23.3 (± 4.8)
	CP subtype, uni-/bilateral	29/26[¶]
Physical activity and cardiopulmonary fitness	Dynamic activities, % of a 24h period (SD)	8.5 (± 3.0) *(n=48)*[‖]
	PASIPD, MET hours/day (SD)[‡]	12.8 (± 8.3) *(n=53)*[§]
	VO2peak, L/min(SD)	2.4 (± 0.8) *(n=44)*[#]
	VO2peak, ml/min/kg (SD)	34.9 (± 9.1) *(n=44)*[#]

[‡] Percentage time per 24-hour of walking, cycling, wheelchair propulsion and general noncyclical movement.
[§]The PASIPD was not performed by 3 participants.
[‖]Eight participants did not have a measurement of 24-hour or longer.
[¶]Of one participant data about CP subtype was missing.
[#]Twelve participants did not reach the criteria for maximal exercise testing
CP = cerebral palsy; GMFCS = Gross Motor Function Classification System; BMI = Body Mass Index; SD = standard deviation; PASIPD = Physical Activity Scale for Individuals with Physical Disabilities

Table 2. Fatigue and comparison between unilateral and bilateral CP.

	Total (n = 56)[†]	Unilateral CP (n = 29)[†]	Bilateral CP (n = 26)[†]	P[‡]
Fatigue				
FSS score, mean(SD)	3.7 (± 1.4)	3.1 (± 1.3)	4.2 (± 1.4)	<0.01[*]
FSS ≥ 4.0, n(%)	22 (39.3)	10 (34.4)	12 (46.2)	0.38
FSS ≥ 5.1, n(%)	7 (12.5)	1 (3.4)	6 (23.1)	0.03[*]

[*] Significant (p ≤ 0.05) difference between unilateral and bilateral CP group.
[†]Of one participant data about CP subtype was missing.
[‡]P-values of independent sample t-tests (FSS score) or Chi square-test (proportion of fatigue) for differences between the unilateral and bilateral CP group are presented.
CP = cerebral palsy; FSS = fatigue severity scale; SD = standard deviation.

Fatigue

Fatigue scores of the total sample are shown in Table 2. Mean FSS score was 3.7 (SD 1.4 range 1.1 to 6.8). Of all participants 39.3% was fatigued, including 12.5% severely fatigued.

Correlates of fatigue

Table 3 shows the relations between level of fatigue and correlates. A significant relation (p<0.01) was found between fatigue and CP subtype, persons with bilateral CP (FSS=4.2 (SD 1.4)) are more

Table 3. Correlates of fatigue

	Correlates	β uncorrected	95% Confidence Interval for β		P	β corrected*	95% Confidence Interval for β		P
			Lower Bound	*Upper Bound*			*Lower Bound*	*Upper bound*	
Personal and CP related factors	**Age**	0.12	-0.14	0.39	0.37				
	Gender‡	-0.20	-0.46	0.06	0.13				
	GMFCS-level‡	0.23	-0.03	0.49	***0.08§***				
	BMI	0.00	-0.22	0.22	0.99				
	CP subtype‡	0.39	0.14	0.64	**<0.01†**				
Physical activity and cardiopulmonary fitness	**% dynamic activities#**	0.03	-0.26	0.31	0.86	0.08	-0.19	0.35	0.55
	PASIPD	-0.07	-0.35	0.20	0.62	0.01	-0.24	0.26	0.92
	VO2peak	-0.29	-0.58	0.00	***0.06§***	-0.27	-0.59	0.04	***0.10§***

*Correlates are corrected for age, gender, GMFCS-level, BMI and CP subtype, as these variables confounded the relations (change of more than 10% in β)

†Significant ($p \leq 0.05$) relation between correlate and fatigue

‡ Categorical correlates were coded in the following manner: gender: female=0, male=1; GMFCS-level: GMFCS-level 1 = 0, GMFCS-level 2 and 3 = 1; CP subtype: unilateral=0, bilateral=1;

§Trend ($p \leq 0.10$) for a relation between correlate and fatigue

#Percentage time per 24-hour of dynamic activities.

CP = cerebral palsy; GMFCS = Gross Motor Function Classification System; PASIPD = Physical Activity Scale for Individuals with Physical Disabilities; BMI = Body Mass Index;

fatigued in comparison with unilaterally affected persons (FSS=3.1 (SD 1.3)). The proportion of severely fatigued participants was also higher in the bilateral CP group (23.1% bilateral against 3.4% unilateral); (p=0.03), see Table 2. The univariate regression analysis showed a trend between fatigue and GMFCS-level (p=0.08). Age, gender and BMI did not relate significantly with fatigue.

Objectively measured daily PA level was 8.5% (SD 3.0%), which represents 123 minutes of PA per day (Table 1). Mean PASIPD score of the 53 participants who completed the PASIPD questionnaire was 12.8 (SD 8.3) MET hours/day. Objectively or self-reported daily PA were not related to fatigue (Table 3).

The mean VO2peak score of the 44 participants who met the objective criteria for maximal exercise was 2.4 (SD 0.8) L/min, which is 15% lower (p<0.01) than calculated healthy norm-values for aerobic capacity.[38] Mean maximum load was 173 (±69) W. The mean score on the Borg-scale was 6.5 (heavy to very heavy exercise). Other aspects of cardiopulmonary fitness are described elsewhere.[39] The regression analysis of fatigue and cardiopulmonary fitness showed a trend (p=0.06) (Table 3), also after correction for confounders (p=0.10).

DISCUSSION

Fatigue

On average, adolescents and young adults with CP were more fatigued (FSS=3.6) than the healthy population (FSS=3.0).[6, 29] The proportion of fatigued and severely fatigued participants with CP was twice as high in comparison with healthy persons (proportion fatigued: respectively 39% versus 18%. Proportion severely fatigued: respectively 13% versus 5%).[6, 29] Although reference values for fatigue are based on an adult population, we think these might be appropriately applied as a reference for our young study sample, since age and fatigue seemed not related, according to Valko et al.[6] and the present study. The high levels of fatigue in the present sample indicate that fatigue is already a common problem at a young age in persons with CP. Therefore, rehabilitation programmes should focus more on fatigue at this age.

Subgroups at increased risk

Participants with bilateral CP were more fatigued and therefore seem to be a subgroup at risk for higher levels of fatigue. Participants with GMFCS-level II or III seem to be more fatigued than participants with GMFCS-level I, although this relation was not significant. BMI, age and gender were not significantly related to fatigue. This indicates that level of fatigue is more affected by CP-related characteristics than personal characteristics. The mean level of fatigue of the bilaterally affected persons in the sample was comparable with a previous study among adults with bilateral CP and higher than in the healthy population.[4] The mean level of fatigue of the unilaterally affected persons was comparable with the

healthy population.[6, 29] Nevertheless the percentage of fatigued participants in the subsample with unilateral CP was twice as high as in the healthy population.[6] A possible explanation for this difference in fatigue between persons with uni- and bilateral CP might be a difference in physical strain. Persons with bilateral CP are likely to have a higher strain during walking and could therefore experience more fatigue.[40]

Fatigue related to daily PA or cardiopulmonary fitness

From a rehabilitation perspective, focusing on daily PA and cardiopulmonary fitness is of interest. Similar to studies in adults with CP, the present younger sample showed low levels of daily PA.[16, 41] The lack of a relation between daily PA and fatigue is also in agreement with studies in adults with CP.[5, 9, 16] Due to high levels of physical strain during walking in persons with CP, they possibly lower their levels of daily PA in order to conserve energy or to prevent fatigue.[40] One could hypothesise that this compensation strategy might explain the absence of the relation between daily PA and fatigue in persons with CP. The low levels of aerobic capacity in comparison to healthy norm values are in agreement with previous research in children, adolescents and adults with spastic CP.[16, 18, 19] Although we found a trend that persons with a higher aerobic capacity were less fatigued; we did not find significant evidence for such a physical origin of fatigue. In contrast, Opheim et al. found a relation between deterioration in walking function and fatigue in adults with CP and hypothesised that the fatigue in adults with CP was of physical origin.[9] Fatigue is a multifactorial problem. Beside the known factors also other factors may play a role. For example, persons with CP are at an increased risk for sleep disorders.[42] Possibly these sleep disorders cause fatigue. Also other factors like behavioural factors, stress, depression, pain or medication may have a stronger influence on fatigue than cardiopulmonary fitness itself. Therefore, rehabilitation programmes which aim to lower the levels of fatigue should presumably incorporate a multifactorial approach.

Study limitations

A limitation of the current study is the use of questionnaires to determine fatigue. Recall-bias may have occurred due to questionnaire use. Nevertheless, no alternatives are available to determine experienced fatigue. We possibly have overestimated daily PA and cardiopulmonary fitness because of selection bias. Persons who are paying more attention to cardiopulmonary fitness and daily PA (and therefore possibly having higher levels of cardiopulmonary fitness and daily PA) may have been more likely to participate in the study. Nevertheless, levels of daily PA and cardiopulmonary fitness were still subnormal. Due to exclusion of participants performing sub-maximal exercise during aerobic capacity measurements, the remaining participants possibly give an overestimation of the level of cardiopulmonary fitness. Since personal or CP related characteristics and FSS-scores of the excluded group were comparable with those included, the included sample does not seem to be a selection. Thus we assume the results to be generalisable to persons with CP of this age. Finally, we have to take in consideration that the study has a cross-sectional design, so we cannot conclude about the course

in time and cause-effect relations of fatigue with other factors. A longitudinal study is necessary to gain more insight in these cause-effect relations.

Conclusions

Fatigue is a common problem in adolescents and young adults with spastic CP. Almost 40% experienced fatigue. Especially participants with bilateral CP are at risk for high levels of fatigue. Besides high levels of fatigue, levels of cardiopulmonary fitness and daily PA were low in adolescents and young adults with spastic CP. Nevertheless, cross-sectional relations between fatigue and cardiopulmonary fitness or daily PA were not significant. According to these results, a rehabilitation programme to decrease fatigue is important in adolescents and young adults with CP and should presumably incorporate a multifactorial approach.

Clinical messages:

- 40% of the adolescents and young adults with spastic CP were fatigued, including 12,5% severely fatigued.
- Persons with bilateral CP were more fatigued than persons with unilateral CP.
- A rehabilitation programme to decrease fatigue should presumably incorporate a multifactorial approach.

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chapter 8

Can a lifestyle intervention improve physical behaviour among adolescents and young adults with spastic cerebral palsy? A randomised controlled trial

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ABSTRACT

Aim

Optimal physical behaviour is important, as physical inactivity contributes to functional deterioration and reduced social participation. Nevertheless, research showed that persons with cerebral palsy (CP) have low physical activity levels. The objective is to evaluate the effectiveness of a lifestyle intervention on physical behaviour.

Method

Fifty-seven persons (36 completed the total study) with spastic cerebral palsy (age range 16-25 years; 27 males, 30 females), classified as Gross Motor Function Classification System levels I-IV were included in this randomised controlled trial. Twenty-nine participants had a unilateral CP and 27 had a bilateral CP. A six-month lifestyle intervention consisting of fitness training and counselling on physical behaviour and sports participation was evaluated. Physical behaviour was objectively measured using ambulatory activity monitors. Self-reported physical activity was determined using the Physical Activity Scale for Individuals with Physical Disabilities.

Results

The intervention did not affect the objectively measured physical activity during the intervention (Beta=0.34, CI=-1.70 to 2.37) or at follow-up (Beta=0.30, CI=-1.99 to 2.59). Self-reported physical activity was positively affected during the intervention period (Beta=7.61, CI=0.17 to 15.05); however, this effect was not maintained at follow-up (Beta=3.65, CI=-3.05 to 10.36).

Interpretation

The lifestyle intervention was ineffective in eliciting a behavioural change toward more favourable physical behaviour in adolescents and young adults with spastic CP.

What this paper adds

- An active lifestyle and sports participation intervention had no meaningful effect on objectively measured outcomes of physical activity or sedentary behaviour.
- The participants' self-reported physical activity (primarily sports participation) improved after 6 months, but this effect was lost after 12 months.

INTRODUCTION

Physical activity (PA), defined as any bodily movement produced by the muscles that results in increased energy expenditure,[1] serves as primary and secondary prevention against several chronic diseases.[2] Independent of moderate to vigorous PA level, prolonged periods of sedentary behaviour (any waking activity characterised by an energy expenditure ≤ 1.5 metabolic equivalents and a sitting or reclining posture)[3] negatively affects the metabolic and cardiovascular systems.[4] Consequently, favourable physical behaviour, consisting of sufficient PA with little sedentary time, is recommended for optimal health.

For persons with cerebral palsy (CP), optimal physical behaviour may be even more important. Physical inactivity contributes to functional deterioration[5] and may reduce social participation.[6] Nevertheless; research shows that CP populations have low PA levels compared to able-bodied persons.[7, 8] In addition, sedentary time is twice the recommended level among adolescents with CP.[8]

Physical activity level during childhood influences eventual adult lifestyle.[9] Therefore, achieving recommended PA levels and reducing sedentary behaviour seems important at young age. Despite the unfavourable physical behaviour profile typical of persons with CP, little attention has been given to this issue. Various environmental and personal barriers and facilitators play a key role in the physical behaviour of adolescents with CP.[10] There is evidence that counselling sessions to discuss barriers and facilitators are effective in modifying physical behaviour in adult populations with physical disabilities.[11]

In addition to unfavourable physical behaviour, persons with CP have low levels of cardiopulmonary fitness,[12] and they are likely to benefit from exercise programmes to improve these fitness levels.[13] Improved cardiopulmonary fitness may indirectly contribute to higher PA levels by lowering the physical strain of daily activities.[12] Therefore, it can be speculated that individual counselling about PA and sedentary behaviour, combined with physical fitness training, is beneficial to improve physical behaviour in persons with CP.

To our knowledge, the effectiveness of an intervention to improve physical behaviour in adolescents with CP has been studied only by Maher et al.[14] They evaluated an internet-based intervention and their results were inconclusive. In contrast to their study, the present study evaluates a more comprehensive, face-to-face intervention that we expect to be more effective than an internet-based intervention. This intervention is offered in outpatient rehabilitation departments for young adults in rehabilitation centres in The Netherlands. The current study is part of the LEARN 2 MOVE 16-24 study[15] and evaluates the effectiveness of the Active Lifestyle and Sports Participation (ALSP) intervention on physical behaviour in adolescents and young adults with spastic cerebral palsy.

METHODS

Design overview

The study used a multi-centre, single blind, randomised controlled design. Assessors who were blinded to group allocation performed measurements. The study design has been described in detail elsewhere.[15]

Setting and participants

Reviewing health records at four rehabilitation centres and two rehabilitation departments at university hospitals throughout the western and central regions of The Netherlands identified eligible participants. Persons with unilateral or bilateral CP were eligible if they met each of the following inclusion criteria: 1) age 16 to 24 years; 2) GMFCS level I to IV; and 3) a spastic type of CP as measured with the modified Ashworth Scale.[16] Persons were excluded if they had any of the following: 1) disabilities other than CP that affect daily PA or cardiopulmonary fitness; 2) contraindication to (maximal) exercise;[17] 3) PA level obtained at the baseline measurement exceeds the mean PA level + 2 SD of a CP population,[7] corresponding with 263 minutes of physical activity per day; or 4) severe cognitive disorders or insufficient comprehension of the Dutch language. An informational letter and invitation to participate were sent to eligible persons. All participants provided written informed consent. The medical ethics committee of the Erasmus Medical Centre approved the study and all participating centres granted local approval.

Randomisation and intervention

After baseline measurement, participants were stratified by the Gross Motor Functioning Classification System (GMFCS)[18] to obtain an equal distribution of gross motor functioning between the experimental and control groups. Within each stratum and for each participating centre, participants were randomly allocated (1:1) to these groups. Participants were assigned in chronological order of enrolment. The generation of the allocation sequence, participant enrolment, and group assignment were performed by the first author of this study. A computer performed the actual randomisation process by syntax for SPSS Statistics. The experimental group received the ALSP intervention. The control group received no intervention to improve physical behaviour and cardiopulmonary fitness, which is the usual care in The Netherlands. The control group was, however, allowed to continue their regular treatments (e.g. physical therapy). These regular treatments were registered using questionnaires and their frequency and duration did not change over time.

The ALSP intervention aims to permanently increase physical fitness and PA levels and reduce sedentary behaviour. The intervention is targeted at adolescents and young adults with physical disabilities and promotes a more active lifestyle. The ALSP intervention consists of three parts; 1) A progressive weekly supervised centre-based and weekly home-based physical fitness training programme with a focus

on increasing levels of cardiopulmonary fitness and muscle strength are offered and guided by a physical therapist for a period of 3-months; 2) counselling on daily PA, which is based on motivational interviewing. Barriers and facilitators of PA in daily life are discussed and increasing PA and minimising sedentary behaviour are encouraged during these sessions. In total, 6 monthly sessions with a duration of 30 minutes are offered and guided by a personal coach (physical therapist / movement therapist); and 3) counselling on sports participation is carried out to find accessible, suitable and appropriate sports and sports facilities conveniently located in each participant's environment. In total, a movement therapist offers two to four sports counselling sessions over a period of 6-months depending on the participants' desires. Furthermore, optional sport-specific training is offered, which includes practice opportunities to match sports to participants' interests and abilities. Details of the ALSP lifestyle intervention have been described elsewhere.[15]

Outcomes and follow-up

All measurements were performed three times: 1) prior to the intervention (T0); 2) directly after finishing the intervention, which was six months after the start of the intervention (T6); and 3) a follow-up measurement 6-months after finishing the intervention (T12).

Objective measurement of movement behaviour

To objectively measure daily PA level and sedentary time, participants wore the VitaMove system (2M Engineering, Veldhoven, The Netherlands) (Figure 1). This system is based on ambulatory

Figure 1. VitaMove activity monitor

monitoring of signals from body-fixed accelerometers (Freescale MMA7260Q, Denver, USA). From the accelerometer signals, the duration, rate, and moment of occurrence of postures and movements can be automatically and separately detected. Furthermore, from each measured signal, information on the variability of the acceleration signal (motility, which is related to the intensity of body-segment movements) can be obtained. A detailed description of the measurement procedure has been presented elsewhere.[15] The VitaMove system is found to be valid to quantify physical behaviour and to detect inter-group differences in daily PA levels in able bodied persons and in persons with a variety of physical disorders, among which leg amputations, failed back surgery, and chronic heart failure, all with validity coefficients around 0.9.[19] Participants wore the VitaMove system (8x4x1cm) for three consecutive weekdays using elastic belts. A successful measurement day was defined as a measurement period of 24 consecutive hours.

The VitaMove system was set up at each participant's home to minimise influence on normal physical behaviour. To avoid measurement bias, we instructed participants to continue their ordinary daily life. Furthermore, the principles of the activity monitor were explained to the participants only after all measurements were made. The following data were analysed from these measurements:

1. Duration of daily PA expressed as a percentage of a 24-hour period. Daily PA comprises walking, running, cycling, wheelchair propulsion (including hand-cycling) and non-cyclic movement.
2. Duration of sedentary time, which comprises lying and sitting, and is expressed as a percentage of the waking part of the day.
3. Mean motility of physical activities, including walking, running, cycling, wheelchair propulsion and non-cyclic movements. This motility indicates movement intensity and is expressed in units of gravitational force (g).
4. Number of total continuous walking and sitting bouts lasting greater than 5 seconds. Distribution of continuous walking and sitting bouts with a pre-defined duration (5-10 sec; 10-60 sec; 1-10 min; 10-30 min; or greater than 30 min) was analysed.

Self-reported daily physical activity level

The Physical Activity Scale for Individuals with Physical Disabilities (PASIPD)[20] was included as measure of self-reported PA. The PASIPD is a 13-item, 7-day recall questionnaire developed for people with physical disabilities. It consists of questions about leisure time, as well as household-related and work-related PA. We used the Dutch version of the PASIPD, which integrates lawn work and gardening into one item about gardening. The total PASIPD score was calculated by multiplying the average hours per day for each item by a metabolic equivalent (MET) value associated with the intensity of the activity. The PASIPD was included in the study to measure self-reported PA and self-reported sports participation. The validity of the PASIPD is poor (coefficient of 0.37) when compared to objective measurement of PA.[21] However, similar low correlations between objective and subjective activity measurements have been found in the general population.[11]

Statistical analysis

Fifty participants were required to detect a 30-minute per day difference in objectively measured PA between the control and experimental groups, with a power of 0.8 and an alpha of 0.05. To allow for drop-outs, we aimed to recruit 60 participants. A difference of 30 minutes of PA was chosen because we considered this a clinically relevant difference. This power calculation was based on data from previous research in a CP population conducted by our research group.[7]

Chi square tests were performed to test for baseline differences in gender, CP type (unilateral or bilateral) and GMFCS distribution between control and intervention groups. Independent sample *t*-tests were performed to test for baseline differences in age, body mass and height between control and intervention groups.

To determine intervention effects, Generalised Estimating Equation (GEE) analyses with exchangeable correlation structures were performed for each outcome measure following an intention to treat protocol. Group allocation, baseline values, measurement time and an interaction variable between group allocation and measurement time were added to the GEE model to compare group outcomes for specific time intervals. These time intervals were the intervention period (T0 to T6) and the total time period (T0 to T12). The control group was used as the reference group for all analyses. IBM SPSS Statistics version 20 (Chicago, IL) was used for statistical analyses.

