Functioning, Disability, Health and Quality of Life in Adults with Cerebral Palsy more than 25 years after Selective Dorsal Rhizotomy

A Long-term Follow-up Study during Adulthood

BY

BERENDINA EGBERTINE VEERBEEK

NEUROSCIENCE INSTITUTE
DIVISION OF NEUROSURGERY
DEPARTMENT OF SURGERY
FACULTY OF HEALTH SCIENCES
UNIVERSITY OF CAPE TOWN

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SUPERVISORS

Dr Nelleke G Langerak MSc (Biomed Health Sc., Hum Mov Sc.), PhD (Biomed. Eng.)

Prof Robert P. Lamberts MSc (Pedagogy, Hum Mov Sc.), PhD (Exercise Sc.), FECSS

Prof A Graham Fieggen FCS (SA) (Neurosurg.), MSc (Neuroscience), MD (Neurosurg.)

SUPERVISORS

Dr Nelleke Gertrude Langerak

Neuroscience Institute, Division of Neurosurgery, Department of Surgery, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town, South Africa

Prof Dr Robert Patrick Lamberts

Institute of Sport and Exercise Medicine & Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg. Cape Town, South Africa

Division of Exercise Science and Sports Medicine, Department Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town, South Africa

Prof Anthony Graham Fieggen

Neuroscience Institute, Division of Neurosurgery, Department of Surgery, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town, South Africa

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DECLARATION

I, Berendina Egbertine Veerbeek, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgments indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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I started this entire process out of the love for learning, my urge to contribute to a greater useful cause and just because I love a challenge. What I found out along the way is *'The more you know, the more you do not know'* - Aristotle. More and more questions arose and I love to keep wondering. To ask the right question is already half of the answer. It was a challenging but beautiful journey which I could have not completed with the support of several people who either contributed to the content, the process or welcoming distractions.

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'You are bigger than your disability; do not allow your disability to define you'

'No fear, only faith'

'When something is important enough, you do it even if the odds are not in your favour'

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Met jou kan ik de wereld aan

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2017 N.G. Langerak, T. N. Mann, **B.E. Veerbeek**, A.G Fieggen, J du Toit, R.P. Lamberts. Gait pattern of children with bilateral lower limb spasticity due to HIV encephalopathy and CP – Is there a difference? *Developmental Medicine and Child Neurology,* 59(S2): S27-28

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THESIS CONFERENCE PRESENTATIONS

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*(**BE Veerbeek**, RP Lamberts*, AG *Fieggen, NG Langerak)*

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*(**BE Veerbeek**, RP Lamberts, AG Fieggen, NG Langerak)*

Australasian academy of cerebral palsy and developmental medicine (AUSACPDM) conference, Auckland, New Zealand, 21-24 March 2018

Oral presentation: ***B.E. Veerbeek*** *'Level of habitual physical activity in adults with bilateral spastic CP>25 years after Selective Dorsal Rhizotomy'*

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2017 **Surgical Research Day – University of Cape Town, Cape Town, South Africa, 17 November 2017**

Oral presentation: ***B.E. Veerbeek*** *'Thirty years after Selective Dorsal Rhizotomy: Level of physical pain and influence on daily activities in adults with bilateral spastic Cerebral Palsy'*

(***BE Veerbeek**, RP Lamberts, AG Fieggen, NG Langerak)*

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*(**BE Veerbeek**, RP Lamberts, AG Fieggen, NG Langerak)*

LIST OF ABBREVIATIONS

2DGA	2 Dimensional Gait Analysis
3DGA	3 Dimensional Gait Analysis
BMI	Body Mass Index
CP	Cerebral Palsy
CT	Computerized Tomography
FMS	Functional Mobility Scale
GDI	Gait Deviation Index
GPS	Gait Profile Score
GMFCS	Gross Motor Function Classification System
GMFM	Gross Motor Function Measure
HHD	Handheld Dynamometer
HREC	Human Research Ethics Committee
HRQoL	Health-related Quality of Life
HADS	Hospital Anxiety and Depression Scale
IC	Initial Contact
ICF	International Classification of Function, Disability and Health
IQR	Interquartile Ranges
LIFE-H	Life Habits Questionnaire
MCS	Mental Health Component Score
MRI	Magnetic Resonance Imaging
ND	Non-Dimensional
ODI	Oswestry Disability Index
PCS	Physical Health Component Score
ROM	Range of Motion

SD	Standard Deviation
SDR	Selective Dorsal Rhizotomy
SF-36v2	Short Form-36 Health Survey version 2
SES	Social Economical Status
TFO	Time to Foot Off
TUG	Timed Up and Go
TD	Typically Developing

INTRODUCTION AND LITERATURE REVIEW

HISTORY

The group of permanent neuromuscular disorders we know today as cerebral palsy (CP) has been studied since ancient times. First descriptions of CP were documented by Egyptians, Greeks, and Romans, although they did not know its cause or how to treat it. The British surgeon William John Little was the first to initiate an in-depth exploration of CP. Consequently, the term 'Little's Disease' emerged amongst the public since the 1830s for the description of CP. One of the first articles William John Little published was entitled 'On the influence of abnormal parturition, difficult labors, premature birth, and asphyxia neonatorum, on the mental and physical condition of the child, especially in relation to deformities', published in 1862 [1]. Based on this he also attempted the first definition of CP; 'a birth injury as a result of difficulties during labor in which the child has been partially suffocated'. A Canadian physician, William Osler, further advanced Little's work and chose to use the term cerebral palsy based on the Latin words for 'brain' and 'paralysis'. In 1889 he published a book titled 'Cerebral Palsies of Children' [2]. Sigmund Freud, an Austrian neurologist and psychiatrist, made a great contribution in the field of CP after Olser. He was the first to recognize that antepartum and postpartum factors could cause CP as well and not only factors during birth as Little proposed. He also associated a variation of disorders to CP including intellectual disabilities and visual disturbances. What is remarkable is that several of Freud's ideas are still part of the current definition of CP [3].

DEFINITION

Cerebral palsy is the most common cause of physical disability in childhood [4]. Definitions developed over time to capture the most correct description of the aetiology and manifestation of this group of neuromuscular disorders. The most recent and widely adopted definition of CP was developed and published by an international expert panel in 2007:

'Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that is attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition,

communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems' [5].

Examples of accompanied disturbances/comorbidities that are associated with an increased prevalence in people with CP are intellectual disability, visual impairment, language and speech disorders, dysarthria, auditory limitations, eating and swallowing disorders, urinary disorders, gastrointestinal disorders, anxiety, depression and cardiovascular problems [5, 6, 7, 8].

CLASSIFICATION

Classification of children diagnosed with CP is challenging due to the broad definition of CP. The most commonly used classification systems used are anatomic, physiological and functional. The anatomic classification is based on the anatomic distribution of CP and includes hemiplegia, diplegia and quadriplegia [9]. The physiological classification refers to the types of CP, which are classified by the type of movement impairment and location of brain damage. The four types include: spastic (cerebral cortex), athetoid/dyskinetic (basal ganglia), ataxic (cerebellum) or mixed type CP [10] (Figure 1.1). The spastic type is the most common, affecting about 80% of people with CP and is most prevalent in the form of spastic diplegia (indicating that both legs are affected and the arms may be affected to a lesser extent) [11]. Spastic diplegia is frequently related to the ischemic brain injury 'periventricular leukomalacia (PVL)', which usually affects the descending motor fibers of the cerebral cortex [12].