RESULTS

Between October 2009 and September 2011, we identified a target population of 456 adolescents and young adults with CP in the patient registers of the participating centres. Many had not received treatment at a rehabilitation centre in many years. Therefore, the contact information accuracy was uncertain. A total of 183 potential participants responded to our invitation, of whom 57 (31%) consented to participate, and 36 completed the study (Figure 2). Participants were included from December 2009 up to September 2011. Baseline personal and clinical characteristics are presented in Table 1. No significant differences were noted between control and intervention groups with respect to personal or clinical characteristics. The participants that completed the intervention attended, on average, 89% of supervised counselling and fitness training sessions. No adverse events were reported. The intended three-day measurement period of the VitaMove system was not always achieved. This was mainly due to technological issues (Table 2).

The observed data over time are presented in Table 3. The results of the corresponding GEE analyses are presented in Table 4. No effect of the intervention was found on the primary outcomes of objectively measured physical behaviour. Between T0 and T6, the PASIPD significantly increased in

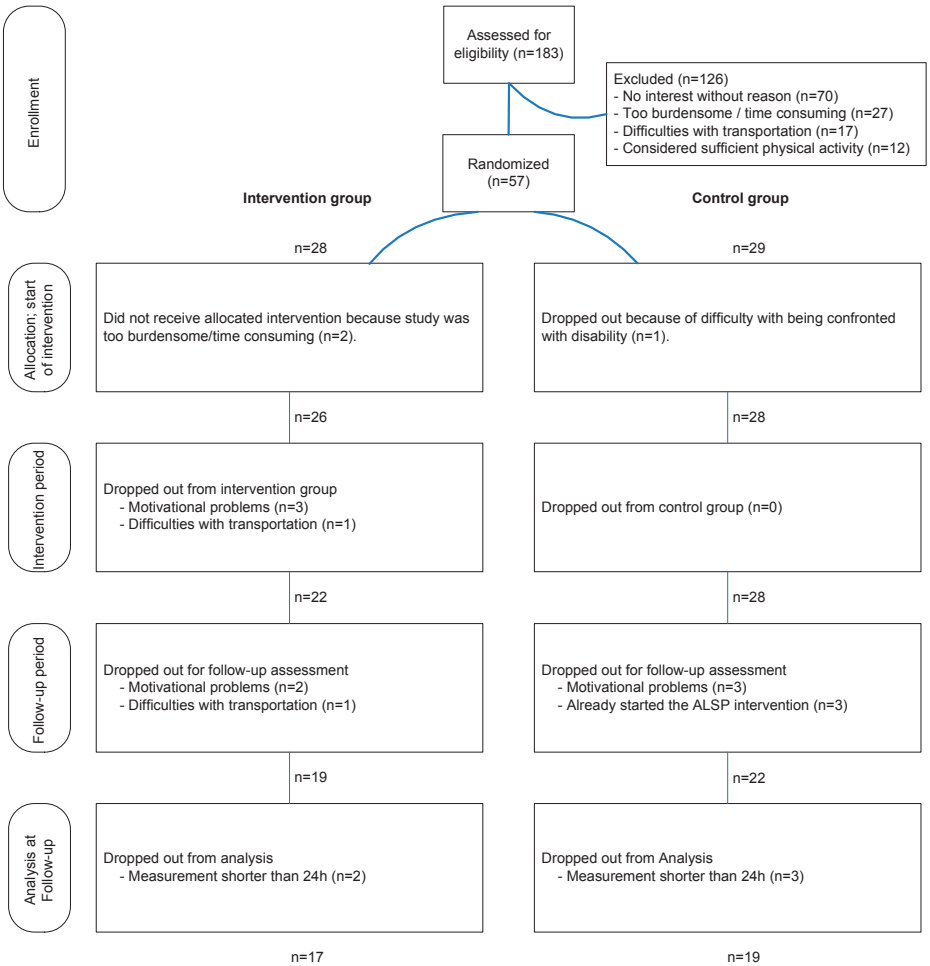

Figure 2. Flowchart of participants through the study.

the intervention group compared to the control group (difference=7.61, p=0.05). Post hoc analyses showed that this increase in PASIPD score was attributable to a difference in strenuous sports and leisure activities (difference=5.43, p=0.03). The number of sitting bouts with a duration of 0-10 sec and 10-60 sec between T0 and T6 both increased in the intervention group compared to the control group (difference=10.47, p=0.03 and difference=15.38, p=0.03, respectively).

Table 1. Baseline participant of the complete study sample and specified per allocated group. P-values are given for differences between the control and intervention group. Reported as n or mean ± SD

	All	Control	Intervention	P-value
N	57	29	28	-
Gender (M / F)	27 / 30	15 / 14	12 / 16	0.50
Age (years)	20 ± 3	20 ± 3	20 ± 3	0.64
Height (cm)	170 ± 10	170 ± 9	169 ± 11	0.66
Body mass (kg)	67 ± 18	65 ± 18	70 ± 18	0.24
CP type (unilateral / bilateral)*	29 / 27	15 / 14	14 / 13	0.79
GMFCS** level† (I / II / III / IV)	33 / 18 / 5 / 1	16 / 9 / 3 / 1	17 / 9 / 2 / 0	0.75

* Type of CP for one participant is unknown

** Gross Motor Function Classification System

Table 2. Drop-outs, failed measurements and successful measurements, per measurement time. For the successful measurements, the distribution of the number of measurement days with the VitaMove system is displayed.

Measurement time	Participant drop-outs (n)	Failed measurements (n)	Successful measurements (n)			
			1 day	2 days	3 days	Total
T0	0	8	6	25	18	49
T6	7	9	8	17	16	41
T12	21	0	9	13	14	36

DISCUSSION

The ALSP intervention was ineffective in changing objectively measured movement behaviour, despite of the unfavourable initial movement behaviour of our study sample.[22] Furthermore, post hoc individual level analyses showed that the numbers of persons that improved or worsened on objectively measured PA were equally distributed between the control and intervention groups. An increase in the number of sitting bouts with short duration was found in the intervention group after following the intervention, which did not lead to an increase in the total number of sitting bouts or sedentary time. The current study did find a significant intervention effect for self-reported PA, which was attributable to increased strenuous sports and leisure activities. However, this effect was not maintained during the follow-up period.

The positive change for self-reported PA is consistent with that reported from a similar lifestyle intervention in adults with physical disabilities.[23] The discrepancy in results of the present study are consistent with results on an internet-based lifestyle intervention for adolescents with CP by Maher et al.[14] They found modest short-term effects for objectively measured PA; however, this positive effect was not present at the 12-week follow-up. Furthermore, they reported no effect of the intervention on self-reported PA. In conclusion, it seems hard to achieve a behavioural change towards more

Table 3. Observed data over time, specified per allocated group. Reported as mean ± SD (n)

Outcome measure	Intervention group			Control Group		
	T0	T6	T12	T0	T6	T12
Dynamic activities (% of 24h period)	8.80±3.12 (24)	8.53±4.30 (20)	9.13±3.35 (19)	8.26±2.94 (25)	7.88±3.77 (21)	7.92 ± 4.63 (17)
Sedentary time (% of wakening part of the day)	41.09±16.77 (24)	43.91±14.90 (20)	38.69±6.67 (19)	46.16±12.67 (25)	46.05±13.07 (21)	46.76±12.52 (17)
Standing (% of 24h period)	13.09±5.44 (24)	12.41±5.77 (20)	10.78±4.58 (19)	10.67±5.11 (25)	9.17±5.73 (21)	9.88±6.53 (17)
Total sitting periods (# / 24h)	102.74±38.76 (24)	121.12±68.61 (20)	99.48±32.25 (19)	115.23±53.46 (25)	106.94±59.91 (21)	117.38±49.78 (17)
Sitting periods >30min (# / 24h)	3.02±1.72 (24)	2.73±1.76 (20)	3.22±2.19 (19)	4.01±2.05 (25)	3.61±1.95 (21)	3.90±2.25 (17)
Total walking periods (# / 24h)	237.19±95.28 (24)	216.66±99.85 (20)	229.54±106.99 (19)	199.35±85.46 (25)	198.60±115.11 (21)	174.08±106.28 (17)
Motility of dynamic activities	44.91±7.37 (22)	42.28±7.25 (16)	42.72±10.73 (19)	43.18±8.74 (25)	40.19±8.52 (20)	36.06±9.25 (14)
PASIPD* score (MET hr/day)	12.75±8.09 (27)	20.29±14.07 (19)	17.09±10.86 (20)	12.56±8.69 (27)	14.12±10.38 (25)	15.78±11.48 (19)

* PASIPD = Physical Activity Scale for Individuals with Physical Disabilities

Table 4. Longitudinal generalised estimating equation results. N represents the number of total cases eligible for longitudinal analysis. Results are specified for effects between T0-T6 and effects between T6-T12. All analyses were adjusted for baseline differences between groups. The control group is marked as reference group for all analyses.

	N	Difference T0-T6	P-value	95% CI		DifferenceT0-T12	P-value	95% CI	
Dynamic activities	120	0.34	0.75	-1.70	2.37	0.30	0.80	-1.99	2.59
Sedentary time	120	-0.84	0.42	-2.90	1.21	-1.34	0.12	-3.02	0.34
Standing	120	0.51	0.15	-0.18	1.20	-.20	0.54	-0.84	0.44
Total # sitting periods	120	23.62	0.18	-10.64	57.89	-13.22	0.15	-31.14	4.71
# Sitting bouts >30 min / 24h	120	-0.49	0.36	-1.54	0.56	-0.15	0.82	-1.44	1.15
# Walking bouts / 24h	120	4.71	0.88	-56.81	66.23	25.23	0.36	-28.62	79.08
Motility of dynamic activities	107	1.81	0.53	-3.81	7.42	5.77	0.14	-1.92	13.45
PASIPD*	131	7.61	0.05	0.17	15.05	3.65	0.29	-3.05	10.36

* PASIPD = Physical Activity Scale for Individuals with Physical Disabilities

favourable physical behaviour among adolescents and young adults with CP. This conclusion is in line with those from studies on the general population that also reported difficulties in changing physical behaviour.[24]

It has been established that self-reported PA levels, as measured with the PASIPD, are often overestimated and poorly correlate with objective PA measures in adults with physical disabilities.[21] This overestimation may explain the discrepancy between objectively measured and self-reported PA in the present study. Self-reported PA overestimation may be even higher among those following the ALSP intervention, as they may feel compelled to respond in a socially desirable way. However, Maher et al. found opposite results in their internet-based lifestyle intervention study, wherein objectively measured PA effects were not supported by self-reported PA results.[14] The present study used a more comprehensive, face-to-face intervention and focused on total physical behaviour, including sedentary behaviour. Despite this more comprehensive approach, we found no change into more favourable physical behaviour.

Strengths and limitations

The strength of the present study is that it is one of the first studies that evaluates a lifestyle intervention among adolescents and young adults with CP. Furthermore, the 6-month follow-up period is an important strength. The applied VitaMove system provides detailed information on physical behaviour and is one of the few accelerometers that can reliably distinguish cycling (a popular activity in The Netherlands) and wheelchair propulsion.

There are some noteworthy limitations of using the VitaMove system to measure daily PA level. We intended to measure PA over a three-day period; however, this was not uniformly achieved due to technological challenges and user errors. Nevertheless, White et al. have shown that a 24-hour VitaMove system measurement is adequate to reliably determine activities and postures.[25] The extent to which such short measurement periods are representative for common movement behaviour is questionable. Participants were asked to keep a diary so that we could correct periods of non-wearing time. Furthermore, to analyse objectively measured physical behaviour, we assumed that participants went directly to bed after taking off the VitaMove system each day. This probably did not always match reality, which may have led to an underestimation of PA and an overestimation of sedentary time. However, this error is expected to be consistent over time and between groups and would apply to all ambulant measurement systems that can be removed by the participants.

Loss to follow-up was 39% in the intervention group and 34% in the control group (Figure 2). A type II error may have occurred in the longitudinal analysis due to a higher than expected dropout rate. However, we do not expect that the results would have differed with fewer participant drop-outs considering that the clinically relevant differences on our primary outcome measures are not included

in the 95% CI of the analyses. Due to multiple testing in the present study, one should be careful to draw strong conclusions from single significant findings.

We may have overestimated everyday PA level because of selection bias. Persons with CP who are interested in PA and sports (and possibly have a higher baseline PA level) may have been more likely to participate than those with low interest. Despite this possible selection bias, participants' initial PA levels were low and sedentary time was high.

Clinical implications

In the future, several improvements can be implemented to the ALSP intervention to attempt to increase its effectiveness. Considering that persons have difficulties in estimating their physical behaviour, applying a simple accelerometer as intervention tool provides instant feedback on one's physical behaviour, which might be a useful addition to the intervention as instrument for individual goal-setting. In light of recent evidence concerning sedentary behaviour,[8] PA counselling should address both interrupting prolonged periods of sedentary time in addition to decreasing overall sedentary time.

The parents may have had a major role in deciding whether to participate in the offered lifestyle intervention. Cases in which the parents consider participation more important than the participants will eventually lead to dropouts. Therefore, intrinsic motivation to participate in such a lifestyle intervention should be measured initially, which could significantly improve the compliance.

Conclusions

We found a significant positive effect of the ALSP intervention on self-reported PA level directly following the intervention. However, this effect was not present at the 12-month follow-up. Furthermore, there were no effects of the ALSP intervention on PA level, movement intensity or sedentary time, as objectively measured with the VitaMove system. Therefore, we conclude that the ALSP intervention was ineffective in eliciting a behavioural change toward more favourable physical behaviour among adolescents and young adults with spastic cerebral palsy.

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Chapter 6

Can a lifestyle intervention improve physical fitness in adolescents and young adults with spastic cerebral palsy? A randomised controlled trial

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ABSTRACT

Objective

Sufficient physical fitness is required for primary and secondary prevention of chronic diseases and to prevent premature death. Research has shown that children, adolescents and bilaterally affected adults with CP have low physical activity levels compared to able-bodied persons. Regular exercise programmes generally only achieve short-term effects. The objective of the present study is to evaluate both the short and long term effectiveness of a lifestyle intervention on physical fitness in adolescents and young adults with CP.

Design

Single blind, randomised controlled trial.

Setting

Six university hospital/clinics in The Netherlands.

Participants

Fifty-seven adolescents and young adults with spastic cerebral palsy classified in GMFCS level I-IV, of whom 42 completed the study.

Intervention

A six-month lifestyle intervention consisting of physical fitness training combined with counselling sessions focused on physical behaviour and sports participation.

Main outcome measures

Physical fitness including measures of cardiopulmonary fitness, muscle strength and body composition.

Results

Favourable short and medium-term effects were found for peak oxygen uptake, oxygen uptake and load on the anaerobic threshold and waist circumference. Favourable long-term effects were found for sum of skinfolds, systolic blood pressure and total cholesterol.

Conclusions

This exploratory study showed that a lifestyle intervention was effective in improving cardiopulmonary fitness and body composition. Effects of body composition were maintained on the long term. However, the intervention needs to be optimised to increase muscle strength and for long term retention of effects on aerobic capacity.

INTRODUCTION

Sufficient physical fitness and physical activity (PA) are major contributors to a healthy lifestyle for the general population,[1] particularly because of their inverse relationship to total and cardiovascular mortality.[2] For persons with cerebral palsy (CP), defined as "a group of permanent disorders of the development of movement and posture, causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain",[3] sufficient physical fitness and PA is likely to be even more important. Additional to health benefits, sufficient physical fitness and PA is believed to maintain and optimise daily life performance[4] and prevent developing secondary health problems in adulthood.[5] Nevertheless, research consistently shows that people with CP have low levels of physical fitness[6-9] and PA.[10-13]

During adolescence, there are many changes in life with substantial impact on the development of the adult lifestyle.[14, 15] Therefore, improving physical fitness and incorporating sufficient PA at this age seem an appropriate goal to benefit the person through the lifespan. Important health-related components of physical fitness are cardiopulmonary fitness, body composition and muscle strength.[16] Children, adolescents and young adults with CP benefit on all these measures of physical fitness directly following interventions, as described in two systematic reviews.[17, 18] However, both reviews indicate that cardiopulmonary fitness tends to return to baseline at follow-up.[17, 18] Also, benefits to muscle strength were no longer present at follow up in two out of five studies in the review of Verschuren et al.[17] Apparently, offering a temporary intervention focused on improving physical fitness is insufficient to maintain improvements in physical fitness over the long-term in persons with CP. A behavioural change toward a more active lifestyle may be more effective over the long-term. Counselling sessions appear promising to achieve behavioural changes among persons with physical disabilities.[19, 20] Therefore, the Active Lifestyle and Sports Participation (ALSP) intervention was developed in The Netherlands to increase physical fitness and PA through behavioural change in adolescents and young adults with childhood-onset physical disabilities.[21] The present study is part of the LEARN 2 MOVE 16-24 study[22] and its aim is to evaluate the effectiveness of this ALSP intervention on physical fitness in adolescents and young adults with spastic cerebral palsy. Effects of the intervention on other outcome measures, like PA, fatigue, participation and quality of life will be presented in forthcoming publications. By offering an exercise programme combined with PA counselling to achieve behavioural changes towards more PA, effects on physical fitness are expected on both the short and long-term.

METHODS

Study design

The present study is a multi-centre trial with randomised controlled design. To obtain equally distributed gross motor functioning between experimental and control groups, stratification of participants was performed using the Gross Motor Functioning Classification System (GMFCS).[23] Random allocation of participants to these groups (1:1) was performed for each participating centre and within each stratum. The ALSP intervention was received by the experimental group, whereas no intervention to improve physical behaviour and fitness was received by the control group. Individuals allocated to the control group continued their regular treatments. These regular treatments consisted of physiotherapy for slightly over 80% of control group participants and had an average duration of 2 hours per week. However, in contrast to the ALSP intervention, these regular treatments were not aimed at increasing fitness or PA levels. Assessors which performed the study measurements were blinded to group allocation.

Setting and Participants

Review of health records at four rehabilitation centres and two rehabilitation departments at university hospitals throughout the western-central part of The Netherlands identified eligible participants. Persons were eligible if they met the following inclusion criteria: 1) diagnosed with spastic unilateral or bilateral CP; 2) age 16 to 24 years; and 3) GMFCS level I to IV. Persons were excluded if they had any of the following: 1) disabilities other than CP affecting cardiopulmonary fitness or PA; 2) contraindication to (maximal) exercise;[24] 3) Exceeding the mean PA level + 2 SD of a CP population[10] as measured with an accelerometry based activity monitor,[25] corresponding to 263 minutes of PA per day; or 4) insufficient understanding of the project caused by severe cognitive impairment or insufficient comprehension of the Dutch language. An informational letter, including an invitation to participate, was sent to eligible persons. Three weeks later, non-responders received a reminder letter. Written informed consent was provided by all participants. The study was approved by the medical ethics committee of the Erasmus Medical Centre. All participating centres granted local approval.

We identified a target population of 456 adolescents and young adults with CP in the patient registers of participating centres. Many patients had not received care at a rehabilitation centre for many years. Therefore, the accuracy of their contact information was uncertain. A total of 183 potential participants responded to our invitation, of whom 57 (31%) consented to participate, and 42 completed the study (Figure 1).

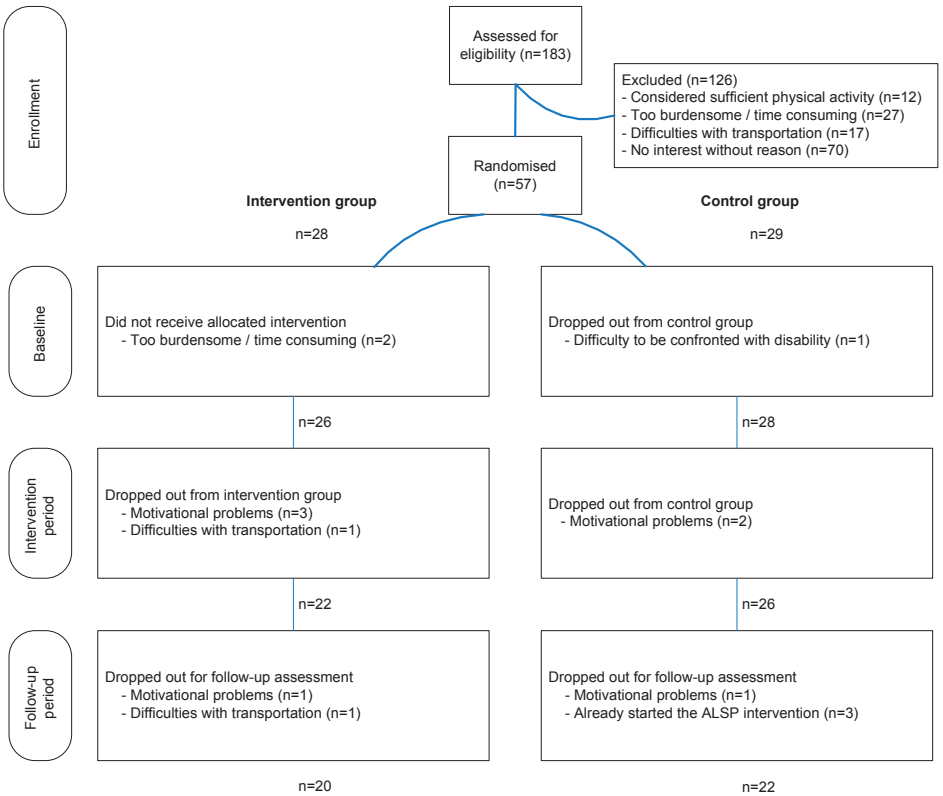

Figure 1. Flowchart of participants through the study.

Intervention

The ALSP intervention aims to permanently increase physical fitness and PA levels and reduce sedentary behaviour. The intervention is targeted at adolescents and young adults with physical disabilities and promotes a more active lifestyle. The ALSP intervention consisted of three parts; 1) weekly supervised centre and weekly home-based physical fitness training with a focus on increasing levels of cardiopulmonary fitness and muscle strength were offered by a physical therapist for a period of 3 months; 2) counselling on daily PA, which was based on motivational interviewing.[26] Barriers and facilitators of PA in daily life were discussed and increasing PA and minimising sedentary behaviour were encouraged during these sessions. In total, six monthly sessions with a duration of 30 minutes were offered and were guided by a personal coach (physical therapist / movement therapist); and 3) counselling on sports participation was carried out to find accessible, suitable and appropriate sports and sports facilities conveniently located in each participant's environment. In total, two to four sports counselling sessions were offered by a movement therapist over a period of six months depending on the participants' desires. Furthermore, optional sport-specific training was offered, which included

Table 1. Time schedule of the Active Lifestyle and Sports Participation intervention.

Week	Measurements	Counselling on daily PA	Fitness training		Sports advice
			Supervised	Home-based	
Week 1	Pre-test (T0)	PA session 1			
Week 2			Training 1	Training 2	
Week 3			Training 3	Training 4	Sports session 1
Week 4			Training 5	Training 6	
Week 5		PA session 2	Training 7	Training 8	
Week 6			Training 9	Training 10	
Week 7			Training 11	Training 12	
Week 8			Training 13	Training 14	
Week 9			Training 15	Training 16	
Week 10		PA session 3	Training 17	Training 18	Sports session 2
Week 11			Training 19	Training 20	
Week 12			Training 21	Training 22	
Week 13			Training 23	Training 24	
Week 14	Post-test 1 (T3)				
Week 15		PA session 4			
Week 16					
Week 17					(Sports session 3)
Week 18					
Week 19					
Week 20		PA session 5			
Week 21					
Week 22					
Week 23					
Week 24					(Sports session 4)
Week 25		PA session 6			
Week 26	Post-test 2 (T6)				
Week 52	Follow-up test (T12)				

Note: After 13 weeks the possibility of continuing fitness training in the day-tot-day situation will be explored for each participant

practice opportunities to match sports to participants' interests and abilities.[21] A time schedule of the ALSP intervention is presented in Table 1. Details of the ALSP lifestyle intervention have been described elsewhere.[22]

The training frequency of the ALSP intervention did not meet guidelines for cardiopulmonary exercise training.[27] However, the content of the counselling and sport-specific training were considered as they also required time and physical effort. Therefore, a training frequency of two times a week was assumed to be practically feasible for the ALSP intervention to respect the load/capacity ratio of participants.

Measurements

All measurements were performed at four points in time: 1) prior to randomisation (T0); 2) directly after completing the fitness training portion of the intervention, which was three months after starting the intervention (T3); 3) directly after completing the entire intervention, including counselling: this was six months after starting the intervention (T6); and 4) a follow-up measurement six months after finishing the intervention (T12). Three components of physical fitness were measured in the present study; cardiopulmonary fitness, body composition and muscle strength.

Cardiopulmonary fitness

Peak oxygen uptake (VO_{2peak}) was measured using a progressive ramp protocol during cardiopulmonary exercise testing (CPET). This test was performed on electronically braked cycle or arm-crank ergometers, depending on each person's primary mode of ambulation during daily life, so as to elicit the highest oxygen uptake levels.[28] VO_{2peak} was expressed in mL/min and defined as the highest mean oxygen uptake during 30 seconds of exercise. The ventilatory equivalent method was used to estimate oxygen uptake at the ventilatory anaerobic threshold (AT) and was expressed in mL/min.[29] Furthermore, the maximum load and the load at anaerobic threshold were analysed and expressed in Watts. We applied two objective criteria for maximal exercise: 1) A maximum HR of at least 175 beats per minute, which represents 90% of the predicted maximum HR in adolescents with CP;[30] and 2) a respiratory exchange ratio (RER) ≥ 1.1.[31] A detailed description of the applied CPET protocol is available elsewhere.[22]

Body composition

Height was measured in a standing position. In case of joint contractures, length was measured joint-to-joint in a lying position. A Seca scale[a] was used to obtain body mass of ambulatory participants and an electronic Cormier sitting scale[b] was used to weigh non-ambulatory participants. Waist circumference (cm) was measured in ambulatory persons mid-way between the iliac crest and the lowest rib while standing, whereas this was measured in a sitting position for non-ambulatory persons. A Harpenden skinfold caliper[c] was used to measure skinfold thickness (biceps, triceps, subscapular and suprailiac). These measurements were repeated twice on the left side of the body.

Vacutainer needles were used to draw non-fasting blood samples of 10-mL, which were collected in evacuated serum separator tubes II. High density lipoprotein (HDL) cholesterol, total serum cholesterol (TC), and the ratio between TC and HDL were determined from the blood samples.

Muscle strength

Muscle strength of the knee extensors, hip abductors and hip flexors was measured in ambulatory participants, whereas the muscle strength of the elbow extensors and shoulder abductors was measured in non-ambulatory participants. Measurements were performed bilaterally with a hand-

held dynamometer,[d] using the "break" testing method.[32] Three trials were performed per muscle group, with trial durations of approximately four seconds and one minute of rest between each trial. The mean value of the trials for both sides was calculated for each muscle group. A detailed description of the applied protocol to obtain muscle force is available elsewhere.[22]

Statistical analysis

As the current study is part of the LEARN 2 MOVE 16-24 study,[22] the power analysis was performed on PA as this a primary outcome measure of the total RCT. Therefore, the study was not powered for the outcomes analysed in this study, and we will consider our results as exploratory. To detect a change of 30 minutes per day in total daily PA between the control and experimental groups with a power of 0.8 and an alpha of 0.05 we had to include 50 participants. We aimed to recruit 60 participants to allow for dropouts. ACSM guidelines for healthy adults recommend at least 30 minutes of moderate intense physical activity for 5 times a week, preferably in bouts of at least 10 minutes.[33] Because activities in persons with CP are more burdensome than in healthy persons[34] these guidelines may not be suitable for the CP population. Because of this and the inactive lifestyle as found in CP,[10, 13] we considered a daily 30-minute change in PA (regardless of the intensity and duration of continuous bouts) as a clinically relevant effect of the intervention. The power analysis was based on data from our previous research.[10]

Chi-square tests were used to test for differences at baseline with respect to gender, CP distribution (unilateral or bilateral CP) and GMFCS level between control and intervention groups. Independent sample *t*-tests were used to test for differences at baseline with respect to age, body mass, height, VO_{2peak}, waist circumference and muscle strength.

We used generalised estimating equation (GEE) analyses, which was more appropriate than using repeated measures ANOVA due to missing data in our dataset. Furthermore, GEE was preferred above Linear Mixed Models as it is slightly more robust for relatively small sample sizes.[35] GEE analyses were applied for each outcome measure[35]. For these analyses, identity link functions were used and exchangeable correlation structures were assumed. Group allocation, baseline values of the particular outcome variable, measurement time and an interaction variable between group allocation and measurement time were added to the GEE equation to be able to compare group outcomes for specific time intervals. These time intervals were the exercise training period (T0 to T3), total intervention period (T0 to T6) and the follow-up period (T6 to T12). In case of significant effects of the intervention between the control and intervention group, additional GEE analyses were performed per group to gain insight into the within-group effect of the ALSP intervention. These models were specified per group and included 'measurement time' as factor. The presented differences from these GEE models represent the difference between groups over the specified time-period. The control group was the referent group for all analyses. SPSS statistics[e] was used for all statistical analyses.

RESULTS

Personal and clinical characteristics of the study sample at baseline are presented in Table 2 for the complete study sample and specified per allocated group. Apart from waist circumference (p=.04), none of the characteristics differed between control and intervention groups. Participants who completed the intervention attended, on average, 89% of the supervised training sessions.

In total, 28 of 178 CPET measurements did not meet the objective criteria for maximal exercise (13 measurements from the control group and 15 measurements from the intervention group) and thus were not analysed. These 28 measurements (from 18 participants) included all CPET measurements performed on the arm-crank ergometer (8 measurements), on which it appeared to be impossible to reach maximal exercise due to physical disabilities of participants. For the remaining 20 measurements, participants appeared to lack motivation for maximal exercise. Waist circumference was measured during standing in all but two participants. Blood observation was incomplete because: collection was impossible at one centre (28 observations), lack of consent (24 observations) and logistic reasons (42 observations). Thus, 84 blood observations remained out of 178 for analysis. Muscle strength was measured on the lower extremity for all but four non-ambulatory participants (three from the control group and one from the intervention group), in which muscle strength was measured on the upper extremity. Due to the low number of upper extremity measurements, no analyses were performed on upper extremity muscle force.

Table 2. Baseline participant characteristics. Data are presented as N or mean (SD).

	All	Control group	Intervention group	P-value
N	57	29	28	-
Gender (M / F)	27 / 30	15 / 14	12 / 16	0.50
Age (years)	20 (3)	20 (3)	20 (3)	0.64
Body mass (kg)	67 (18)	65 (18)	70 (18)	0.24
Height (cm)	170 (10)	170 (9)	169 (11)	0.66
CP distribution (unilateral / bilateral)*	29 / 27	15 / 14	14 / 13	0.79
GMFCS† level (I / II / III / IV)	33 / 18 / 5 / 1	16 / 9 / 3 / 1	17 / 9 / 2 / 0	0.75
Peak oxygen uptake (mL/min)	2397 (780)	2533 (824)	2260 (725)	0.25
Waist circumference (cm)	83 (14)	79 (12)	87 (15)	0.04
Total lower extremity muscle strength (N)	1397 (515)	1482 (630)	1307 (352)	0.24
Total upper extremity muscle strength (N)	461 (34)	466 (40)	448	0.74

* CP distribution for one person from the control group is unknown

† Gross Motor Function Classification System

Table 3. Outcome measures for intervention and control groups. Data are presented as mean (SD)

	Group*	n T0/T3/T6/T12	T0	T3	T6	T12
Cardiopulmonary fitness						
Maximum load (W)	I	22/17/21/15	163 (64)	172 (64)	174 (58)	166 (63)
	C	22/20/19/15	183 (74)	184 (77)	183 (84)	188 (88)
Maximum heart rate (bpm)	I	20/17/16/14	185 (15)	183 (23)	183 (16)	184 (14)
	C	19/18/18/15	192 (9)	190 (11)	181 (20)	182 (21)
VO_{2peak}† (mL/min)	I	22/17/21/15	2260 (725)	2515 (737)	2456 (583)	2315 (519)
	C	22/20/21/15	2533 (824)	2553 (862)	2396 (861)	2549 (864)
VO_2 on AT‡ (mL/min)	I	20/16/19/14	1488 (491)	1796 (483)	1603 (551)	1706 (427)
	C	20/19/19/13	1664 (695)	1626 (634)	1501 (481)	1953 (691)
Load on AT (W)	I	20/16/18/14	91 (42)	111 (46)	102 (48)	113 (47)
	C	20/19/16/11	113 (58)	105 (55)	103 (47)	151 (65)
O_2pulse (mL/beat)	I	20/17/15/13	13.4 (3.6)	14.7 (3.5)	15.5 (4.3)	14.3 (3.5)
	C	19/17/18/12	14.4 (5.0)	14.5 (4.6)	14.3 (4.9)	15.3 (4.9)
MaxVE (L/min)	I	22/17/16/15	89 (32)	98 (33)	94 (30)	95 (240
	C	22/20/16/15	101 (34)	101 (33)	80.81 (31)	105 (47)
Body composition						
Weight (kg)	I	28/22/23/20	70.3 (18.4)	74.0 (18.5)	72.9 (17.8)	70.7 (15.0)
	C	29/25/22/22	64.6 (17.6)	66.0 (18.2)	66.5 (18.7)	67.4 (19.9)
Waist circumference (cm)	I	28/21/22/18	87 (15)	86 (15)	86 (14)	84 (13)
	C	28/26/25/21	79 (12)	82 (13)	82 (13)	80 (15)
Sum of skinfolds (mm)	I	28/22/23/20	72.4 (31.1)	69.5 (28.8)	74.0 (33.2)	64.8 (25.4)
	C	29/26/24/21	58.9 (27.9)	61.5 (28.1)	60.8 (29.7)	64.8 (32.2)
Systolic blood pressure (mmHg)	I	28/22/23/19	119.9 (17.7)	121.1 (12.3)	119.2 (13.6)	115.9 (14.2)
	C	29/26/24/21	119.4 (17.6)	117.0 (16.8)	116.0 (16.4)	122.9 (15.1)
Diastolic blood pressure (mmHg)	I	28/21/23/19	78.0 (9.3)	76.0 (8.0)	77.2 (8.3)	74.8 (11.8)
	C	29/26/24/21	75.2 (8.6)	69.9 (11.7)	77.5 (9.2)	73.9 10.6)
Total cholesterol (mmol/L)	I	14/8/10/11	4.17 (0.54)	4.19 (0.52)	3.68 (0.51)	3.27 (0.67)
	C	10/10/12/9	4.58 (0.61)	4.30 (0.63)	4.46 (0.94)	4.32 (0.86)
HDL cholesterol (mmol/L)	I	14/8/10/11	1.29 (0.28)	1.37 (0.22)	1.42 (0.35)	1.41 (0.21)
	C	10/10/12/9	1.44 (0.31)	1.36 (0.33)	1.36 (0.26)	1.44 (0.25)
Cholesterol ratio (mmol/L)	I	14/8/10/11	3.28 (0.74 (14)	3.15 (0.72)	2.67 (0.42)	3.08 (0.66)
	C	10/10/12/9	3.36 (0.94)	3.35 (1.05)	3.37 (0.94)	3.13 (0.96)
Muscle strength						
Hip flexion (N)	I	26/21/21/18	417 (15)	449 (160)	429 (121)	501 (187)
	C	25/22/21/19	477 (20)	474 (139)	443 (153)	486 (118)
Hip abduction (N)	I	26/20/19/16	461 (15)	482 (143)	469 (128)	476 (108)
	C	25/21/20/18	483 (24)	449 (176)	480 (195)	508 (215)
Knee extension (N)	I	24/18/18/15	463 (12)	494 (126)	468 (124)	494 (144)
	C	25/20/20/19	522 (25)	484 (136)	457 (147)	516 (211)
Shoulder abduction (N)	I	1/1/1/1	222	250	250	282
	C	3/3/2/3	267 (67)	167 (41)	105(25)	139 (27)
Elbow extension (N)	I	1/1/1/1	226	179	191	263
	C	3/3/-/3	198 (60)	221 (68)	-	232 (43)

* I= intervention group, C= control group.

† Peak oxygen uptake

‡ Anaerobic threshold

Table 4. Longitudinal generalised estimating equation results for between-group analyses. All analyses were adjusted for baseline differences between groups for that particular outcome variable. The difference represents the difference over time of the intervention group compared to the control group for the specified time intervals.

Components of physical fitness	Difference T0-T3	P-value	95% CI		Difference T0-T6	P-value	95% CI		Difference T6-T12	P-value	95% CI	
Cardiopulmonary fitness												
Maximum load (W)	-0.3	0.97	-15.5	14.9	7.7	0.19	-3.8	19.2	0.3	0.97	-13.2	13.7
Maximum heart rate (bpm)	2.53	0.52	-5.2	10.3	4.1	0.35	-4.5	12.7	2.9	0.40	-3.9	-9.6
VO_{2peak}* (mL/min)	89.3	0.35	-98.8	277.4	195.2	**<0.01**	57.3	333.1	-118.2	0.14	-274.5	40.1
VO_2 on AT† (mL/min)	299.6	**<0.01**	94.2	505.0	325.5	**<0.01**	102.4	548.5	-219.7	0.23	-574.2	134.9
Load on AT (W)	26.5	**<0.01**	9.1	43.9	35.6	**<0.01**	16.0	55.2	-28.8	0.3	-61.1	17.4
O2pulse (mL/beat)	0.7	0.25	-0.5	1.8	1.7	0.07	-0.1	3.6	-1.0	0.12	-2.1	0.3
MaxVE (L/min)	5.6	0.21	-3.1	14.3	11.4	0.2	-5.4	28.1	-7.8	0.4	-24.3	8.8
Body composition												
Weight (kg)	0.5	0.51	-1.1	2.2	-0.6	0.46	-2.2	0.9	-0.8	0.62	-4.0	2.4
Waist circumference (cm)	-3.7	**0.04**	-7.2	-0.2	-2.6	0.15	-6.1	0.9	0.4	0.85	-3.9	4.7
Sum of skinfolds (mm)	-2.2	0.48	-8.4	4.0	0.2	0.96	-7.6	8.0	-11.2	**<0.01**	-19.0	-2.9
Systolic blood pressure (mmHg)	2.9	0.4	-3.7	9.5	1.5	0.68	-5.6	8.6	-10.2	**0.03**	-19.2	-1.2
Diastolic blood pressure (mmHg)	5.2	0.1	-0.3	10.6	-3.0	0.24	-7.9	1.9	0.7	0.83	-6.1	7.5
Total cholesterol (mmol/L)	-0.18	0.27	-0.50	0.14	-0.50	0.07	-3.22	-0.01	-0.55	**0.05**	-1.04	-0.07
HDL cholesterol (mmol/L)	0.12	0.13	-0.03	0.26	0.01	0.98	-0.21	0.21	0.09	0.34	-0.09	0.26
Cholesterol ratio (mmol/L)	-0.42	0.07	-0.88	0.04	-0.49	0.11	-1.08	0.10	0.18	0.44	-0.28	0.65
Muscle strength												
Hip flexion (N)	-16.1	0.63	-81.3	49.2	1.4	0.97	-63.0	66.0	29.0	0.51	-56.5	114.5
Hip abduction (N)	2.4	0.94	-59.6	64.5	-38.6	0.17	-93.1	15.9	-10.8	0.71	-68.1	46.5
Knee extension (N)	17.8	0.64	-56.7	92.4	23.7	0.57	-58.6	106.1	37.7	0.33	-38.0	113.4

* Peak oxygen uptake

† Anaerobic threshold

Table 5. Longitudinal generalised estimating equation results for within-group analyses for both the control and intervention group and specified per time frame. The difference represents the difference over time within groups.

	Control group				Intervention group			
	Difference	P-value	95% CI		Difference	P-value	95% CI	
T0-T3								
VO_2 on AT* (mL/min)	-52.9	0.51	-209.2	103.3	218.2	**<0.01**	58.0	378.4
load on AT (W)	-9.1	0.19	-22.6	4.5	15.7	**0.02**	2.7	28.6
Waist circumference (cm)	2.1	**<0.01**	0.6	3.6	-2.5	0.11	-5.6	0.6
T0-T6								
VO_{2peak}† (mL/min)	-119.5	**0.02**	-215.8	-23.3	94.0	0.17	-41.7	229.6
VO_2 on AT (mL/min)	-240.6	**0.01**	-424.5	-56.7	110.3	0.25	-79.1	300.0
Load on AT (W)	-25.8	**<0.01**	-44.1	-7.6	13.6	0.05	-0.2	27.3
T6-T12								
Sum of skinfolds (mm)	-3.2	0.24	-8.5	2.1	8.0	**0.01**	1.6	14.3
Systolic blood pressure (mmHg)	-7.3	0.06	-14.8	0.2	2.8	0.29	-2.4	8.0
Total cholesterol (mmol/L)	0.26	0.10	-0.1	0.6	-0.3	0.17	-0.7	0.1

* Anaerobic threshold

† Peak oxygen uptake

The observed data over time are presented in Table 3 and Table 4 shows the results of the associated longitudinal analyses. For specific time intervals, we found significant effects of the intervention for the experimental group compared with the control group (Table 4). Significant increases in cardiopulmonary fitness were found for the intervention group for VO_2 on AT (difference=300, p<0.01) and load on AT (difference=27, p<0.01) between T0 and T3. Furthermore, VO_{2peak} (difference=195, p<0.01), VO_2 on AT (difference=325, p<0.01) and load on AT (difference=36, p<0.01) increased in the intervention group compared to the control group between T0 and T6. For body composition, a decrease in waist circumference was found for the intervention group between T0 and T3 (difference=-4, p=0.04). Furthermore, during the follow-up period, decreases in sum of skinfolds (difference=-12, p=0.01), systolic blood pressure (difference=-10.18, p=0.03) and total cholesterol (difference=-0.55, p=0.05) were found for the intervention group compared to the control group. No significant effects were found for muscle strength. Table 5 shows the results of the within-group analyses.