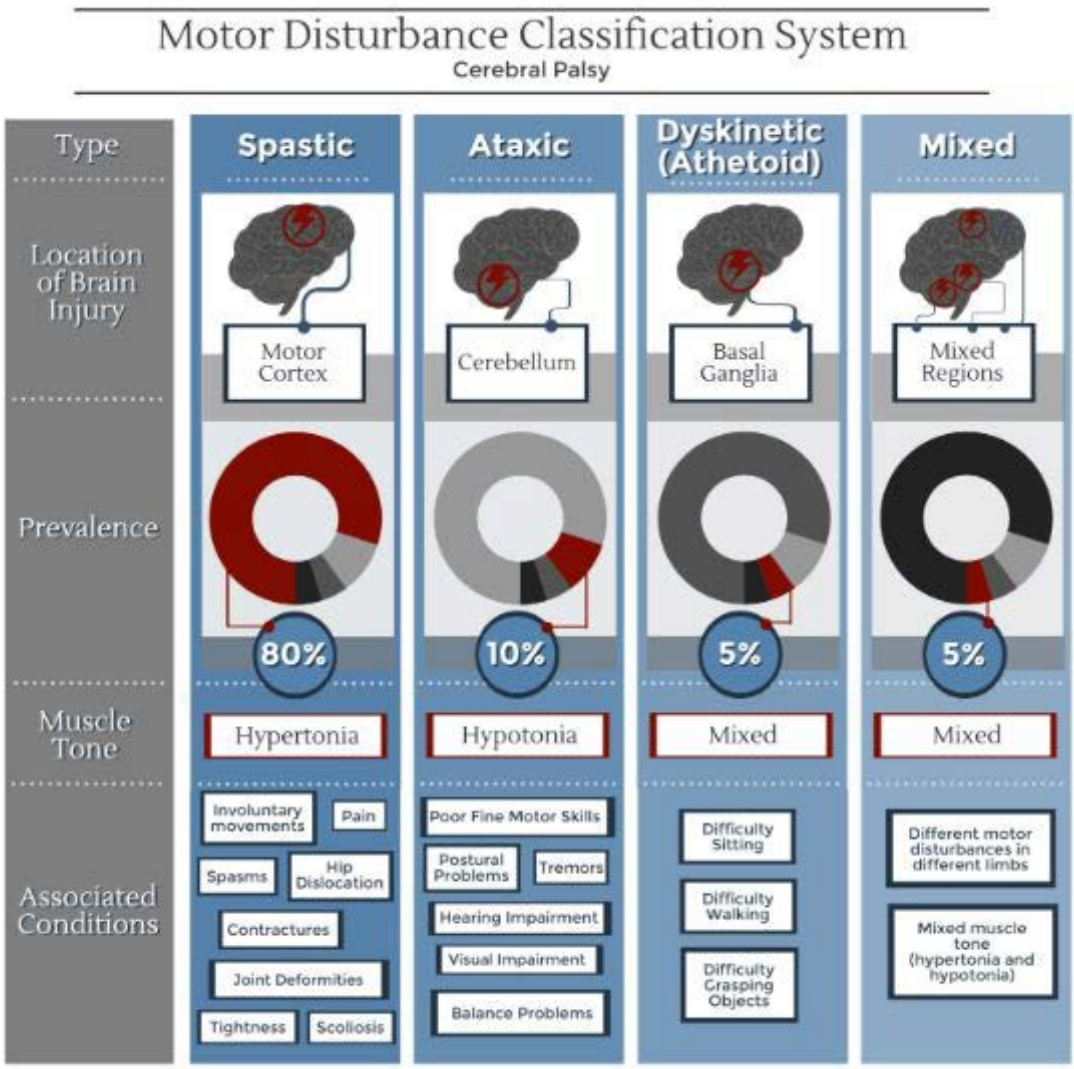

Figure 1.1 *Physiological classification of CP: type of movement impairment and location of brain damage (adapted from Reiter & Walsh, PC - www.abclawcenters.com)*

The most commonly used functional classification is The Gross Motor Functional Classifications System (GMFCS) [13]. The GMFCS is a five-level classification of severity based on gross motor function, where level I reflect the highest level of functioning and Level V the most impaired level of functioning. Additionally, each level has functional descriptions for age groups 1-2 years; 2-4 years; 4-6 years, 6-12 years and 12-18 years (Figure 1.2). The GMFCS has been reviewed for stability in adults with CP [14] and emphasizes the concepts inherent in the World Health Organization's International Classification of Functioning, Disability and Health model (ICF-model) [13].