DISCUSSION

In our sample of adolescents and young adults with spastic CP, VO_{2peak} at baseline was 17% lower (p<0.01) compared to individually calculated healthy norm-values for peak cardiopulmonary fitness, using the formula of Jones et al.[36] This finding is consistent with previous results of decreased peak

cardiopulmonary fitness in persons with CP.[37-39] ALSP intervention effects were promising for several cardiopulmonary fitness outcomes. VO_2 on AT and load on AT increased directly after completing the physical fitness training of the intervention (T3), and remained through the total intervention period (T6), while the physical fitness training had a duration of only three months. VO_{2peak} intervention effects were also present for the entire 6-month intervention period. In contrast to regular exercise programmes,[17,18] ALSP intervention effects were maintained for at least three months following physical fitness training. This persistence is likely to be attributable to the counselling sessions regarding incorporation of exercise and PA into daily life. However, these effects were no longer present at follow-up, half a year after intervention completion. Booster strategies, such as phone, mail or internet support could facilitate long-term effectiveness and could be added to the ALSP intervention, as these strategies seem effective for maintaining long-term lifestyle intervention effects.[40] We found improvements of 10% to 30% for the intervention group on outcomes of cardiopulmonary fitness. This is reasonable when compared to previously published results on intervention studies,[41] especially when the low training frequency of the ALSP intervention is taken into account. These effects may contribute to higher PA levels by lowering the physical strain of daily activities.[6]

Participants completing the ALSP intervention experienced decreases in waist circumference (T0-T3), sum of skinfolds (T6-T12) and systolic blood pressure (T6-T12) compared to the control group. In contrast to effects on cardiopulmonary fitness, effects on body composition are retained on the long term. A recent study found more hypertension and obesity in adults with CP than a healthy reference sample.[42] Therefore, the ALSP intervention may help participants lower their risk for cardiovascular disease. Furthermore, our results show that baseline lipid profiles are lower compared to those of a Dutch reference sample.[43] Such favourable lipid profiles have also been found in adults with CP.[42] Despite participants having favourable baseline lipid profiles, total cholesterol decreased in the intervention group compared to the control group during the follow-up period.

No effects of the ALSP intervention were found on muscle strength. This lack of a difference is consistent with results from a meta-analysis of resistance training protocols which showed that such interventions are ineffective in children and adolescents with CP.[44] However, a different review found that children and adolescents with CP may benefit from resistance training.[17] These conflicting results led to a study which aimed to optimise resistance training protocols for children and adolescents with CP.[45] The ALSP resistance training protocol met almost all suggestions presented in that optimisation study. The lack of improvement in muscle strength in the present study may be due to the relatively low training frequency for the ALSP intervention.

The results of the within group analyses in Table 5 show that the between-group effects that we have found in the present study are not always attributable to within-group changes of the intervention group, but can also result of within-group changes in the control-group.

The results of the present study suggest that offering a lifestyle intervention has positive results on physical fitness. By offering a combination of fitness training and counselling on daily PA and sports participation, the retention of treatment effects are positively influenced as compared to regular fitness training. This offers opportunities for clinical practice in order to keep physical fitness at level after intervention completion. However, optimisation of the ALSP intervention is required to retain effects on cardiopulmonary fitness at follow-up. The retention of results on the mid-term for cardiopulmonary fitness and on the long term for body composition is likely to be attributable to the offered counselling sessions on PA and sports. However, the design of the present study is not suitable to attribute results to specific intervention components. This merits more specific testing in future studies. Furthermore, the present study provided exploratory results for future studies and study designs.

Study limitations

The six participating centres did not have the same breath-by-breath analysers available. Therefore, two different types of analysers were used to determine VO_{2peak}. However, over the study course, each participant was tested with the same equipment, and calibration of the analysing systems was performed prior to each measurement. Furthermore, both applied systems were found to be valid by testing them against the Douglas-bag method resulting in explained variances of 0.97 and 0.96.[46, 47] Waist circumference was measured in a sitting position in persons using a wheelchair; this method could have led to incorrectly high waist circumference measures compared to those measured in the standing position. However, each participant was measured using the same method over time. Furthermore, waist circumference was measured during standing in all but two participants, which makes this possible measurement error negligible. Skin fold thickness was measured on the left side of the body. However, it could be possible that an involved side would not have the same anthropometric features as a non-impaired side. For practical reasons, non-fasting blood samples were collected. However, evidence exists that fasting minimally alters levels of TC and HDL-C.[48-50] Furthermore, non-fasting values for TC and HDL-C are considered to be appropriate by the NCEP ATP III guidelines.[51]

As power calculation was performed on PA, intervention effects on physical fitness should be regarded as exploratory. Loss to follow-up was 29% in the intervention group and 24% in the control group (Figure 1). Due to this higher than expected drop-out rate, a type II error may have occurred in the longitudinal analysis. Finally, one should be careful to draw strong conclusions from single significant findings, due to multiple testing in the present study.

Conclusions

This exploratory study showed that the ALSP intervention yielded positive short and medium-term effects on peak oxygen uptake, oxygen uptake and load on the anaerobic threshold and waist

circumference. Long-term effects were found for sum of skinfolds, systolic blood pressure and total cholesterol. The intervention was ineffective in increasing muscle strength and needs to be optimised to increase muscle strength and for long term retention of effects on aerobic capacity.

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Chapter 10

A lifestyle intervention improves fatigue, mental health and social support among adolescents and young adults with cerebral palsy: Focus on mediating effects

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ABSTRACT

Objective

To evaluate the effect of a lifestyle intervention on fatigue, participation, quality of life, gross motor functioning, motivation, self-efficacy, and social support and to explore mediating effects of physical behaviour and physical fitness.

Design

A randomised controlled trial with intention to treat analysis.

Setting

Rehabilitation centres and university hospitals in The Netherlands.

Subjects

Adolescents and young adults with spastic cerebral palsy.

Interventions

A six-month lifestyle intervention that consisted of physical fitness training combined with counselling sessions focused on physical behaviour and sports participation.

Main measures

Fatigue, social participation, quality of life and gross motor functioning.

Results

The lifestyle intervention was effective in decreasing fatigue severity during the intervention (difference=-6.72, p=0.02) and in increasing health-related quality of life with respect to bodily pain (difference=15.14, p=0.01) and mental health (difference=8.80, p=0.03) during follow-up. Furthermore, the domain participation and involvement of the social support increased during both the intervention (difference=5.38, p=0.04) and follow-up (difference=4.52, p=0.03) period. Physical behaviour or physical fitness explained the observed effects for 22.6%, 9.7% and 28.1% of improvements on fatigue, bodily pain and mental health, but had little effect on social support (2.6%).

Interpretation

Fatigue, bodily pain, mental health and social support can be improved using a lifestyle intervention among adolescents and young adults with cerebral palsy. Furthermore, substantial mediating effects were found for physical behaviour and physical fitness on fatigue, bodily pain and mental health.

INTRODUCTION

Increasing exercise and physical activity adolescents and young adults with cerebral palsy is important because they are known to have unfavourable physical behaviour profiles,[1] consisting of low physical activity, high sedentary time,[2] and subnormal physical fitness.[3] These unfavourable factors are associated with adverse effects on medical state[4, 5] and can affect perceived level of fatigue,[6] social participation[7, 8], quality of life.[9, 10] and gross motor functioning.[11, 12] Because physical behaviour and physical fitness are modifiable, increases may positively affect levels of fatigue, social participation, health-related quality of life and gross motor functioning. Furthermore, personal and environmental factors such as self-efficacy, intrinsic motivation and social support for exercise behaviour are likely to be linked with (changes in) physical behaviour and physical fitness among persons with physical disabilities.[13] However, there is only little evidence on the effectiveness of interventions to modify physical behaviour and physical fitness among adolescents and young adults with cerebral palsy and therefore, persons with cerebral palsy tend not to receive regular treatment in this area.[14]

The LEARN 2 MOVE 16-24 study[15] evaluates effects of the Active Lifestyle and Sports Participation intervention in adolescents and young adults with spastic cerebral palsy. This lifestyle intervention aims to optimise participants' physical behaviour and increase physical fitness levels. Effects of the intervention on these primary outcomes are presented in previous publications.[16, 17] The current study focuses on the intervention's secondary effects on fatigue, participation, health-related quality of life and gross motor functioning. Also, additional changes of self-efficacy, intrinsic motivation and social support for exercise behaviour were studied. In case of significant effects of the Active Lifestyle and Sports Participation lifestyle intervention for any of these secondary outcome measures, the mediating effects of physical behaviour and physical fitness on this specific outcome measure were explored.

METHODS

The study used a multi-centre, single blind, randomised controlled design. The measurements were performed by assessors who were blind for group allocation. The study design has been described in detail elsewhere.[15]

Setting and participants

To determine eligibility, we reviewed health records at four rehabilitation centres and two rehabilitation departments at university hospitals throughout the western and central regions of The Netherlands. Persons with spastic cerebral palsy were eligible if they met each of the following inclusion criteria: 1) age 16 to 24 years; and 2) Gross Motor Functioning Classification System (GMFCS)[18] level I to IV.

Persons were excluded if they had any of the following: 1) disabilities other than cerebral palsy that affect daily physical activity or cardiopulmonary fitness; 2) contraindication to (maximal) exercise;[19] 3) physical activity level at baseline that exceeds the mean physical activity level + 2 SD of a cerebral palsy population,[1] corresponding with 263 minutes of physical activity per day; or 4) severe cognitive disorders or insufficient comprehension of the Dutch language that would impede understanding of instructions for the intervention and assessments.

An informational letter and invitation to participate were sent to eligible persons. A reminder letter was sent three weeks later to non-responders. All participants provided written informed consent. The medical ethics committee of the Erasmus Medical Centre approved the study and local approval was granted by all participating centres.

Randomisation and intervention

Following baseline measurement, participants were stratified according to GMFCS level to obtain an equal distribution of gross motor functioning between the experimental and control groups. Within each stratum and for each participating centre, participants were randomly allocated (1:1) to these groups. Participants were assigned in chronological order of enrolment by using a series of numbers and each number had a randomly allocated group associated with it. As the patient was registered, he was allocated to the next number and then the group was revealed. The experimental group received the Active Lifestyle and Sports Participation intervention. The control group received no intervention to improve physical behaviour and cardiopulmonary fitness, which is usual care in The Netherlands.

The Active Lifestyle and Sports Participation intervention, which was developed for adolescents and young adults with physical disabilities, lasted six months. This intervention aimed to permanently improve physical behaviour and increase physical fitness. It consisted of: 1) counselling on daily physical activity and sedentary behaviour, which was guided by a personal coach to discuss barriers and facilitators of physical behaviour; 2) physical fitness training, which consisted of supervised centre and home-based training and focused on increasing cardiopulmonary fitness and muscle strength; and 3) counselling on sports participation to find suitable, accessible and appropriate sports and sports facilities in the person's day-to-day environment. This intervention has been described in detail elsewhere.[15]

Measurements

All measurements were performed thrice: 1) prior to starting the intervention; 2) immediately following the intervention, which was six months after the start of the intervention; and 3) a follow-up measurement six months after finishing the intervention.

Fatigue

Two widely used measures of fatigue were applied in this study: the Dutch version of the Fatigue Severity Scale (FSS)[20] and the fatigue sub-scale (CIS-f) of the Checklist Individual Strength (CIS-20r).[21] These two questionnaires likely measure different aspects of perceived fatigue. The FSS focuses on the impact of fatigue on specific types of functioning and the CIS-f measures the severity of perceived fatigue.[22] The FSS is a nine-item, 1-week recall, self-administered questionnaire with scores ranging from 1 to 7. The total score is the mean of nine items and ranges from 1 (no signs of fatigue) to 7 (most disabling fatigue). Internal consistency, reliability, validity and sensitivity of the FSS have been established.[20] The CIS-f is a 2-week recall questionnaire, assessing fatigue severity during the two weeks prior to assessment, with scores ranging from 1 to 7. The score of the CIS-f is the sum score of these eight questions and ranges from 8 to 56, with higher scores indicating more fatigue. Reliability, validity and sensitivity of the CIS have been established.[23]

Social Participation

Social Participation was assessed using the short version of the Life Habits Questionnaire (LIFE-H 3.0), which includes 69 life habits covering 12 categories (daily activities and social roles): nutrition, fitness, personal care, communication, housing, mobility, responsibilities, interpersonal relationships, community life, education, employment, and recreation.[24] Scoring is based on two specific aspects of participation: (1) the degree of difficulty in performing life habits (no difficulty, with difficulty, with substitution, or not accomplished); and (2) the type of assistance required performing the habit (no help, technical assistance or adaptation, or human assistance). Both elements are combined in a scale ranging from 0 to 9, with 0 indicating total handicap and 9 indicating optimal activity or participation. The mean scores for the two sub domains (i.e. daily activities and social roles) were calculated. The Life-H has been shown to have moderate to good psychometric properties in adults with physical impairments.[25]

Health-related quality of life

The 36-item Short-Form health survey (SF-36)[26] was used to measure health-related quality of life. The Short-Form 36 is a validated, self-administered questionnaire used internationally to measure health status with respect to several domains: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, pain, mental health, vitality and general health perception. All raw scores were linearly converted to a 0 to 100 scale, with higher scores indicating higher levels of functioning or well-being. The Dutch language version of the SF-36 has shown good reliability and validity.[26]

Gross motor functioning

Gross motor functioning was measured using the Gross Motor Function Measure 66 item sets.[27] These item sets derive a GMFM-66 score by testing a subsample of GMFM-66 items and entering them into

the Gross Motor Ability Estimator computer scoring programme. The Gross Motor Function Measure 66 item set has shown good reliability and validity.[27]

Social support for Exercise Behaviour

Social support is measured with the Social Support for Exercise Behaviour Scale. This scale consists of 18 items with scores ranging from 1 to 5, covering 3 domains that address the social support of family and friends: Family support: participation and involvement, Family support: rewards and punishments, and Friends support: exercising together. Total score and domain scores were calculated by summing up the scores of the questions in the particular domains. The Dutch language version of the Social Support for Exercise Behaviour Scale has shown moderate reliability.[28]

Self efficacy and Motivation

Self-efficacy is determined using the General Self-efficacy scale.[29] This scale consists of 10 questions with scores ranging from 1 to 4. All responses are summed up to obtain the total score. Intrinsic motivation is measured with the Intrinsic Motivation Inventory.[30] This inventory consists of 29 items on a 7 point scale. The response on all items was summed up to obtain the total score.

Potentially mediating variables

Four potentially mediating variables on intervention effects were specified: peak oxygen uptake, objectively measured physical activity level, objectively measured sedentary time, and self-reported physical activity level. Peak oxygen uptake was measured during progressive maximal exercise testing, and defined as the highest mean oxygen uptake during 30 seconds of exercise. An accelerometry-based ambulatory monitoring system (VitaMove) was used to objectively quantify physical behaviour over a 3-day period. From these measurements, the amounts of physical activity and sedentary time were determined. Self-reported physical activity level was measured using the Physical Activity Scale for Individuals with Physical Disabilities.[31] More detail on how these potential mediating variables were measured is given elsewhere.[15]

Statistical analyses

The current study is part of the LEARN 2 MOVE 16-24 study,[15] and therefore the power analysis was performed on physical activity. Fifty participants were required to detect a clinically relevant difference of 30 minutes per day in physical activity between control and intervention groups, with a power of 0.8 and an alpha of 0.05.

Chi square tests and Independent sample *t*-tests were applied to test for differences between groups at baseline. General Estimation Equation (GEE) analyses with exchangeable correlation structures were used to analyse the effect of the intervention. Group allocation, baseline values, measurement time and an interaction variable between group allocation and measurement time were added to the

GEE model to compare the outcomes of the intervention group with the control group for specific time intervals. These time intervals were specified as the intervention period and the total period. The control group was specified as the reference group for all analyses. IBM SPSS Statistics version 20 (Chicago, USA) was used to perform statistical analyses.

In case of significant intervention effects between the control and intervention groups, additional analyses were performed to analyse possible mediating effects of peak oxygen uptake, objectively measured physical activity level, objectively measured sedentary time, and self-reported physical activity level. Mediation was expressed as the percentage of change in the intervention effect(s) after adding the potential mediator to the GEE model.

RESULTS

Between October 2009 and September 2011, we identified a target population of 456 adolescents and young adults with cerebral palsy in the registers of participating centres. Many eligible persons had not visited the rehabilitation centre for many years. Therefore, the accuracy of their address information was uncertain. A total of 183 potential participants responded to our invitation, of whom 57 (31%) consented to participate, and 41 completed the study (Figure 1). Personal and clinical characteristics at baseline are presented in Table 1. No significant differences were found between the control and intervention group at baseline. Participants who completed the intervention completed a mean of 89% of the supervised counselling and fitness training sessions.

Table 1. Baseline personal and clinical characteristics. P-values refer to differences between the control and intervention groups.

	Total (N = 57)	Control group (N = 29)	Intervention group (N = 28)	P-value
Gender (M / F)	27 / 30	15 / 14	12 / 16	0.50
Age (years)	20 ± 3	20 ± 3	20 ± 3	0.64
Height (cm)	170 ± 10	170 ± 9	169 ± 11	0.66
Body mass (kg)	67 ± 18	65 ± 18	70 ± 18	0.24
CP type (unilateral / bilateral)*	29 / 27	15 / 14	14 / 13	0.79
GMFCS** level (I / II / III / IV)	33 / 18 / 5 / 1	16 / 9 / 3 / 1	17 / 9 / 2 / 0	0.75

* CP type was unknown for one person in the control group

** Gross Motor Function Classification System

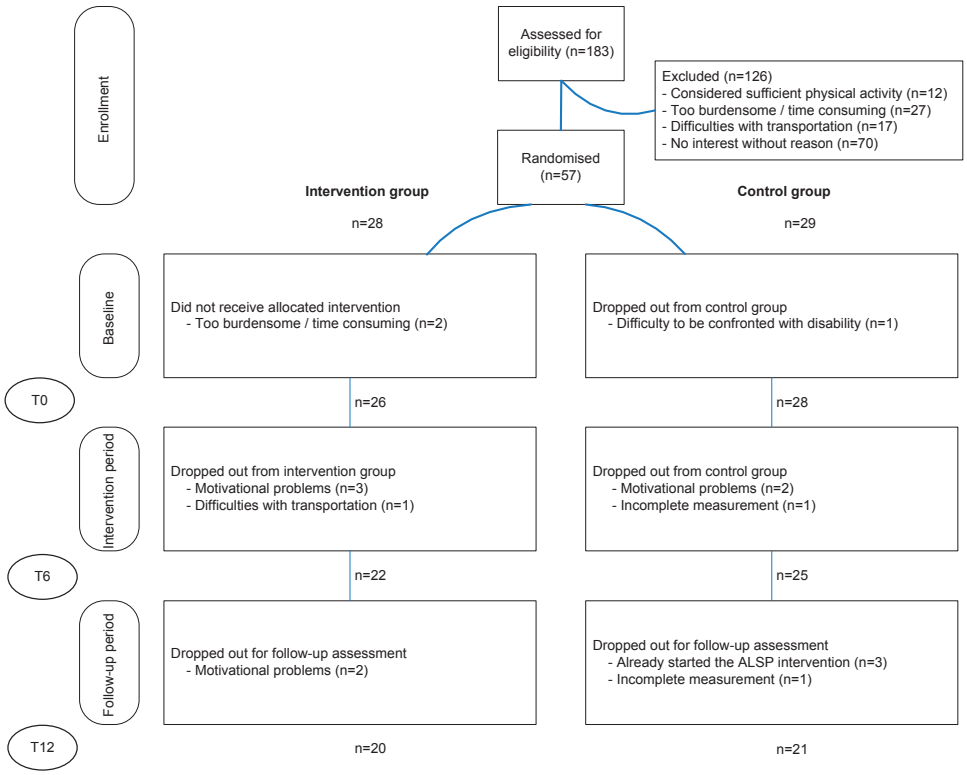

Figure 1. Flowchart of participants through the study. T0, T6 and T12 respectively represent the baseline, end of intervention, and follow-up measurement.

Intervention effects

The observed data over time are presented in Table 2, and corresponding GEE analysis results are shown in Table 3. During the intervention period, fatigue severity, as measured by the CIS-f, decreased in the intervention group compared to the control group (difference=-6.72, p=0.02). An intervention effect was noted for bodily pain during the total period (difference=15.14, p=0.01) in favour of the intervention group. Perceived mental health differed between groups during the intervention period (difference=8.00, p=0.03) and total period (difference=8.80, p=0.03). Furthermore, Family support for exercise behaviour (participation and involvement) increased during both the intervention (difference=5.38, p=0.04) and total (difference=4.52, p=0.03) period. No intervention effects were noted for fatigue, as measured with the FSS, gross motor functioning, self-efficacy, motivation, limitation in participation in life areas, or health-related quality of life domains other than mental health and bodily pain.