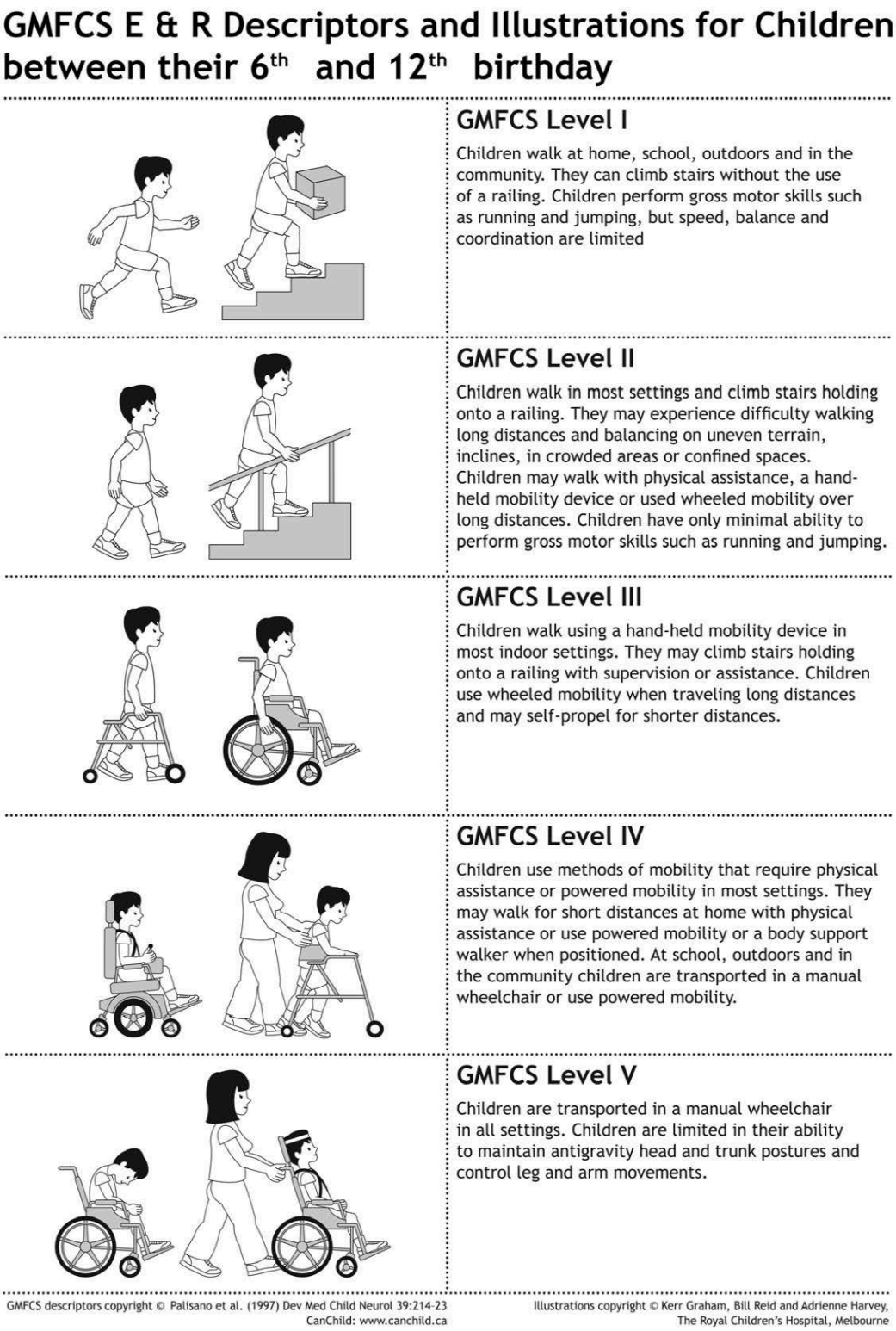

Figure 1.2 *Gross Motor Function Classification System (GMFCS) expanded and revised for children with cerebral palsy, ages 12-18 years. Image copied from www.canchild.ca*

EPIDEMIOLOGY AND ETIOLOGY

The overall prevalence of CP worldwide is approximately 2 per 1,000 live births [15]. The reported estimated prevalence rate in Africa is approximately from 2 -10 per 1000 live births, although very little has been published about the prevalence rates in African countries and the studies that report prevalence rates vary widely in methodology [16].

Prematurity or low birth-weight is one of the major risk factors reported in European or American studies [17], while in African cohorts, birth asphyxia, kernicterus, and neonatal infections were the most common reported etiologies [10]. Generally, there are multiple causal pathways for disturbances in the brain leading to CP. These can occur during prenatal (e.g. intoxication, infection), perinatal (e.g. hypoxic-ischemia) and postnatal (e.g. infection, trauma) period until the first birthday [4]. Recently a growing body of evidence suggests that genomic abnormalities could cause CP [18]. There is also a growing body of research to suggest that maternal obesity may increase the risk of CP in offspring [19, 20].