Table 2. Fatigue, participation and health-related quality of life outcome measures for intervention and control groups

Outcome measure	Intervention group			Control group		
	T0	T6	T12	T0	T6	T12
Fatigue (FSS)	3.65±1.38 (n=28)	3.52±1.29 (n=22)	3.50±1.08 (n=18)	3.64±1.41 (n=29)	3.53±1.05 (n=24)	3.70±1.42 (n=21)
Fatigue (CIS-f)	26.75±10.84 (n=28)	21.91±8.90 (n=22)	24.56±11.16 (n=18)	25.34±11.22 (n=29)	28.70±11.86 (n=23)	29.05±12.88 (n=20)
Participation, daily activities	7.87±1.08 (n=27)	7.74±1.18 (n=19)	7.73±1.50 (n=20)	8.14±0.97 (n=28)	8.31±0.84 (n=25)	8.27±0.89 (n=18)
Participation, social roles	7.77±1.40 (n=26)	7.51±1.83 (n=19)	8.08±1.98 (n=19)	8.25±0.88 (n=27)	8.35±0.82 (n=24)	8.51±0.59 (n=17)
HRQoL, physical functioning	64.81±26.44 (n=27)	78.86±18.96 (n=22)	79.72±19.44 (n=18)	76.72±20.54 (n=29)	77.50±27.11 (n=24)	76.90±26.34 (n=21)
HRQoL, role physical	80.56±27.15 (n=27)	78.41±35.60 (n=22)	84.72±33.36 (n=18)	75.00±34.72 (n=29)	73.96±37.94 (n=24)	69.05±46.03 (n=21)
HRQoL, bodily pain	82.59±21.60 (n=27)	82.09±25.07 (n=22)	88.61±18.39 (n=18)	80.75±23.75 (n=28)	75.78±22.45 (n=24)	73.55±19.29 (n=20)
HRQoL, general health	71.08±18.39 (n=26)	75.18±17.39 (n=22)	74.50±18.22 (n=18)	69.90±23.19 (n=29)	66.09±23.57 (n=23)	66.85±22.80 (n=20)
HRQoL, vitality	54.44±15.53 (n=27)	58.41±8.78 (n=22)	53.61±11.22 (n=18)	55.54±11.25 (n=28)	57.71±14.37 (n=24)	54.00±12.73 (n=20)
HRQoL, social functioning	85.19±13.44 (n=27)	90.34±11.53 (n=22)	86.03±15.23 (n=17)	82.76±21.24 (n=29)	89.06±17.02 (n=24)	90.00±17.01 (n=20)
HRQoL, role emotional	87.65±22.92 (n=27)	96.97±9.81 (n=22)	98.15±7.86 (n=18)	79.31±37.18 (n=29)	90.28±28.62 (n=24)	87.30±32.45 (n=21)
HRQoL, mental health	75.26±13.90 (n=27)	82.36±8.52 (n=22)	81.56±10.81 (n=18)	76.69±16.32 (n=29)	74.67±15.99 (n=24)	73.40±15.59 (n=20)
Gross motor functioning (GMFM-66)	82.57±12.07 (n=28)	82.44±11.48 (n=23)	85.50±12.41 (n=18)	83.76±14.38 (n=27)	85.22±11.62 (n=23)	85.15±12.27 (n=20)
Social support (SSEBS, total score)	46.04±10.80 (n=26)	48.67±10.15 (n=21)	48.78±12.88 (n=18)	49.86±13.46 (n=29)	42.38±10.33 (n=24)	44.50±10.03 (n=20)
Family support: participation & involvement (SSEBS)	20.46±7.57(n=28)	24.19±7.02 (n=21)	24.94±9.36 (n=18)	25.34±9.59 (n=29)	19.58±7.49 (n=24)	20.50±7.42 (n=20)
Family support: rewards and punishments (SSEBS)	13.31±1.32 (n=26)	13.57±0.98 (n=21)	13.50±1.25 (n=18)	13.62±1.08 (n=29)	13.25±1.26 (n=24)	13.25±1.33 (n=20)
Friends support: exercising together (SSEBS)	10.79±6.40 (n=28)	10.90±5.78 (n=21)	10.33±5.30 (n=18)	10.90±5.35 (n=29)	9.54±4.68 (n=24)	10.75±5.11 (n=20)
Motivation (IMI , total score)	89.93±19.61 (n=28)	86.44±21.65 (n=18)	89.18±23.46 (n=17)	87.15±18.43 (n=27)	87.05±20.45 (n=21)	87.44±21.18 (n=16)
Self-efficacy (GSE, total score)	29.46±4.34 (n=28)	30.58±5.19 (n=19)	30.12±6.72 (n=17)	30.10±4.90 (n=29)	29.17±5.43 (n=24)	30.65±4.34 (n=20)

T0 = Baseline measurement
T6 = Measurement directly after intervention completion (6 months after inclusion)
T12 = Follow up measurement (12 months after inclusion)
FSS = Fatigue Severity Scale
CIS-f = fatigue subscale of the Checklist Individual Strength
HRQoL = health-related quality of life
SSEBS = Social support for exercise behaviour scale
IMI = Intrinsic motivation inventory
GSE = General self efficacy scale
GMFM = Gross motor function measure

Table 3. GEE analysis results for T0-T6 differences and T0-T12 differences. All analyses were adjusted for baseline differences between groups on each variable. The control group is the reference group for all GEE analyses.

Outcome measure	Difference T0-T6 (95% CI)	Difference T0-T12 (95% CI)
Fatigue (FSS)	-0.19 (-0.63, 0.25)	-0.53 (-1.08, 0.02)
Fatigue (CIS-f)	**-6.72 (-12.44, -0.99)**	-5.84 (-12.93, 1.26)
Participation, daily activities	-1.04 (-0.34, 0.13)	-0.22 (-0.50, 0.07)
Participation, social roles	-0.21 (-0.55, 0.12)	0.04 (-0.60, 0.53)
HRQoL, physical functioning	3.11 (-8.31, 14.53)	5.45 (-5.13, 16.04)
HRQoL, role physical	4.15 (-15.10, 23.40)	16.27 (-8.65, 41.20)
HRQoL, bodily pain	5.47 (-7.12, 18.06)	**15.14 (3.44, 26.85)**
HRQoL, general health	7.41 (-3.81, 18.62)	10.28 (-1.42, 21.98)
HRQoL, vitality	1.64 (-4.96, 8.23)	-0.40 (-6.92, 7.71)
HRQoL, social functioning	1.76 (-5.88, 9.41)	-3.08 (-12.64, 6.49)
HRQoL, role emotional	5.94 (-5.01, 16.90)	11.09 (-1.22, 23.39)
HRQoL, mental health	**8.00 (0.96, 15.05)**	**8.80 (0.99, 16.61)**
Gross motor functioning	-1.94 (-4.69, 0.82)	-0.08 (-1.99, 1.83)
Social support, total score	5.50 (-12.84, 1.83)	4.87 (-0.89, 10.62)
Family support: participation & involvement	**5.38 (0.03, 10.74)**	**4.52 (0.39, 8.65)**
Family support: rewards and punishments	-0.31 (-1.12, 0.49)	0.34 (-0.32, 1.00)
Friends support: exercising together	1.80 (-1.24, 4.83)	-0.611 (-3.71, 2.49)
Motivation	0.34 (-10.45, 11.13)	-0.20 (-9.24, 8.85)
Self-efficacy	0.91 (-2.11, 3.92)	0.96 (-1.86, 3.77)

T0 = Baseline measurement
T6 = Measurement directly after intervention completion (6 months after inclusion)
T12 = Follow up measurement (12 months after inclusion)
FSS = Fatigue Severity Scale
CIS-f = fatigue subscale of the Checklist Individual Strength
HRQoL = health-related quality of life
GMFM = Gross motor function measure
SSEBS = Social support for exercise behaviour scale
IMI = Intrinsic motivation inventory
GSE = General self efficacy scale
Bold text indicates statistical significance

Mediating effects

Results of the additional analyses on mediating effects are shown in Table 4. Physical behaviour explains intervention effects on fatigue severity (22.6%) (CIS-f), bodily pain (9.3%) and perceived mental health (28.1%), whereas physical fitness explains 16.0%, 9.7% and 22.6%, respectively, of intervention effects for those same outcome measures. Intervention effects on social support were mediated for only 2.6% by physical fitness, whereas no mediating effects of physical behaviour was found.

Table 4. Mediating effects of physical behaviour and fitness on fatigue, bodily pain and mental health

Mediating variables*	Outcome measures			
	Fatigue (CIS-f)	Bodily pain (SF-36)	Mental health (SF-36)	Family support exercise behaviour (SSEBS)
Peak oxygen uptake	16.0%	9.7%	22.6%	2.6%
Objectively measured physical activity level	6.2%	-	26.8%	-
Objectively measured sedentary time	5.9%	-	28.1%	-
Self-reported physical activity level	22.6%	9.3%	25.3%	-

* expressed as a percentage of change in the intervention effect after adding the potential mediator to the GEE model.
CIS-f = fatigue subscale of the Checklist Individual Strength
SF-36 = 36-item Short-Form health survey
SSEBS = Social support for exercise behaviour scale

DISCUSSION

To our knowledge, this is the first longitudinal study to evaluate the effect of a lifestyle intervention on fatigue, social participation, gross motor functioning and health-related quality of life in adolescents and young adults with cerebral palsy, and study the mediating effects of physical behaviour and fitness. The lifestyle intervention was effective in reducing fatigue severity and in increasing health-related quality of life with respect to bodily pain and mental health in the intervention group compared to the control group. In addition, the intervention increased the family support for the person's exercise behaviour, by participating and being involved in planning exercise activities. No intervention effects were noted for limitations in social participation, gross motor functioning or other health-related quality of life domains. Furthermore, motivation and generic self-efficacy were not altered by following the lifestyle intervention.

Additional analyses showed that the observed differences in family support for exercise between the intervention and control groups could be explained to a little extent by specific variables of physical fitness and physical behaviour. On the other hand, the observed differences between the intervention and control groups on the remaining parameters could be explained to a considerable extent by single variables of physical fitness and physical behaviour, specifically by self-reported physical activity and physical fitness. Apparently, self-reported physical activity and physical fitness levels are substantial mediators of the effect of the Active Lifestyle and Sports Participation intervention on fatigue, bodily pain and mental health. Therefore, apart from their direct health benefits, these results

stress the importance of favourable physical behaviour and sufficient physical fitness for adolescents and young adults with cerebral palsy.

At baseline, participants were more fatigued compared to the general population, as measured by FSS (3.6 vs. 3.0)[20] and CIS-f (26.0 vs. 24.4).[32] Thus, fatigue in persons with cerebral palsy may be a problem even at a young age. The Active Lifestyle and Sports Participation intervention was effective in decreasing fatigue severity during the intervention period. This finding is consistent with results from Vogtle et al., who found that fatigue levels in ambulatory adults with cerebral palsy decreased following an exercise training programme.[6] However, Vogtle et al. found these effects during both intervention and follow-up periods, whereas observed effects in the present study did not persist into the follow-up period of our current study. To facilitate long-term effectiveness, booster strategies, such as phone, mail or internet support, could augment the Active Lifestyle and Sports Participation intervention, as these strategies seem effective for maintaining lifestyle intervention effects over the long term.[33]

In contrast to CIS-f scores, FSS scores did not change following the Active Lifestyle and Sports Participation intervention. This discrepancy may reflect different constructs of fatigue assessed by these questionnaires. The FSS measures the impact of fatigue on specific types of functioning, whereas the CIS-f more specifically measures the severity of the perceived fatigue.[22] In adults with cerebral palsy, fatigue may not affect functioning comparably to able-bodied persons because their functioning could have been adapted or limited from an early age.

At baseline, mean scores for difficulty in daily activities and social roles on the Life-H 3.0 were 7.9 and 7.8, respectively. These scores are somewhat higher than participation levels among adults with bilateral spastic cerebral palsy, who have mean scores of 7.5 and 7.7, respectively, on these domains.[34] These higher social participation levels could be explained by the large percentage of persons with unilateral cerebral palsy in the current study, as well as their younger age. The Active Lifestyle and Sports Participation intervention was not effective in decreasing restrictions in daily activities or social roles. This finding partially contrasts with those of van Wely et al. among school-aged children with cerebral palsy, who found positive long-term effects on activities in and around the house (domestic life) following a lifestyle intervention.[8] Similar to our study, these children did not experience improvements in performance of mobility and leisure activities related to moving outside the house, in the local community, in the wider environment or in sports.

Baseline scores for health-related quality of life domains (except bodily pain) among our adolescent and young adult participants with cerebral palsy were lower compared to Dutch reference values.[26] This finding is consistent with studies on adolescents[35] and adults with cerebral palsy,[10, 36, 37] which also show subnormal levels of perceived health-related quality of life, specifically in physical functioning.

Exercise has been shown to reduce pain in adults with cerebral palsy,[38] and to increase cerebral palsy-specific health-related quality of life over time in children.[9] Cerebral palsy-specific health-related quality of life evaluates self-perceived pain and fatigue, in addition to functional level in movement, balance, upper-limb activities, speech and communication. Positive effects on pain and fatigue were confirmed by results of the present study, as fatigue severity and perceived bodily pain decreased following the Active Lifestyle and Sports Participation intervention. In addition, the present lifestyle intervention was effective in improving mental health. Despite low baseline health-related quality of life, other health-related quality of life domains did not change following the Active Lifestyle and Sports Participation intervention.

Gross motor functioning score as assessed with the Gross Motor Function Measure-66 was around 83 at baseline. This is higher compared to another study on adolescents with cerebral palsy.[39] The relatively high score on gross motor functioning is possibly explained by the relative lack of severity of the included sample of the present study. Bartlett et al. found that pain and gross motor functioning are related in adolescents with cerebral palsy.[39] In the present study, the observed intervention effect on pain severity did not led to significant changes in gross motor functioning.

Loss to follow-up was 39% in the intervention group and 34% in the control group (Figure 1). A type II error may have occurred in the longitudinal analysis due to a higher drop-out rate than expected. We were not able to perform the remaining measurements on the persons that dropped out of the study. Due to multiple testing in the current study, one should be careful to draw strong conclusions from single significant findings.

Although a sample size of 57 is relatively large considering the prevalence of spastic cerebral palsy, the absolute number is quite small. However, we do not expect that the results would have differed with fewer participant drop-outs considering that the clinically relevant differences on non-significant outcome measures are not included in the 95% CI of the analyses.

Our study participants had relatively high gross motor functioning (89% had GMFCS level I or II) and intellectual functioning (I.Q. >70). It can be hypothesised that lifestyle intervention effects can be affected by levels of gross motor and intellectual functioning. Future research is required to clarify the effectiveness of lifestyle interventions in study samples with lower levels of gross motor functioning and intellectual functioning.

Clinical messages

- The Active Lifestyle and Sports Participation intervention was effective in decreasing fatigue and in increasing social support and health-related quality of life regarding bodily-pain and self-perceived mental health.

- The observed effects of the Active Lifestyle and Sports Participation intervention were to a considerable extent mediated by physical behaviour and fitness.

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Chapter 11

Cost-utility analysis of a lifestyle intervention in adolescents and young adults with spastic cerebral palsy

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ABSTRACT

Objective

To evaluate the cost-utility of a lifestyle intervention among adolescents and young adults with CP.

Design

Single blind, randomised controlled trial.

Setting

Six university hospital/clinics in The Netherlands.

Participants

Fifty-seven adolescents and young adults with spastic cerebral palsy classified in GMFCS level I-IV.

Interventions

A six-month lifestyle intervention consisting of physical fitness training combined with counselling sessions focused on physical behaviour and sports participation.

Main Outcome Measures

Data on quality of life, direct medical costs and productivity costs were collected using standardised questionnaires. Quality adjusted life years were derived from the short-form 36 questionnaire using the short-form 6D.

Results

Quality of life remained stable over time for both groups. No significant differences between groups were found for direct medical costs or productivity costs. A cost-utility ratio of -€23.664 per QALY was found for the lifestyle intervention compared to no treatment.

Conclusions

Results of the present study are exploratory, but indicate that implementing a lifestyle intervention for CP-population might be cost-effective or cost-saving as compared to offering no intervention to improve physical behaviour and fitness. However, the large ranges of uncertainty for the cost-utility ratio should be taken into account and, therefore, results should be interpreted with caution.

INTRODUCTION

Cerebral palsy (CP) is the most common cause of physical disability in paediatric rehabilitation medicine.[1] Representing a group of permanent disorders of the development of movement and posture, it causes activity limitation that is attributed to non-progressive disturbances that occurred in the developing foetal or infant brain.[2] For the general population, sufficient levels of physical activity (PA) and physical fitness are known to provide psychological and physiological benefits.[3, 4] An active lifestyle may be even more important in persons with CP since it is assumed that it optimises and maintains their physical performance in daily life[5] and prevents the development of secondary health problems later in life.[6] Nevertheless, research has consistently shown that people with CP have low levels of physical fitness,[7-10] low levels of PA[11-14] and high sedentary time.[15] The Active Lifestyle and Sports Participation (ALSP) intervention has been developed in The Netherlands, aiming to improve physical behaviour and fitness in adolescents and young adults with childhood onset physical disabilities.[16] The effectiveness of this intervention is being studied in adolescents and young adults with spastic CP in the LEARN 2 MOVE 16-24 study.[17]

Economic evaluations are a prerequisite for the reimbursement and implementation of interventions in many Western countries since it provides valuable information on the relative efficiency compared to usual care. Costs are preferably determined from a societal perspective in which all relevant costs are included,[18] such as costs incurred by patients and informal caregivers. For example, productivity costs often account for significant proportions of total healthcare expenditures.[19] Following the ALSP intervention might reduce these productivity costs, which could possibly compensate for the additional cost of the intervention.

The cost-utility of a lifestyle intervention has, to our knowledge, never been evaluated in an adolescent or young adult population with CP. The lacking of such analyses could possibly explain why lifestyle interventions are rarely implemented in rehabilitation medicine in The Netherlands. Therefore, the aim of the present study was to estimate the cost-utility of a lifestyle intervention compared with usual care in adolescents and young adults with spastic CP.

MATERIAL & METHODS

This cost-utility study was performed in conjunction with the multi-centre randomised clinical trial of the LEARN 2 MOVE 16-24 study, of which more details can be found in the study design protocol.[17] In short, adolescents and young adults with spastic unilateral or bilateral CP were eligible if they met each of the following inclusion criteria: 1) age 16 to 24 years; 2) GMFCS level I-IV; and 3) a spastic type of CP as measured with the Modified Ashworth Scale.[20] Exclusion criteria were: 1) disabilities

other than CP that affected daily PA or aerobic capacity; 2) contraindication to (maximal) exercise; 3) PA level at baseline exceeding 2SD scores above the mean PA level of a CP population; or 4) severe cognitive/intellectual disorders or insufficient comprehension of the Dutch language that hamper the understanding of instructions of the intervention and assessments. The study had a multi-centre, single blind, randomised controlled design. After baseline measurement, participants were stratified according to their level on the Gross Motor Functioning Classification System (GMFCS)[21] to obtain an equal distribution of GMFCS levels between the experimental and control group. Within each stratum and for each centre, participants were randomly allocated (1:1) to these groups. The experimental group received the ALSP intervention. The control group received no intervention to improve physical behaviour and fitness, which is usual care in The Netherlands. All participants provided written informed consent. The medical ethics committee of the Erasmus Medical Centre approved the study and local approval was granted by all participating centres.

Intervention

The 'Active Lifestyle and Sports Participation' intervention had a duration of 6 months and was developed for adolescents and young adults with physical disabilities.[16] This intervention aimed to permanently increase PA and fitness levels and to reduce sedentary time by promoting behavioural changes toward a more active lifestyle and consisted of three parts: 1) counselling on daily PA, which was based on motivational interviewing and guided by a personal coach to discuss barriers and facilitators of physical behaviour; 2) physical fitness training, which consisted of supervised centre and home-based training and focused on increasing aerobic capacity and muscle strength; and 3) counselling on sports participation to find suitable, accessible and appropriate sports and sports facilities in the person's day-to-day environment. The intervention has been described in detail elsewhere.[17]

Measurements

The present paper focused on cost-utility which was primarily conducted from a societal perspective, but healthcare perspective was also appraised. Data on quality of life, direct medical costs and productivity costs were collected using standardised questionnaires: 1) prior to starting the intervention (T0); 2) directly after finishing the intervention, which is 6 months after the start of the intervention (T6); and 3) at follow-up, six months after finishing the intervention (T12). All costs were based on Euro 2009 cost data from the Dutch manual for cost research.[22] The primary outcome measures of the randomised clinical trial are levels of PA and physical fitness. Results of the effectiveness of the ALSP intervention on these outcome measures will be reported in forthcoming publications.

Quality of life

Quality of life was measured using the Short Form-36 (SF-36, version 1 US).[23] However, the SF-36 questionnaire cannot directly be used in economic evaluations because it does not produce

a preference based single index able to be combined with life duration in order to obtain quality adjusted life years (QALYs), the metric used in cost-utility analysis.[24] Therefore, SF-36 responses were converted into SF-6D utility scores using the University of Sheffield algorithm. The SF-6D is an algorithm for describing health and is composed of six multi-level dimensions (physical functioning, role limitation, social functioning, pain, mental health and vitality). This index ranges from 0 to 1 and introduces preference weights to generate health state utility values needed to construct QALYs.[25]

Intervention costs

The intervention costs included a consultation by a rehabilitation physician and utilisation of allied healthcare. The total number of contacts was multiplied by the 2009 reference unit prices of the corresponding health care service to calculate the total intervention costs.[26]

Direct medical costs

We used the Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness' (TiC-P) to collect data on direct costs.[27] The first part of the TiC-P consists of questions on the number of contacts with health care providers in the previous 3 months. Bottom-up methodology was used to calculate the total direct medical costs; that is, the total number of medical contacts (outpatient visits, hospital length of stay, etc.) was multiplied by the 2009 reference unit prices of the corresponding health care service. Furthermore, the TiC-P questionnaire determined frequency and dosage of medication use. Wholesale medication costs were valued by a Dutch government website.[28] To estimate the costs over the period of half a year, we used linear extrapolation, i.e. we assumed that the quartile costs measured at T6 and T12 could be taken as representative to calculate costs of the preceding six months. The annual costs were calculated by adding up the costs per half year. This way, the yearly overall direct medical costs of patients with spastic CP was assessed.