Although it appears that the frequency of CP amongst very low birth weight infants decreased [21], a trend towards a steady prevalence was found most probably related to improved screening, diagnosis, registration and advances in neonatal and medical care [22]. Progress is being made in further prevention of the brain injury. For example, administration of magnesium sulphate during premature labor and cooling of high-risk infants can reduce the rate and severity of CP [4].

AGING AND SECONDARY COMPLICATIONS OF CP

Almost all higher functioning children with CP survive into adulthood which reflects that life expectancy of individuals with CP have become similar to that of typically developing (TD) adults [4]. Cerebral palsy is the most common cause of childhood-onset, lifelong physical disability in most countries, and people with CP are considered as one of the world's largest populations with a physical impairment [23]. Although the brain injury that initially causes CP is not progressive, the clinical manifestation might change throughout the life span [23]. Secondary conditions which may develop over time as a consequence of the primary condition, contractures, hip subluxations and dislocations, spinal deformities, foot

deformities, gait disorders, pain, fatigue and the development of osteoporosis [23, 24, 25, 26, 27, 28].

Other issues that have been commonly reported throughout the lifespan in adults with CP are a lower perceived health-related quality of life compared to the general population, functional deterioration, an inactive lifestyle, and restrictions in participation in work, intimate relationships and housing [28]. In addition, due to inactive lifestyles and reduced cardiorespiratory endurance in individuals with CP, adults with CP seem also to be more prone to chronic non-communicable diseases [29, 30]. These diseases are related to cardio vascular (e.g. ischemic heart disease, stroke), cardio metabolic (e.g. diabetes, hypertension) and pulmonary systems (e.g. asthma) [31, 32, 33, 34].

One of the biggest challenges during the lifespan of individuals with CP is healthy aging; to prevent or minimize the secondary effects of CP on the musculoskeletal system (e.g. bone deformities due to spasticity) as well as to improve functional status and quality of life [35, 36]. Effective treatment in childhood is essential to prevent secondary complications and guidance and management throughout lifespan is essential to support healthy aging. The aging process inevitably interacts with the motor disorder associated with CP, but systematic, large-scale follow-up studies describing the natural history of CP over the life course are lacking [23]. Recently there is more research and focus on CP management regarding healthy aging to support physical, mental, and emotional wellbeing and goals for desired social participation over the life course [37].

MANAGEMENT

General

Currently, no treatment options are available to cure the brain damage observed in CP. ‘Management’ instead of ‘treatment’ of CP is therefore a more accurate term. Cerebral palsy varies in type, and severity of impairment, which makes a standard protocol for CP management difficult. Therefore, it requires a multidisciplinary approach to address associated movement disorders and its consequences [38]. A comprehensive management plan usually focuses on the primary conditions (e.g. muscle tone, range of motion, gross motor function), secondary conditions (e.g. contractures, spinal deformities) and

comorbidities (e.g. epilepsy, speech disorders, anxiety) in order to maximize mobility, independence and quality of life. Physical therapy and adaptive equipment are basic management options and based on individuals' needs medication, surgical interventions and specialist treatments maybe required [36].

Spasticity

Spasticity is the most prevalent primary condition, estimated to be present in 80% of people with CP (Figure 1.1) [24]. Spasticity is a stretch reflex disorder which occurs as a consequence of a central lesion that damages the upper motor neurons, manifested clinically as an increase in muscle tone that becomes more apparent with rapid stretching movement [39]. Muscle function is dependent on the muscle stretch reflex, which works through excitation of anterior horn motor neurons and continuous sensory feedback from each muscle by the muscle spindle to the spinal cord regarding its length and tension. In more detail, when a limb muscle is stretched muscle spindles respond by sending action potentials to the spinal cord via sensory neurons. In the case of spasticity, the feedback system between muscle spindles and motor neurons is disrupted because of the upper motor neuron lesion. This lesion distorts communication between the brain and the spinal cord, causing disinhibition of the spinal reflexes and abnormal muscle activation occurs [40, 41]. However, besides this explanation of spasticity, it seems highly likely that there are more mechanisms operative in causation of spasticity, which still needs to be fully revealed [41].

There is an importance to specifically treat spasticity to prevent secondary abnormalities related to spasticity like deformities of lower extremities, contractures, joint dysplasia and pain, which can have an influence on gait and level of functioning. Overall, spasticity management can facilitate optimal physical development [42, 43].