Productivity costs

The productivity costs were measured with the second part of the TiC-P, which includes the short form of the Health and Labour questionnaire (SF-HLQ) for collecting data on productivity losses.[29] The SF-HLQ consists of three modules that measure productivity losses: costs due to absence from paid work, reduced efficiency at paid work, and difficulties with job performance at unpaid work.

The days of absence from paid work were valued by the friction method (elasticity factor = 0.8)[30] and were calculated taking the number of days and hours of paid employment per week into account. Reference prices were applied to value the absence from paid work, which ranged from €8.67/hr to €34.03/hr depending on gender and age.[31]

The Osterhaus method was applied to calculate costs associated with reduced efficiency at paid work.[32] This method multiplies the number of days hindered with one minus the indicated efficiency

for these days. Respondents with paid jobs were asked to estimate the number of extra hours they should have worked to compensate for the health-related work productivity loss incurred. Reference prices were applied to value these extra hours of work, which ranged from €8.67/hr to €34.03/hr depending on gender and age.[31]

An impediment score was estimated to assess the amount of difficulty experienced in performing unpaid work. Unpaid work was defined as household work, shopping, childcare and work around the house. Hours of unpaid work that were taken over by others were valued by €8.64/hr for unpaid help and €31.94/hr for paid help.[31]

Statistics

Differences between the intervention and control group were assessed by means of independent sample t-tests (for normally distributed variables) or Pearson chi square tests and Mann-Whitney U-tests (for variable fractions). Using non-parametric bootstrapping (2500 observations at random from the available patient sample), the degree of uncertainty for costs, QALY's and the cost utility plane was examined on the so called cost-utility plane. In addition, an acceptability curve was generated to indicate the probability that the intervention has lower incremental costs per QALY gained than various thresholds for the maximum willingness to pay for an extra QALY.

Table 1. Clinical characteristics at baseline of the complete study sample and specified per allocated group. P-values are given for differences between the control and intervention group.

	All	Control group	Intervention group	P-value
N	57	29	28	-
Gender (M / F)	27 / 30	15 / 14	12 / 16	0.50
Age (years)	20 ± 3	20 ± 3	20 ± 3	0.64
Height (cm)	170 ± 10	170 ± 9	169 ± 11	0.66
Body mass (kg)	67 ± 18	65 ± 18	70 ± 18	0.24
CP type (unilateral / bilateral)*	29 / 27	15 / 14	14 / 13	0.79
GMFCS level (I / II / III / IV)**	33 / 18 / 5 / 1	16 / 9 / 3 / 1	17 / 9 / 2 / 0	0.75
Primary occupation (%)				0.36
School	73	79	68	
Paid work	9	10	7	
Unemployed due to health problems	11	4	18	
Unemployed due to other reasons	7	7	7	
Paid work; primary or secondary	29	28	30	0.87
Average work duration / week (hr)	16.8 ± 12.0	17.8 ± 11.9	12.8 ± 4.5	0.75
Average net income / hour (€)	7.53 ± 2.68	7.76 ± 3.13	7.23 ± 2.21	0.75
Sports participation (%)	60	66	54	0.36
Sports duration / week (hr)	2.1 ± 3.0	2.4 ± 3.6	1.7 ± 2.2	0.34

* CP distribution of one person from the control group is unknown

** Gross Motor Function Classification System

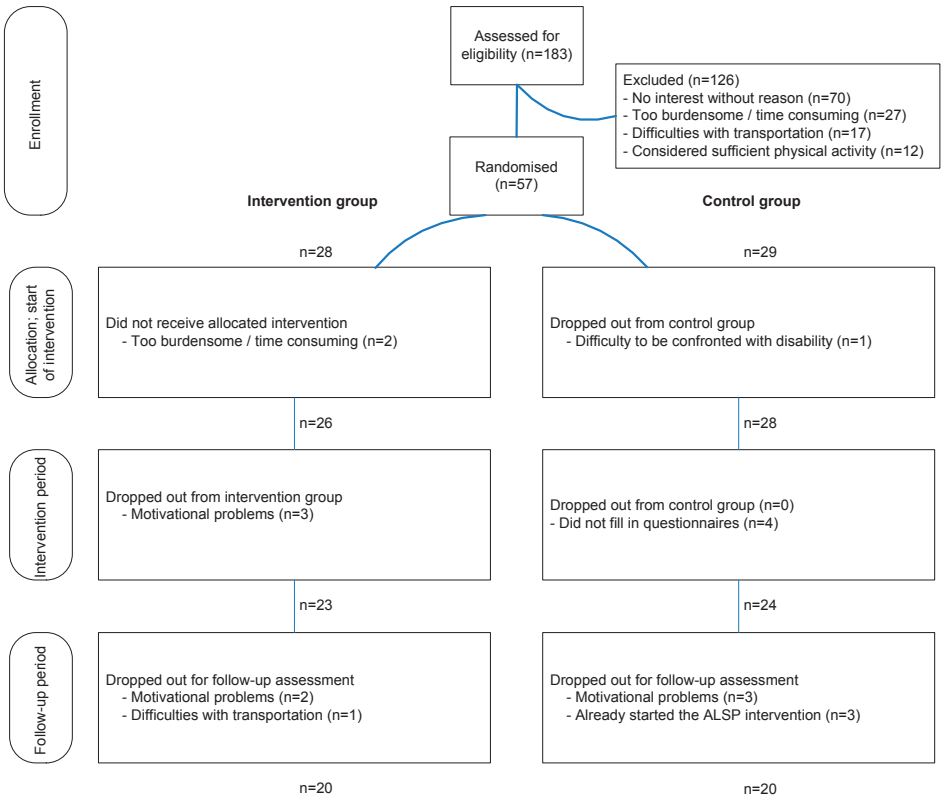

Figure 1. Flowchart of participants through the study.

RESULTS

We identified a target population of 456 adolescents and young adults with CP from the participating centres. Many of them had not been seen at the participating centres for years and therefore, the accuracy of their address information was uncertain. A total of 183 potential participants responded to our invitation, of whom 57 (31%) consented to participate, and 40 completed the total study (figure 1). Participants that completed the intervention followed, on average, 89% of the supervised training sessions. The clinical characteristics at baseline are presented in Table 1 for the complete study sample and specified per allocated group, showing that control and intervention groups did not differ significantly on clinical characteristics.

Quality of life

Figure 2 shows the SF-6D outcomes over time for the intervention and control group. The quality of life scores did not significantly differ between control and intervention groups at any moment in time (Table 2).

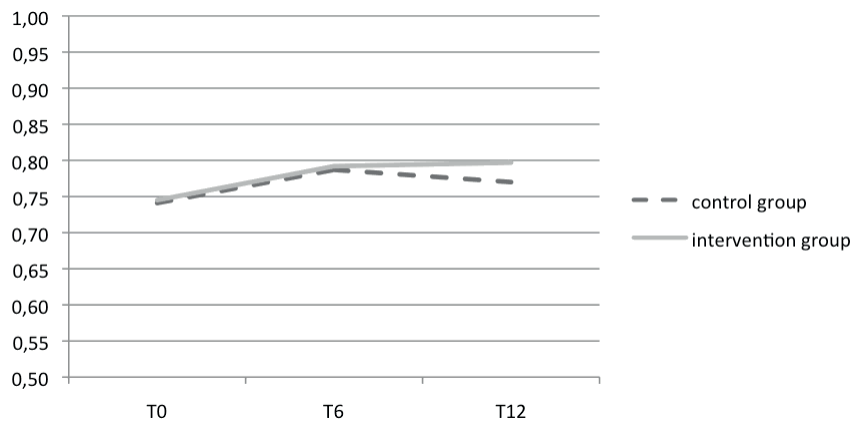

Figure 2. Quality of life (utility values) over time for the intervention and control group as measured with the SF-6D. No significant difference in quality of life was found between groups at any moment in time.

Intervention costs

The total costs of the intervention were €496 per participant. This included one consultation with a rehabilitation physician (€96). Furthermore, twelve fitness sessions of an hour were provided for the fitness training (12 * €50 = €600) which was in group context with, on average, 3 participants at a time (€600 / 3 = €200). Finally, six individual counselling sessions of half an hour on daily activity (6x €25 = €150) and two sessions of half an hour on sports advice (2x €25 = €50) were deployed.

Direct medical costs

A summary of the direct medical costs per 3 months (excluding intervention costs) is given in Table 3. Frequent used healthcare were the general practitioner, psychological care, medical specialists and allied healthcare. At baseline 44% of the intervention group used medication and 38% of the control group. Most frequently used medications were those for pain, epilepsy or spasticity.

The direct medical costs per patient did not differ significantly between the intervention and the control group at the three measurement moments. Annual direct medical costs (excluding intervention costs) for both the intervention and the control group are presented in Table 4. The direct medical costs for the intervention and the control group were €840 (SD 757) and €1602 (SD

Table 2. Quality Adjusted Life Year scores over time specified per allocated group.

	SF-6D index scores (mean ± SD)			p-value
Measurement	Control group	Intervention group	Mean difference	
T0 (n = 28/28)	0.741 ± 0.116	0.745 ± 0.098	-0.004	0.90
T6 (n= 24/23)	0.787 ± 0.125	0.792 ± 0.116	-0.005	0.90
T12 (n= 20/20)	0.770 ± 0.122	0.797 ± 0.087	-0.027	0.42

Table 3. Mean (median) direct medical costs (€) per respondent for the past 3 months per measurement moment.

	T0		T6		T12	
	Intervention (n=28)	*Control (n=29)*	*Intervention (n=22)*	*Control (n=24)*	*Intervention (n=20)*	*Control (n=20)*
General practitioner	22 (0)	14 (0)	18 (0)	25 (0)	18 (28)	19 (0)
Industrial physician	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Medical specialist	55 (0)	40 (0)	66 (0)	16 (0)	63 (0)	24 (0)
Allied healthcare	78 (0)	76 (0)	68 (0)	110 (0)	58 (0)	101 (0)
Psychological care	102 (0)	158 (0)	54 (0)	174 (0)	28 (0)	118 (0)
Social work	39 (0)	16 (0)	0 (0)	89 (0)	3 (0)	23 (0)
Alternative healthcare	0 (0)	20 (0)	0 (0)	37 (0)	0 (0)	29 (0)
Hospital admission	0 (0)	29 (0)	0 (0)	72 (0)	0 (0)	0 (0)
Medication	12 (0)	17 (0)	13 (0)	12 (0)	14 (0)	16 (0)
Total	308 (125)	371 (77)	219 (140)	537 (254)	184 (106)	330 (87)
SD	432	673	259	623	208	620
25 percentile	7	0	0	55	28	0
75 percentile	476	457	334	961	298	464

SD. standard deviation

2156), respectively (p=0.40). No significant differences were found for any of the cost components of the direct medical costs.

Productivity costs

Absence from paid work

Table 5 presents the productivity costs per month due to absence or reduced efficiency at paid or unpaid work. The annual costs due to absence from paid work per patient were €82 (SD 332) and €27 (SD 122) for the intervention and control group, respectively (p=0.80)

Reduced efficiency at paid work

The share of persons with reduced efficiency at paid work is presented in Table 5 and was high at the 6 month measurement for both groups (33% and 22%) and low at the measurement at 12 months (0% for both groups). The differences between both groups were never significantly different. The annual

Table 4. Annual direct medical costs per patient based on the Euro 2009 cost data from the Dutch manual for cost research.

	Mean number of visits or lying days per patient year (n = 20/20)		Median costs per patient		Mean costs per patient		SD		P*
	Control	*Intervention*	*Control*	*Intervention*	*Control*	*Intervention*	*Control*	*Intervention*	
General practitioner	2.9	2.6	56.0	56.0	81.2	72.8	88.0	70.6	0.93
Psychological care	5.8	1.9	0.0	0.0	578.2	174.9	1335.9	519.4	0.68
Industrial physician	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.00
Medical specialist	0.9	2.7	0.0	193.0	86.9	260.6	116.7	416.7	0.21
Allied healthcare	19.7	10.7	0.0	0.0	466.6	267.0	701.6	379.1	0.64
Social work	2.8	0.1	0.0	0.0	182.0	6.5	403.2	29.1	0.07
Alternative healthcare	2.8	0.0	0.0	0.0	146.1	0.0	418.1	0.0	0.08
Hospital admission	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.00
Medication	-	-	4.7	0.0	60.7	58.7	117.0	129.5	0.66
Total	-	-	1001.1	766.2	1601.7	840.5	2155.7	756.7	0.40

*Mann-Whitney U (two tailed)

costs due to reduced efficiency at paid work were €17 (SD 74) and €72 (SD 320) for the intervention and control group respectively (p=0.82).

Reduced efficiency at unpaid work

At baseline about 3.6% of the patients in the intervention group and 13.8% of the patients in the control group had housekeeping tasks taken over. These fractions remained stable during the intervention period and did not differ significantly between the intervention and the control group at any of the measurement moments. The annual costs of taking over housekeeping tasks were €10 (SD 46) and €55 (SD 244) for the intervention and control group, respectively (p=0.99).

Cost utility

Table 6 shows the total annual costs and QALY's for the intervention and the control group. The mean difference in annual total costs was €310 lower for the intervention group compared with the control group (p=0.55). Furthermore, compared to the control group, the intervention group gained 0.0131

Table 5. Productivity costs due to absence or reduced efficiency at paid or unpaid work in the past month per measurement moment (Euro 2009)

	T0		T6		T12	
	Control (n=29)	*Intervention (n=28)*	*Control (n=24)*	*Intervention (n=22)*	*Control (n=20)*	*Intervention (n=20)*
Number of respondents with a paid job	8	8	10	8	6	10
Share of respondents absent (%)	0	0	10.0	12.5	0	10.0
Number of days absent. mean (SD)	0 (0)	0 (0)	0.1 (0.3)	0.1 (0.4)	0 (0)	0.2 (0.6)
Share of respondents with reduced efficiency at paid work (%)	12.5	12.5	22.2	33.3	0.0	0.0
Share of respondents with reduced efficiency at unpaid work (%)	13.8	3.6	4.2	4.5	5.0	10.0
Costs due to absence from work (mean, SD)						
Per respondent with a paid job	0 (0)	0 (0)	9.1 (28.7)	2.7 (7.8)	0 (0)	24.8 (78.3)
Per respondent	0 (0)	0 (0)	3.8 (18.6)	1.0 (4.7)	0 (0)	12.4 (55.4)
Costs due to reduced efficiency at paid work (mean, SD)						
Per respondent with a paid job	2.0 (5.7)	24.7 (70.0)	32.6 (77.4)	7.2 (19.3)	0 (0)	0 (0)
Per respondent	0.6 (3.0)	7.1 (37.4)	13.6 (51.1)	2.6 (11.7)	0 (0)	0 (0)
Costs due to reduced efficiency at unpaid work per respondent (mean, SD)						
Per respondent	14.3(50.0)	0 (0)	5.8 (28.4)	0 (0)	2.2 (9.7)	1.7 (7.7)
Total productivity costs (mean, SD)						
Per respondent	14.9(50.0)	7.1 (37.4)	23.2 (73.0)	3.6 (16.4)	2.2 (9.7)	14.1 (55.5)

QALY (p=0.76). This resulted in a societal average cost-utility ratio of -€23.664 per QALY. However, the variance around this cost-utility ratio was substantial. The bootstrapping method showed that the simulated 95% confidence interval for the cost-utility ratio ranged from -€167.992 to +€129.007. The cost-utility plane (Figure 3) shows that the intervention was dominant in 75% of the cases (positive health effects and cost savings) and inferior for 8% of the cases. The probability that the intervention had positive health effects was 78% (quadrant I & II), the probability for cost savings was 89% (quadrant II & III). The acceptability curve showed a probability of 86% that the cost per QALY were lower than €20.000, which is a generally accepted threshold in The Netherlands.

When only direct medical costs and intervention costs were included, average incremental costs per patient were -€265 for persons following the ALSP intervention and the average costs per QALY was -€20.229. The bootstrapped confidence interval for the cost-utility ratio was again wide, ranging from -€141.368 to +€134.174. The probability for costs savings was 85%. The acceptability curve showed a probability of 83% that the cost per QALY was lower than €20.000; an amount which generally accepted in The Netherlands.

DISCUSSION

To our knowledge, this is the first cost-utility study on a lifestyle intervention for adolescents and young adults with spastic CP. There were no significant differences in annual direct medical costs, annual productivity costs and total annual costs between the intervention and control group. In contrast to findings in the literature,[18, 19] our results suggest that productivity costs contribute little to the total costs. This might be explained by the small proportion or persons in the study sample that had paid work as primary (9%) or secondary (20%) occupation. Another explanation for the low productivity costs may be that CP is a congenital condition. Therefore, in contrast to persons with acute disabilities, persons with CP may have occupations that suit their capabilities, keeping their reduced efficiency costs low. Furthermore, the majority of the participants were living with their parents, possibly explaining the low reduced efficiency costs for unpaid work, as relatives may take over these unpaid tasks anyway. QALY did not significantly differ between the two groups at any time and was fairly constant over time. Apparently, the ALSP intervention had no or minimal effects on this generic outcome. Moreover, the aim of the intervention was to affect clinical outcomes like physical activity or fitness and was not directly targeted at improving generic outcomes like QALY's.

With a cost-utility ratio of -€23.664 per QALY, our study revealed a considerable probability that the ALSP intervention is cost saving or cost effective as compared with offering no intervention to improve movement behaviour and fitness. This is in line with results of a review on cost-utility studies of lifestyle interventions in the healthy population.[33] However, the small variance in QALY's between

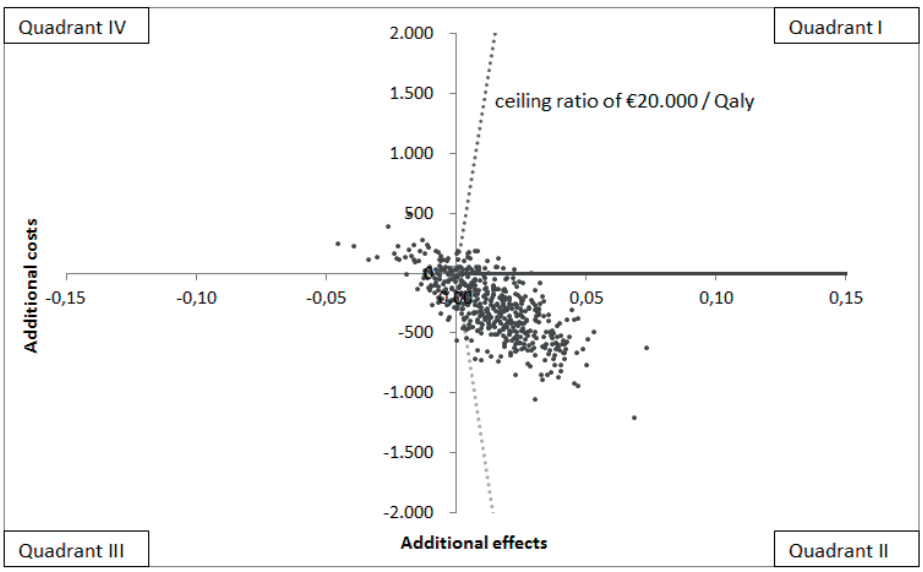

Figure 3. Cost-utility plane. The joint distribution of costs (y-axis) and effects (x-axis) based on the LEARN 2 MOVE trial population were calculated over 2500 replications of the study data using the bootstrap resampling method and plotted on the cost-utility plane. Each point in the scatter plot represents 1 bootstrap iteration. The probability that the intervention had positive health effects is shown in quadrant I & II, whereas the probability for cost savings is found in quadrant II & III. The acceptability curve is represented by the dotted line. All points right from this line fall below the ceiling ratio of €20.000 / QALY.

Table 6. Total annual costs and quality adjusted life years (QALY's) per patient in the intervention and the control group expressed as mean (SD).

	Intervention group	Control group	Incremental	P*
Intervention costs (€) (n = 20/20)	496 (0)	0 (0)	496	-
Direct medical costs (€) (n = 20/20)	841 (757)	1602 (2156)	-761	0.40
Direct medical costs including intervention costs (€) (n = 20/20)	1337 (757)	1602 (2156)	-265	0.45
Total productivity costs (€) (n = 20/20)	109 (343)	154 (494)	-45	0.84
Costs due to absence from paid work (€)	82 (332)	27 (122)	55	0.80
Costs due to reduced efficiency at paid work (€)	17 (74)	72 (320)	-55	0.82
Costs due to reduced efficiency at unpaid work (€)	10 (46)	55 (244)	-45	0.99
Total costs (€) (n = 20/20)	1446 (848)	1756 (2187)	-310	0.55
Quality adjusted life years (QALY) (n = 20/20)	0.7921	0.7790	0.0131	0.76

*Mann-Whitney U (two tailed)

participants, the substantial variance for total costs (Table 5), combined with a small sample size resulted in a wide confidence interval for the cost-utility ratio. This implies considerable uncertainty whether to adopt the ALSP intervention from a cost-utility perspective. The uncertainty analysis, however, indicated that there is a probability of 78% that the ALSP intervention produces positive health effects, 89% that the cost per QALY gained is lower than €20.000 and 86% that the intervention saves societal costs. Although these results are exploratory, they indicate that implementing a lifestyle intervention for CP-population might be cost-effective or cost-saving.

Limitations

We applied Dutch reference unit prices to calculate intervention costs. However, costs which are expected to account for a large proportion of total costs are ideally calculated with micro costing methodology, because this methodology provides cost estimations that most accurately reflect actual costs. As this methodology is time consuming, especially when administrative information systems are absent or inadequate, the use of Dutch reference prices had our preference.