There is a variety of options to address the primary spasticity. The choice of these intervention options depends on the level of invasiveness preferred, whether a reversible or permanent effect is desired and/or if a general or focal approach is required (Figure 1.3).

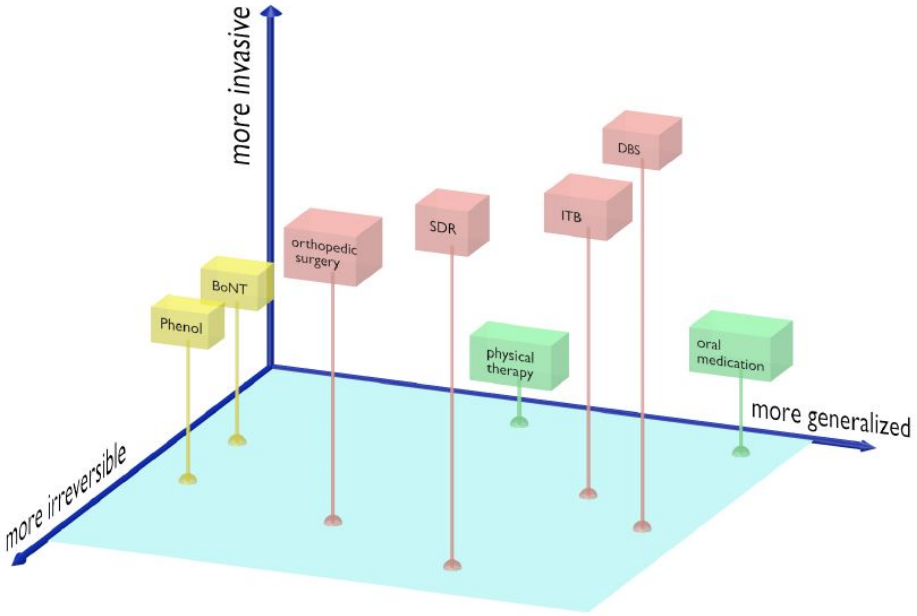

Figure 1.3 *Tone management options in CP. Within the tone management paradigm, options include non-invasive (green), injections (yellow) and surgical (red) (copied from Wang et al. [31]). Abbreviations: BoNT, botulinum toxin; ITB, intrathecal baclofen; DBS, deep brain stimulation; SDR, selective dorsal rhizotomy.*

A systematic review of interventions for CP from Novak *et al.* [44] reported that the best recommended options for spasticity treatment are the reversible option of botulinum toxin injections (BoNT) and diazepam (oral medication) and the non-reversible option of Selective Dorsal Rhizotomy (SDR) (Figure 1.4). A new intervention with potential effectiveness is stem cell therapy; however, this therapy is in the very early stages of development, and more research is needed to show the effectiveness in individuals with spastic CP [45].

Reversible treatment options are not commonly accessible for children with CP living in South Africa, because of high costs and limited accessibility. Therefore, a common management choice is orthopedic surgery in children with CP and spastic diplegia living in South Africa [46]. Another likely treatment regime is SDR (with pre-and post-operative intensive physiotherapy) [47]. SDR is a neurosurgical procedure in which a reduction in spasticity is achieved by the dissection of dorsal nervous roots. Although SDR is accessible for all income groups in South Africa, this management option is limited to a number of children with CP as one has to fulfill strict selection criteria. The reduction in spasticity after a SDR generally leads to a significant reduction in the total amount of required orthopedic surgeries [48, 49, 50], however most patients require a minim~~al~~ of one orthopedic operation

and a few other interventions, such as casting and orthotics, to prevent or address contractures [38, 51] (Figure 1.4).

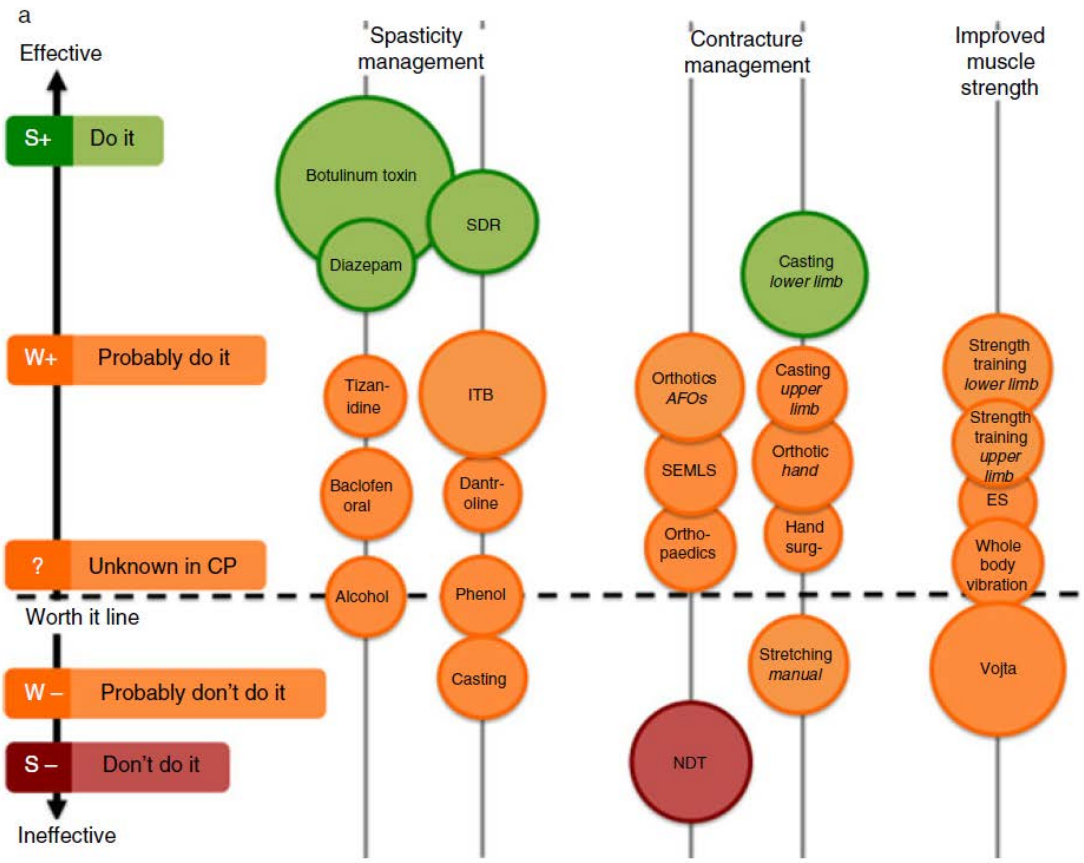

Figure 1.4 *Spasticity and contracture management options and state of the evidence of effectiveness (copied from Novak et al. [33]). Abbreviations: SDR, selective dorsal rhizotomy; ITB, Intrathecal baclofen; AFO's, Ankle foot orthosis; SEMLS; Single-event multilevel surgery; NDT, Neurodevelopmental therapy.*

SELECTIVE DORSAL RHIZOTOMY

History

The first dorsal rhizotomy was performed in humans by Foerster in 1913 [52]. His procedural method of non-selective rhizotomy by complete sectioning of the dorsal nerve roots from L2 level down to S2 level, was abandoned due to the adverse effects of severe sensory deficits and bladder denervation [53]. In the 1960's, Gros refined the procedure by sectioning only a fraction of the sensory nerve roots, thereby preserving sensation [54]. Fasano started using electrical stimulation and electromyography (EMG) monitoring in 1970, to indicate and only cut the fascicles that presumably contribute to the abnormal muscular tone [55, 56]. In the 1980's Warwick Peacock, pediatric neurosurgeon in Cape Town, South Africa, shifted the site of the laminectomy for the procedure from the conus medullaris to the cauda equine [57, 58]. This allowed more distal opening and access to cauda equine, which makes rootlet identification easier in order to prevent complications like bladder and bowel dysfunction. In 1986, after performing more than 100 SDR procedures at Red Cross War Memorial Children's hospital in Cape Town, he moved to Los Angeles and taught this technique globally. Over the last few decades different variations of this technique have been proposed. Park shifted the site back to the conus to perform a more limited laminectomy [59]. He advocates that this results in a smaller scar, less spinal instability and a quicker recovery, although it is more difficult to identify rootlet levels. Sindou, a neurosurgeon from France, was concerned about the long segment exposure required by the Peacock technique (L2–S2) and developed with Georgoulis the Keyhole interlaminar dorsal rhizotomy (KIDr) technique in 2014, which allows minimal spinal ligamentous injury, while still allowing accurate nerve root identification at the exit foraminae [60]. Despite the development of different techniques, the 'Peacock technique' (Figure 1.5) is still widely used. Originally Peacock performed a L2 to L5 laminectomy and then SDR on L2 to S1 (he always left S2 intact) [57, 58]