The power of this cost-utility study was poor, as reflected in the wide confidence intervals for cost differences, implying that the study results should be interpreted with caution. This uncertainty is a common problem in cost-utility studies performed alongside randomised controlled trials, in which sample sizes are based on detecting relevant differences in clinical effects. Because the distribution of cost data is typically heavily skewed, large study populations are needed[34] which often results in unfeasibly large required sample sizes.

Conclusion

Results of the present study are exploratory, but indicate that implementing a lifestyle intervention for CP-population might be cost-effective or cost-saving as compared to offering no intervention to improve physical behaviour and fitness. However, the large ranges of uncertainty for the cost-utility ration should be taken into account and, therefore, results should be interpreted with caution. Further research with larger samples is required to reduce the uncertainty of these estimations.

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Chapter 12

General Discussion

The primary aim of this thesis was to evaluate both the short-term and long-term effectiveness of the Active Lifestyle and Sports Participation (ALSP) intervention on physical behaviour and physical fitness among adolescents and young adults with spastic cerebral palsy (CP). Additionally, the intervention's effectiveness on fatigue, participation, health-related quality of life (HRQoL) and gross motor functioning was studied. Baseline levels of movement behaviour, physical fitness and fatigue were described and compared with those for a non-disabled population to understand the physical condition of adolescents and young adults with spastic CP. Furthermore, insight into working mechanisms was gained by analysing cross-sectional and longitudinal interactions between physical behaviour, physical fitness and fatigue level. The present chapter will interpret the study results and discuss them within the context of the published literature. Methodological issues related to the study will be discussed. Finally, the present chapter describes the clinical implications of the study, as well as suggestions for future research.

RESULT INTERPRETATION AND LITERATURE PERSPECTIVE

The effectiveness of the ALSP intervention on physical behaviour was inconclusive. A significant intervention effect for self-reported PA level was noted during the intervention period. However, this effect was not maintained at follow-up and not supported by objective PA measures. Therefore, we conclude that the ALSP intervention was ineffective in eliciting favourable changes in physical behaviour among adolescents and young adults with spastic CP. The scarce literature stresses the difficulty of achieving long-term physical behaviour changes among persons with CP.[1] Difficulties in changing physical behaviour have been reported frequently for the general population as well.[2] The major obstacle in changing physical behaviour is likely the considerable time commitment, especially for persons with physical disabilities. A large proportion of the day is devoted to time spent at school or work, and little time remains for spontaneous PA. Additionally, various personal and environmental barriers and facilitators determine the extent to which youth with CP participate in physical activity.[3]

Regarding the inconclusive results of our PA outcome measures, self-reported PA was measured with the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD) questionnaire. PASIPD questions addressed activities in the context of household, gardening, nurturing and work, which were not applicable to a large proportion of our relatively young study participants. Other PASIPD questions addressed light, medium and strenuous activities, as well as activities requiring muscle force. Therefore, PASIPD results in our study may be interpreted as sports outcome measures. This interpretation may explain why self-reported PA differed from objectively measured PA, which included both daily living and sports-related activities. Another difference between the applied outcome measures of physical behaviour is that the PASIPD questionnaire included weekend days, whereas the objective PA measurements included only weekdays. It could be argued that changes in physical behaviour

occurred during the weekend when there were fewer school and work commitments. Furthermore, it has been established that self-reported PA levels are often overestimated and correlate poorly with objective PA measures in adults with physical disabilities.[4] Self-reported PA overestimation may be even higher among those following the ALSP intervention, as they may feel compelled to respond in a socially desirable way. Furthermore, intervention group participants may be more aware of physical behaviour compared to control group participants, and consequently report more PA. Hence, studies that evaluate lifestyle interventions using only self-reported PA[5, 6] should be interpreted carefully.

Results of the ALSP intervention on physical fitness are more easily interpreted. The ALSP intervention yielded several beneficial effects on outcomes of cardiopulmonary fitness, body composition and lipid profiles among our study participants. Improvements of 10% to 30% in cardiopulmonary fitness were noted for the intervention group compared to the control group. This improvement is reasonable when compared to previously published intervention studies among persons with CP.[7] In contrast to those in regular exercise programmes,[8, 9] those participating in the ALSP maintained intervention effects for at least three months following physical fitness training. This persistence is likely attributable to the counselling sessions designed to get participants to incorporate exercise and PA into daily life. However, the effects on cardiopulmonary fitness were no longer present six months following intervention completion. Booster strategies, such as phone, mail or internet support may facilitate long-term effectiveness and could be added to the ALSP intervention, as these strategies seem effective for maintaining long-term lifestyle intervention effects.[10]

The ALSP intervention was effective in reducing self-perceived fatigue severity and in improving HRQoL with respect to bodily pain and mental health. However, no intervention effects were noted for limitations in participation or HRQoL domains other than bodily pain and mental health. Additional analyses showed that the observed differences between the intervention and control groups could be explained to a considerable extent by single physical behaviour and physical fitness variables, where self-reported PA and physical fitness were stronger mediators than objectively measured PA and sedentary time. Apparently, self-reported physical activity and physical fitness levels are substantial mediators of ALSP intervention effects on fatigue, bodily pain and mental health. Therefore, apart from direct health benefits, these results stress the importance of achieving and maintaining favourable physical behaviour and physical fitness in adolescent and young adult populations with CP.

In searching for clinically applicable alternatives to cardiopulmonary exercise testing, we found that the 6MWT is weakly related to VO_{2peak}, which was accompanied by a rather large standard error of estimate (SEE). Due to this SEE magnitude, the regression model was of limited value for predicting VO_{2peak} in individual patients. This finding is consistent with studies in persons with pulmonary disease[11, 12] and heart failure.[13] Compared to able-bodied persons, the 6MWT distance is likely decreased among persons with CP due to decreased walking capacity[14, 15] caused by spasticity, impaired balance and

reduced muscle strength.[14, 16-18] The severity of walking disability varies greatly among persons with CP. This wide variation may explain the weak relationship between VO_{2peak} and 6MWT distance in persons with CP. Therefore, we conclude that the 6MWT is inadequate to estimate peak cardiopulmonary fitness in adolescents and young adults with CP. This conclusion is consistent with similar studies among patients with stroke, wherein the authors concluded that the 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness.[19]

Objectively measured PA levels were low among our adolescent and young adult study participants, which is consistent with previous research in children[20, 21] and adults[22] with CP. Also consistent with previously published studies, PA level did not differ between participants with GMFCS levels I and II.[23-25] However, studies that have included persons with GMFCS levels III and IV have shown significant associations between GMFCS level and PA level.[23, 26, 27] Although we did not test for significance, PA level seemed to be lower among persons with GMFCS level III compared to GMFCS levels I and II. Furthermore, we found that adolescents and young adults with CP spent more time sedentary compared to healthy adults.[28] This finding is consistent with findings from another study that reported that sedentary time is twice the recommended level among adolescents with CP.[29] In addition to unfavourable physical behaviour, various physical fitness components were low among our study participants compared to the general population. These low physical fitness levels have also been described in children and adults with CP.[30-32] Remarkably, physical fitness and physical behaviour outcomes did not differ between persons with GMFCS levels I and II. Apparently, differences in gross motor functioning between persons classified in GMFCS level I and II are not large enough to cause differences in measured parameters of physical behaviour and physical fitness.

Durstine et al. hypothesised that unfavourable physical behaviour, subnormal physical fitness levels and fatigue interact with each other, leading to a vicious cycle of deconditioning in persons with chronic disabilities.[33] In contrast to this rationale, we did not find cross-sectional relationships between peak oxygen uptake or oxygen uptake during walking and total daily walking time in adults with CP. The lack of significant relationships between these outcome measures is consistent with previous studies of children[25] and adults[34] with CP that showed no relationship between peak oxygen uptake and physical activity level. However, we did find an inverse relationship between physical strain during walking and total daily walking time. Two previous studies investigated the relationship between oxygen uptake during walking and PA level in children with CP.[25, 26] Results of these studies and those of the current study suggest that, compared to oxygen uptake during walking, physical strain is more strongly related to PA level in persons with CP. This finding indicates that persons with CP with a high physical strain during walking are likely to walk less in daily life than persons with CP with low physical strain during walking. The practical implication is that health professionals should not focus solely on treatments to improve walking efficiency, but should also consider training interventions to improve maximal aerobic capacity to lower the physical strain of walking. Although longitudinal research is

required to confirm these cross-sectional associations, we assume that decreasing physical strain may positively affect total daily walking time, thereby interrupting the cycle of deconditioning.[33]

More than 40% of our study participants experienced fatigue, with bilaterally affected persons experiencing more fatigue compared to unilaterally affected persons. These high fatigue levels indicate that fatigue is already a major problem at a young age among persons with CP. In contrast to the vicious cycle of deconditioning proposed by Durstine et al.,[33] we found that experienced fatigue was unrelated to outcomes of physical behaviour and physical fitness. The lack of associations mirrors findings for adults with CP.[34-36] Persons with CP may lower their daily PA levels to conserve energy or prevent fatigue that results from high levels of physical strain during walking.[37] One could hypothesise that this compensation strategy may explain the lack of relationship between daily PA or physical fitness and fatigue in persons with CP.

Regarding the cost-utility analysis, no significant differences in annual direct medical costs, annual productivity costs or total annual costs were found between the intervention and control groups. Furthermore, the ALSP intervention had no effect on participant quality of life. The cost-utility ratio of -€23.664 per quality-adjusted life year (QALY) shows that the ALSP intervention may be cost-saving or cost-effective compared to offering no intervention to improve movement behaviour and fitness. However, the small variance in quality of life between participants, the substantial variance for total costs, combined with a small sample size, resulted in a wide confidence interval for the cost-utility ratio. This result implies considerable uncertainty about whether to adopt the ALSP intervention from an economic point of view. Our uncertainty analysis indicated that there is a probability of 78% that exercise therapy produces positive health effects, 89% that the cost per QALY gained is lower than €20.000 and 86% that the intervention saves societal costs. Whether these results are sufficiently acceptable to adopt the ALSP intervention instead of no intervention to achieve a more active lifestyle is up to rehabilitation physicians, policy makers and patient organisations.

METHODOLOGICAL CONSIDERATIONS

Study design

The study used a multi-centre randomised controlled design. All measurements were blinded, except for the objective measurement of physical behaviour. Research assistants, who performed the measurements, were blinded to group allocation. Obviously, the subjects, intervention counsellors and trainers could not be blinded to group allocation. Therefore, self-reported outcome measures may have been biased because persons allocated to the intervention group may have felt compelled to respond in a socially desirable way.

Study sample and generalisability.

This multi-centre study recruited participants aged 16 to 24 years with spastic CP from four rehabilitation centres (Rijndam Rehabilitation Centre, Rotterdam; De Hoogstraat, Utrecht; and Sophia Rehabilitation, Den Haag & Delft) and two rehabilitation departments at university hospitals (ErasmusMC, Rotterdam; VUmc, Amsterdam) throughout the western and central regions of The Netherlands. These regions include the most densely populated areas of the country. Between October 2009 and September 2012, we identified a target population of 456 adolescents and young adults with CP from the patient registers of participating centres. Because many of these patients had not been seen at the rehabilitation centre for several years, the accuracy of their address information was uncertain. A total of 183 potential participants responded to our invitation, of whom 57 (31%) consented to participate in the study.

We may have overestimated levels of PA and fitness because of selection bias. Persons with CP who are interested in PA and sports (and presumably have higher baseline PA and fitness levels) may have been more likely to participate than those with low interest in PA and sports. Despite this possible selection bias toward recruiting persons with interest in PA and sports, initial PA and fitness levels were low and sedentary time was high.

Outcome measures

Physical activity

There are some noteworthy limitations of using the VitaMove system to measure daily PA levels. Although we intended to measure PA over a three-day period, this was not uniformly achieved because of technological challenges and user errors. Nevertheless, White et al. showed that a 24-hour VitaMove system measurement is adequate to reliably determine activities and postures.[38] However, it is questionable whether short measurement periods containing only weekdays would yield data representative of common movement behaviour.

It is possible that some persons were more likely to experience PA changes during the weekends when their schedules were not limited by school and work. Fortunately, the VitaMove system firmware has improved over time and we are currently able to measure both week and weekend days over a five-day period. Although wearing the VitaMove system may have impeded activities of daily life, participants indicated that they had been able to perform their regular activities, so the influence of the measurement equipment is considered negligible. During swimming, the VitaMove system was removed. However, participant diaries of non-wearing time showed that swimming was a rare activity. Furthermore, to analyse objectively measured physical behaviour, we assumed that participants went directly to bed after removing the VitaMove system each day. This may have led to an underestimation of PA and an overestimation of sedentary time. This limitation is not unique to the VitaMove system,

but applies to all ambulant monitoring systems that can be removed by participants. The resulting error is expected to be consistent over time and equally distributed between control and intervention groups.

Physical fitness

Two different types of breath-by-breath analysers were used to determine VO_{2peak} at the four participating centres. Over the course of the study, each participant was tested with the same devices, which were calibrated with reference gases prior to each measurement. Furthermore, each system demonstrated validity in testing against the Douglas-bag method (explained variances were 0.97 and 0.96).[39, 40] Previous research on persons with CP suggests that the primary mode of ambulation elicits the highest oxygen uptake during maximal exercise testing.[41] However, our study participants who were tested using an arm crank ergometer were unable to deliver a maximal effort, as determined by maximal achieved heart rate and respiratory exchange ratio later in the study. The primary reason for failing to obtain maximal effort was hand slippage from the pedals due to spasticity.

For practical reasons, we did not obtain fasting blood samples. However, there is evidence that non-fasting and fasting levels of total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) differ minimally[42-44] and the NCEP ATP III guidelines consider non-fasting values for TC and HDL-C to be appropriate.[45]

Compliance

Participants who completed the intervention attended, on average, 89% of supervised counselling and fitness training sessions. We determined the compliance and duration and intensity of individual fitness training sessions at the participants' homes with heart rate monitors. These data revealed that compliance with individual fitness training sessions at home was low and that the workout duration and intensity of these sessions were substantially lower than those prescribed.

Statistical power & analyses

Although a sample size of 57 is relatively large considering the prevalence of spastic CP, the absolute number is quite small. Nevertheless, the power of the study sample seemed sufficient for all but one analysis. The power for the cost-utility study was insufficient, as reflected in the wide confidence intervals for cost differences. This is a common problem in cost-utility studies performed alongside randomised controlled trials, in which sample sizes are usually based on detecting relevant clinical differences. Because the distribution of cost data is typically heavily skewed, large study populations are needed to appropriately perform cost-utility analyses.[46]

Sixteen participants were lost to follow-up. A type II error may have occurred in the longitudinal analyses due to a higher than expected drop-out rate. Considering the clinical relevance and p-values

from the analyses, we do not expect that any results would have differed with fewer participant drop-outs.

Due to the multi-centre study design, multi-level analyses with centre-correction were initially performed. However, centre level did not contribute significantly to the model on our primary outcome measures. Therefore, we chose to perform generalised estimating equation (GEE) analyses, which are more robust when analysing small study samples.[47] Finally, due to multiple longitudinal testing, one should be careful to draw strong conclusions from single significant findings.

CLINICAL IMPLICATIONS

Our results showed that adolescents and young adults with spastic CP have unfavourable physical behaviour levels and low physical fitness levels. These findings emphasise the need for intervention. Whereas general practitioners play an important role in improving physical behaviour and fitness among the general population,[48] rehabilitation physicians can fulfil this role for persons with CP. Rehabilitation professionals can inform patients of important health benefits and on how and where to exercise; they can facilitate finding of equipment and programmes, and supervise and assist during exercise. Although interest in lifestyle support has increased among the general population in recent years, it is still uncommon within the practice of rehabilitation medicine. The results of the present study emphasise the importance of engaging rehabilitation medicine providers in these roles.

The ALSP intervention was associated with increased self-reported PA level, physical fitness and improved mental health. In contrast to our hypotheses, the ALSP intervention failed to improve objectively measured PA levels or sedentary behaviour. As persons with CP regularly require treatment regarding physical behaviour and physical fitness, it seems sensible to continue offering the ALSP intervention. Otherwise, these patients must rely on external help, which is likely less structured than the ALSP intervention. However, we feel that the ALSP intervention in its current form leaves room for significant improvements and should be modified to increase its effectiveness. Our suggestions to improve the effectiveness of the ALSP intervention are described in the section 'directions/ recommendations for future research' further on.

The ALSP intervention was offered during the transition into adulthood when life changes substantially impact development of the adult lifestyle.[49, 50] Therefore, improving physical fitness and achieving sufficient PA at this age seem appropriate goals to benefit participants throughout life. However, as important issues such as education, work, housing, social contacts and romantic relationships require attention at this age, it could be argued that the ALSP intervention should be offered later in life as soon as sufficient attention can be given to this issue. In addition, it is likely that older persons

are more able to realize the long-term consequences of favourable physical behaviour and fitness levels. However, it may be more difficult to change behavioural later in life, as persons have already developed their adult lifestyles.

In the present study, the ALSP intervention was evaluated using a comprehensive set of outcome measures. In clinical practice, a smaller set of outcome measures would be sufficient to evaluate individual results. These measurements should include the use of a simple accelerometer/pedometer, a maximal exercise test and measurements of body composition to gain insight into patients' physical behaviour and physical fitness over time. Maximal exercise testing can be performed without oxygen measurement, as the achieved load during testing also indicates fitness level.

Cost-utility results show that the ALSP intervention is most likely cost-effective or even cost-saving in adolescents and young adults with CP. Hopefully, these results influence rehabilitation professionals to offer lifestyle interventions to CP populations.

DIRECTIONS/RECOMMENDATIONS FOR FUTURE RESEARCH

We hypothesised that the ALSP intervention would be particularly effective on the long-term by eliciting behavioural changes toward more favourable physical behaviour. However, this aspect of the intervention was less effective than hypothesised. The ALSP intervention can be improved to increase its effectiveness.

The ALSP intervention, in its current form, may focus too heavily on increasing PA possibly leading to neglecting the participants' load/capacity ratio. Interventions should be tailored to guide participants toward optimal physical behaviour. Close cooperation between rehabilitation professionals is required, and appointing centres to specialise in this area is advised. Another modification, in light of recent evidence concerning sedentary behaviour,[29] would be to use PA counselling to address interruption of prolonged sedentary periods in addition to decreasing overall sedentary time. In consideration of participants' difficulty in estimating physical behaviour, a simple accelerometer or pedometer could be added as an intervention tool to provide instant feedback regarding participants' physical behaviour. This feedback may serve as a useful instrument for augmenting individual awareness and goal-setting. Using such devices has been found effective, when combined with counselling, to increase PA in healthy adults.[51] Moreover, device feedback allows for a competitive element among intervention participants.

Although the ALSP intervention was effective in increasing several components of physical fitness, the exercise programme has room for improvement. The intervention incorporated low frequency

exercise to increase cardiopulmonary fitness by means of endurance-based aerobic training. High intensity interval training should be considered as an exercise strategy to maximise workouts that are limited on time, as has been achieved in cardiac rehabilitation studies.[52] Moreover, this high intensity strategy could complement the existing exercise programme and would be particularly suitable for persons with a minimum basic level of fitness. Heart rate monitor data revealed that the compliance was low with individual fitness training sessions at home and that workout duration and intensity were substantially lower than prescribed. Therefore, we recommend eliminating these home training sessions. Instead, an additional weekly training session at the centre should be considered.

The achieved intervention effects were generally not maintained at follow-up. To counteract this, booster strategies such as phone, mail or internet contact might be added to the ALSP intervention to facilitate long-term effectiveness.[10] These booster sessions would ideally be combined with accelerometer/pedometer information to provide targeted feedback.

We believe that the effectiveness of the ALSP intervention would improve by incorporating the above outlined adaptations. Future research is needed to evaluate the effectiveness of these changes to the ALSP intervention. Although not all components of the intervention may have been equally effective, the current research design is not suitable to attribute results to specific components. Future research could focus on the effectiveness of separate components to improve the overall intervention.

Our study participants had relatively high gross motor functioning (89% had GMFCS level I or II) and intellectual functioning (I.Q. >70). Future research is required to clarify the effectiveness of lifestyle interventions in study samples with lower levels of gross motor functioning and intellectual functioning.

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Summary

The study protocol in **chapter 2** describes the rationale, design, intervention and outcome measures of the six-month lifestyle intervention named 'Active Lifestyle and Sports Participation' (ALSP). It was hypothesised that this lifestyle intervention would have added value for improving physical behaviour and physical fitness compared to regular therapy. Adolescents and young adults (16-24 years) were invited to participate when they had spastic cerebral palsy (CP) and were classified in level I-IV of the Gross Motor Functioning Classification System. The participants were randomly allocated to the intervention group (ALSP intervention) or the control group (no additional therapy). The ALSP intervention consisted of three parts; 1) weekly supervised centre and weekly home-based physical fitness training with a focus on increasing levels of cardiopulmonary fitness and muscle strength; offered by a physical therapist for a period of 3 months; 2) counselling on daily PA, which was based on motivational interviewing. Barriers and facilitators of PA in daily life were discussed and increasing PA and minimising sedentary behaviour were encouraged during these sessions. In total, six monthly sessions with a duration of 30 minutes were offered and were guided by a personal coach (physical therapist / movement therapist); and 3) counselling on sports participation was offered to find accessible, suitable and appropriate sports and sports facilities conveniently located in each participant's environment. In total, two to four sports counselling sessions were offered by a movement therapist over a period of six months depending on the participants' desires. Furthermore, optional sport-specific training was offered, which included practice opportunities to match sports to participants' interests and abilities. Data was collected at baseline, after 3 months, at the end of the intervention (at 6 months), and at follow-up by assessors who were blinded for group allocation. Primary outcome measures were measures of physical behaviour and physical fitness. Secondary outcome measures included fatigue, participation and quality of life. Cross sectional studies on these outcomes are described in chapters 3-7. The results of the longitudinal study are described in chapters 8-10. A cost-utility analysis of the ALSP intervention is described in chapter 11.

Chapter 3 describes a study to determine whether the 6-minute walk test (6-MWT) predicts peak oxygen uptake and whether the 6-MWT is a clinically applicable alternative to cardiopulmonary exercise testing in ambulatory adolescents and young adults with CP. We found that the 6-MWT distance was poorly related to peak oxygen uptake. This finding was accompanied by a rather large standard error of estimate. Therefore, the applied regression model did not allow for prediction of peak oxygen uptake from the 6MWT in individual ambulatory adolescents and young adults with CP. The 6MWT possibly is more suitable as a measure of walking capacity than of physical fitness in persons with CP.

Baseline values of our participants' physical behaviour and physical fitness are described in **chapter 4** and **chapter 5**. Our study sample had a less favourable physical behaviour profile compared to an able-bodied comparison population. Physical behaviour did not differ between persons with GMFCS level I and II and only short sitting bouts were significantly more prevalent in persons with bilateral

CP compared to unilateral CP ($p<0.05$).These results suggest that adolescents and young adults with spastic CP may be at increased risk for health problems related to less favourable physical behaviour. This unfavourable behaviour profile is consistent with the subnormal physical fitness levels that we observed. Measures marked as considerably lower (<75%) in persons with CP compared to reference were: cardiopulmonary fitness, hip flexion and knee extension strength. Compared to participants with unilateral CP, those with bilateral CP had significantly lower cardio-respiratory endurance and hip abductor muscle strength. Comparison between persons with GMFCS level I and II showed only a difference on peak power during cycling-ergometry.

Although PA and physical fitness levels are generally believed to interact, we found no cross-sectional relationships between total daily walking time and peak oxygen uptake or oxygen uptake during walking in adolescents and young adults with CP, as described in **chapter 6**. Nevertheless, physical strain of walking, defined as the oxygen uptake during walking and expressed as a percentage of peak aerobic capacity, was inversely related to total daily walking time. These results imply that persons with CP with a high physical strain during walking are likely to walk less during daily life.

The study described in **Chapter 7** estimated the prevalence of fatigue in adolescents and young adults with spastic CP. In addition, subgroups at risk for fatigue were explored. Forty percent of the participants was fatigued, including 12,5% severely fatigued. Furthermore, participants with bilateral CP were significantly more fatigued than participants with unilateral CP. Daily PA and cardiopulmonary fitness were both low, but were not significantly related to fatigue. The results indicate that fatigue is already present at a relatively young age in persons with CP. Subtype of CP is a determinant of fatigue and we did not find evidence for a physical origin of fatigue.

Results from the longitudinal evaluation of the ALSP intervention on physical behaviour are reported in **chapter 8**. These results show that the intervention increased self-reported PA levels immediately following the intervention. However, this increase was not sustained at follow-up. Furthermore, the ALSP intervention did not affect objectively measured PA level, movement intensity or sedentary time. Therefore, we concluded that, despite the initially unfavourable physical behaviour, the ALSP intervention was ineffective in eliciting more favourable physical behaviour among adolescents and young adults with spastic CP.

The ALSP intervention yielded favourable effects on several outcomes of cardiopulmonary fitness, body composition and lipid profile among our study participants which is described in **chapter 9**. The addition of counselling on PA and sports participation to fitness training resulted in favourable short and medium-term effects on peak oxygen uptake, oxygen uptake and load on the anaerobic threshold and waist circumference. Favourable long-term effects were found for sum of skinfolds,

systolic blood pressure and total cholesterol. However, the intervention needs to be optimised to increase muscle strength and for long term retention of effects on aerobic capacity.

Chapter 10 describes that the ALSP lifestyle intervention was effective in lowering fatigue severity and bodily pain, and in improving mental health. No effects of the ALSP lifestyle intervention were found for participation or HRQoL domains other than bodily pain and mental health. The effects of the ALSP lifestyle intervention on fatigue, bodily pain and mental health were largely mediated by physical behaviour and physical fitness. These mediation effects stress the importance of achieving favourable physical behaviour and sufficient physical fitness levels among adolescents and young adults with CP.

A cost-utility analysis of the ALSP intervention is described in **chapter 11**. Quality of life remained stable over time for both groups. No significant differences between groups were found for direct medical costs or productivity costs. A cost-utility ratio of -€23.664 per QALY was found for the lifestyle intervention compared to no treatment. Results of the study are exploratory, but indicate that implementing a lifestyle intervention for CP-population might be cost-effective or cost-saving as compared to offering no intervention to improve physical behaviour and fitness. However, the large ranges of uncertainty for the cost-utility ratio should be taken into account and, therefore, results should be interpreted with caution.

Finally, **chapter 12** described the main findings of this thesis and discusses the methodological considerations, both strengths and limitations. In this chapter, we also addressed clinical implications and made recommendations for future research.

Samenvatting

Het studieprotocol in **hoofdstuk 2** beschrijft de aanleiding en de opzet van het LEARN 2 MOVE onderzoek. De hypothese was dat de leefstijlinterventie 'Actieve Leefstijl en Sportstimulering' (ALSP) een positief effect heeft op het beweeggedrag en de fysieke fitheid in vergelijking met reguliere therapie. Adolescenten en jongvolwassenen (16-24 jaar) zijn uitgenodigd om deel te nemen indien ze een spastische vorm van CP hebben en geclassificeerd zijn in niveau I tot en met IV van het Gross Motor Functioning Classification System. De deelnemers werden willekeurig toegewezen aan de interventiegroep (ALSP interventie) of de controlegroep (geen extra therapie). De ALSP interventie bestond uit drie onderdelen; 1) Fitness training; dit onderdeel is gericht op het verbeteren van de fysieke fitheid en bestaat uit groepstraining (1 uur per week) in het centrum onder supervisie van een fysiotherapeut en 1 uur per week thuis of in eigen omgeving trainen. Het doel van dit onderdeel van de interventie is het verbeteren van de aerobe capaciteit en de spierkracht en heeft een duur van 3 maanden; 2) Personal counselling; dit onderdeel is gebaseerd op motivational interviewing en richt zich op het optimaliseren van het beweeggedrag. Belemmeringen en bevorderende factoren van fysieke activiteit in het dagelijks leven werden besproken. Daarnaast werd het verhogen van fysieke activiteit en het minimaliseren van sedentair gedrag aangemoedigd. Door middel van 6 maandelijkse counselling-gesprekken met een personal coach (fysiotherapeut / bewegingsagoog) werd aangestuurd op een meer actieve leefstijl in het dagelijks leven; 3) Sportcounselling; dit onderdeel bestaat uit 2 tot 4 gesprekken met een bewegingsagoog waarbij de voorkeuren en mogelijkheden in sportactiviteiten zijn besproken. Daarnaast werden er sport-specifieke workshops aangeboden om verschillende sporten, aangepast aan de individuele capaciteit, aan de deelnemers te introduceren. De duur van dit onderdeel van de interventie is variabel tot een maximum van 6 maanden. De data zijn verzameld op baseline, na 3 maanden, direct na afloop van de interventie (na 6 maanden) en tijdens follow-up (12 maanden) door meetassistenten die blind waren voor de groepstoewijzing van de deelnemers. De primaire uitkomstmaten hebben zich gericht op het beweeggedrag en de fysieke fitheid. Secundaire uitkomstmaten waren vermoeidheid, participatie en kwaliteit van leven. In hoofdstuk 3-7 worden cross-sectionele onderzoeken naar deze uitkomstmaten beschreven. De resultaten van het longitudinale onderzoek zijn beschreven in hoofdstuk 8, 9 en 10. Een kosten-utiliteiten analyse van de ALSP interventie wordt beschreven in hoofdstuk 11.

Hoofdstuk 3 beschrijft het onderzoek waarin is bepaald of de 6-minuten wandeltest (6-MWT) de maximale zuurstofopname kan voorspellen en of de 6-MWT een klinisch toepasbaar alternatief is voor maximale inspanningstesten in ambulante adolescenten en jongvolwassenen met cerebrale parese. We vonden dat de 6-MWT afstand slecht gerelateerd was aan de maximale zuurstofopname. Deze bevinding ging gepaard met een forse afwijking van de schatting. Daarom is het op de 6-MWT afstand gebaseerde regressiemodel niet geschikt voor de individuele voorspelling van de maximale zuurstofopname in ambulante adolescenten en jongvolwassenen met CP. De 6MWT lijkt meer geschikt als uitkomstmaat van loopcapaciteit dan dat het een klinisch toepasbaar alternatief voor maximale inspanningstesten is bij personen met CP.

De baselinegegevens van het beweeggedrag en de fysieke activiteit van de deelnemers zijn beschreven in **hoofdstuk 4 en 5**. De deelnemers hadden een minder gunstig beweeggedrag vergeleken met referentiegroepen. Er is geen verschil in beweeggedrag gevonden tussen personen met GMFCS niveau I en II. Korte zitperioden kwamen significant vaker voor bij personen met bilaterale CP in vergelijking met personen met een unilaterale CP ($p < 0.05$). Deze resultaten suggereren dat adolescenten en jongvolwassenen met spastische CP een verhoogd risico hebben op het ontwikkelen van gezondheidsproblemen door hun ongunstige beweeggedrag. Daarnaast is er ook een subnormale fysieke fitheid gevonden onder de deelnemers. De cardiopulmonaire fitheid en spierkracht (heup-flexie en knie-extensie) waren aanzienlijk lager (<75%) bij personen met CP in vergelijking met referentie groepen. Deelnemers met een bilaterale CP hadden een significant lager cardiorespiratoire fitheid en een lagere spierkracht (heup-abductie) dan personen met een unilaterale CP. De vergelijking tussen personen met GMFCS niveau I en II toonde alleen een verschil in het maximaal geleverde vermogen tijdens de maximale inspanningstest.

Over het algemeen wordt verondersteld dat de mate van fysieke activiteit en fysieke fitheid gerelateerd zijn. Desondanks werd in **hoofdstuk 6** geen cross-sectionele relatie gevonden tussen de totale dagelijkse wandeltijd en de maximale zuurstofopname of de zuurstofopname tijdens het lopen onder jongeren en jongvolwassenen met CP. De fysieke belasting van het lopen, gedefinieerd als de zuurstofopname tijdens het lopen en uitgedrukt als een percentage van de maximale zuurstofopname, was wel omgekeerd evenredig gerelateerd aan de totale dagelijkse wandeltijd. Deze resultaten impliceren dat personen met CP met een hoge fysieke belasting tijdens het lopen waarschijnlijk minder lopen in het dagelijks leven.

De in **hoofdstuk 7** beschreven studie schat de prevalentie van vermoeidheid onder jongeren en jongvolwassenen met spastische CP. Daarnaast werd er naar subgroepen met een verhoogd risico op vermoeidheid gezocht. Veertig procent van de deelnemers was vermoeid, waarvan 12,5% ernstig vermoeid. Deelnemers met bilaterale CP waren significant meer vermoeid dan deelnemers met unilaterale CP. Dagelijkse fysieke activiteit en cardiopulmonale fitheid waren beiden subnormaal, maar waren niet significant gerelateerd aan de mate van vermoeidheid. De resultaten van deze studie tonen aan dat vermoeidheid al op jonge leeftijd aanwezig is bij personen met CP. Het CP subtype is een determinant van vermoeidheid en we hebben geen bewijs gevonden voor een fysieke oorsprong van vermoeidheid.

De longitudinale evaluatie van de ALSP interventie op het beweeggedrag wordt beschreven in **hoofdstuk 8.** De resultaten tonen aan dat zelf-gerapporteerde fysieke activiteit toeneemt na het doorlopen van de interventie. Deze toename was echter niet meer aanwezig tijdens de follow-up meting. Bovendien heeft de ALSP interventie geen effect gehad op het objectief gemeten fysieke activiteiten niveau, de bewegingsintensiteit of de tijd die sedentair is doorgebracht. Dit leidt tot de

conclusie dat de ALSP interventie niet effectief was in het behalen van gewenst beweeggedrag bij adolescenten en jongvolwassenen met spastische CP.

Hoofdstuk 9 beschrijft dat de ALSP interventie gunstige effecten heeft op verschillende uitkomsten van cardiopulmonaire fitheid, lichaamssamenstelling en het lipidenprofiel onder jongeren en jongvolwassenen met CP. Het toevoegen van counselling op beweeggedrag en sport aan de fitness training resulteerde in gunstige korte en middellange termijn effecten op de maximale zuurstofopname, de zuurstofopname en de belasting op de anaerobe drempel en middelomtrek. Gunstige effecten op lange termijn werden gevonden voor de som van de huidplooien, systolische bloeddruk en het totale cholesterol. Echter, de interventie moet worden geoptimaliseerd om spierkracht te verhogen en voor het behoud van effecten op aerobe capaciteit op de lange termijn.

Hoofdstuk 10 beschrijft de effectiviteit van de ALSP leefstijlinterventie in het verlagen van de mate van vermoeidheid en lichamelijke pijn en in het verbeteren van de geestelijke gezondheid. Het doorlopen van de ALSP leefstijlinterventie had echter geen effect op het participatieniveau of op domeinen van de gezondheid gerelateerde kwaliteit van leven, anders dan lichamelijke pijn en geestelijke gezondheid. De effecten van de ALSP leefstijlinterventie op vermoeidheid, lichamelijke pijn en geestelijke gezondheid werden grotendeels gemedieerd door variabelen van het beweeggedrag en de fysieke fitheid. Dit benadrukt het belang van het behalen van gunstig beweeggedrag en voldoende fysieke fitheid bij adolescenten en jonge volwassenen met CP.

Een kosten-utiliteiten analyse van de ALSP interventie is beschreven in **hoofdstuk 11**. De kwaliteit van leven bleef stabiel over de tijd in zowel de controle- als interventiegroep. Geen significante verschillen tussen de groepen zijn gevonden voor directe medische kosten of productiviteitskosten. De berekende kosten-utiliteiten ratio bedroeg -€ 23,664 per QALY voor de ALSP leefstijlinterventie in vergelijking met geen behandeling. Deze resultaten zijn verkennend, maar geven aan dat het implementeren van een leefstijlinterventie voor personen met CP kosteneffectief of zelfs kostenbesparend kan zijn vergeleken met het aanbieden van geen interventie. De resultaten van deze studie moeten echter voorzichtig worden geïnterpreteerd door de grote range van het betrouwbaarheidsinterval van de berekende ratio.

Ten slotte beschrijft **hoofdstuk 12** de belangrijkste bevindingen van dit proefschrift en bespreken we zowel de sterke kanten als de beperkingen van de studies die zijn beschreven in dit proefschrift. In dit hoofdstuk bespreken we tevens de klinische implicaties en aanbevelingen voor toekomstig onderzoek.

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About the author

Jorrit Slaman was born in Gouda on the 16th of November 1983. He attended secondary school at Het Schoonhovens College (VWO) in Schoonhoven, where he graduated in 2002. He started his study Human Movement Sciences in 2003. In 2006 he obtained his Bachelor degree and he completed his master study in 2007 with a thesis on the effects of arm load magnitude on selective shoulder muscle activation. Subsequently, he worked as a junior researcher studying the relations between movement patterns and clinical scores on persons with reversed shoulder prostheses. In September 2008 he started working on the research described in this thesis at the Department of Rehabilitation Medicine and Physiotherapy of the Erasmus MC, Rotterdam as part of the research lines MoveFit and Transition & Lifespan. At present, he is working as a policy worker at Rijndam Rehabilitation Centre and as a Postdoc for the of Rotterdam Neurorehabilitation Research line (RoNeRes) at the Department of Rehabilitation Medicine and Physiotherapy of the Erasmus MC, where his focus is on developing a national stroke database.

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Steenbrink F, Meskers CG, van Vliet B, **Slaman J**, Veeger HE, De Groot JH. Arm load magnitude affects selective shoulder muscle activation. Med Biol Eng Comput. 2009;47:565-72.

PhD Portfolio

PHD. PORTFOLIO SUMMARY

Summary of PhD training and teaching activities			
Name PhD student:	Jorrit Slaman	**PhD period:**	2008-2013
Erasmus MC Department	Rehabilitation Medicine	**Promotor**	Prof.dr. H.J. Stam
Research school	-	**Supervisors**	Dr. H.J.G. van den Berg-Emons Dr. M.E. Roebroeck

1. PhD training

General academic skills		
- Biomedical English writing and Communication	2009	56 hours
- CPO course	2009	8 hours
- BROK course	2010	30 hours
Research skills		
- Introduction to data analysis (NIHES)	2009	30 hours
- Regression analysis (NIHES)	2009	56 hours
- Longitudinal data analysis (EpidM, VU)	2010	32 hours
In depth courses		
- Motivational interviewing (HAN-VDO)	2009	24 hours
- Cerebral palsy; status and developments (VRA)	2010	16 hours
- ECG interpretation	2010	8 hours
Presentations		
- Oral presentation: Effects of age specific physical activity interventions among persons with CP. BOSK / DACD congress, Utrecht.	2009	8 hours
- Poster presentation: Poster presentation: Effects of a lifestyle intervention among youth with CP. BOSK / DACD congress, Utrecht.	2009	8 hours
- Oral presentation: Physical strain of walking in persons with CP. ICAMPAM, Glasgow.	2011	20 hours
- Oral presentation: Physical strain of walking in persons with CP. RACMEM, Maastricht.	2011	20 hours
- Oral presentation: Physical strain of walking in persons with CP. ICPC, Pisa	2012	20 hours
- Oral presentation: Physical strain of walking in persons with CP. DACD, Utrecht	2012	20 hours
- Oral presentation: Predictive value of the 6 minute walk test. DACD, Utrecht	2012	20 hours
- Poster presentation: Predictive value of the 6 minute walk test. EACD, Newcastle.	2013	8 hours

- Poster presentation: Lifestyle intervention effects among youth with CP. EACD, Newcastle.	2013	8 hours
- Oral Presentation: Lifestyle intervention effects among youth with CP. VRA, Noordwijkerhout.	2013	20 hours
International conferences		
- A global status quo on Cerebral Palsy, with a view to the future, Utrecht, The Netherlands	2009	28 hours
- International Conference on Ambulatory Monitoring of Physical Activity and Movement, Glasgow, Scotland	2011	28 hours
- Recent Advances and Controversies in Measuring Energy Metabolism, Maastricht, The Netherlands	2011	28 hours
- International Cerebral Palsy conference, Pisa, Italy	2012	28 hours
- European Academy of Childhood Disability Conference, Newcastle, England	2013	28 hours
Seminars and workshops		
- Introduction and Career Planning day for PhD's, Erasmus, Rotterdam	2008	4 hours
- Rehab on the move; towards interventions to improve physical activity and fitness of young physically disabled persons, Erasmus MC, Rotterdam	2009	4 hours
- Kinderen met cerebrale parese: beloop en behandeling, VUmc, Amsterdam	2009	4 hours
- Workshop motivational interviewing, VUmc, Amsterdam	2009	4 hours
- Dutch Academy for childhood disability, Arnhem	2011	8 hours
- Dutch Academy for childhood disability, Utrecht	2012	8 hours
- VRA Congress, Noordwijkerhout	2013	24 hours
Didactic skills		
- Basic Didactics (RISBO)	2009	32 hours
Other		
- Participating in research meetings department of rehabilitation medicine, Erasmus MC, Rotterdam	2008-2013	200 hours
- Organising research meetings department of rehabilitation medicine, Erasmus MC, Rotterdam	2008-2010	50 hours

2. Teaching activities

Lecturing		
- Introduction to physiology (part of the minor Rehabilitation Medicine for medical students), Erasmus MC, Rotterdam	2008 2010	32 hours 40 hours
- Research skills (part of the minor Rehabilitation Medicine for medical students), Erasmus MC, Rotterdam	2010	16 hours
- Ambulatory activity monitoring (part of the course for rehabilitation physicians in training), Erasmus MC, Rotterdam	2010	16 hours
- LEARN 2 MOVE; design and results physiology (part of the minor Rehabilitation Medicine for medical students), Erasmus MC, Rotterdam	2011	16 hours
- LEARN 2 MOVE; design and results physiology (part of the minor Rehabilitation Medicine for medical students), Erasmus MC, Rotterdam	2012	16 hours
- LEARN 2 MOVE; design and results physiology (part of the minor Rehabilitation Medicine for medical students), Erasmus MC, Rotterdam	2013	16 hours
Supervising practicals and excursions		
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Supervising Master's theses		
- Supervising medical student (thesis on fatigue among youth with cerebral palsy)	2012-2013	50 hours
- Supervising student on human movement technology (thesis on the relation between physical activity and physical fitness)	2010	30 hours
Other		
- Supervising of medical students with review assignments	2010	8 hours
- Supervising AIO research project	2011-2012	30 hours
- Organising member of the PhD-day for human movement scientists, Erasmus MC, Rotterdam	2011	12 hours
Total		**1172 hours**