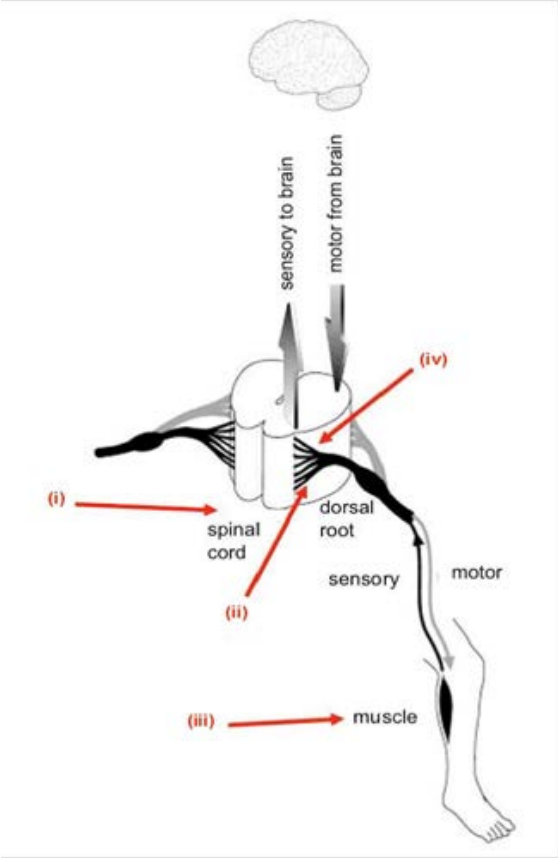

Figure 1.5 *Peacock' SDR technique: (i) laminectomy from L2 to S1 and opening of the dura; (ii) stimulate the posterior rootlets with a 50-Hz train of stimuli at the threshold intensity for muscular contraction; (iii) measure the muscle response with electromyography; and (iv) nerve rootlets associated with a normal response left intact, while those associated with an abnormal response divided (about 50-70% of L2-S1) (adapted from www.uwhealth.org).*

The technique entails using selective dorsal fascicular sectioning as based on electromyographical (EMG) findings, Fasano's principles of EMG interpretation, and the clinical pattern of spasticity [61, 62]. However, the electrophysiological guidance as a necessary component of the SDR has been questioned by clinicians since some studies showed no benefits of using the electrophysiological guidance over no guidance in terms of spasticity reduction and functional outcomes [63, 64]. In addition, concerns were raised regarding increased spinal deformities due to the multilevel laminectomies [65, 66, 67]. This contributed to the fact that SDR was later further modified by doing a laminotomy procedure (replacement of the laminae postoperative and reattachment of the paraspinal muscles). The current SDR practice in Cape Town entails the Peacock technique with electrophysiological guidance and a laminoplasty (laminae are kept attached to the rostral level and put back in pace after dural closure) from L2 to L5 [68].

Selection criteria

Peacock and Arens established a set of selection criteria for SDR to maximize safety and efficacy. Of these criteria they determined that children with spasticity would only benefit from SDR. Other criteria they formulated were that the candidate should have predominant leg involvement, some walking function, a certain level of intelligence and underlying muscle strength. The motivation of the patient and access to intensive physical therapy before and after SDR was also considered important [69, 70]. Contraindications were a diagnosis of athetosis, dystonia, chorea or ataxia, the presence of severe contractures or increased weakness in antigravity muscles.

Grunt *et al.* reviewed selection criteria for SDR and concluded that although many institutions adopted the criteria of Peacock, there are many variations and no international consensus exists [71]. The differences in the main goal of SDR contribute to these variations. Commonly the predominant aim of SDR is to reduce muscle tone to maximize mobility and independence for ambulant children with CP (GMFCS level I-III). Recently some institutions perform SDR procedures in children classified as GMFCS level IV and V with the aim to improve caregiving and pain relief [72].

SDR appears most beneficial when operated on in early childhood, just after the steepest increase of gross motor function development which typically takes place during the first four years [73]. Two randomized controlled trials report spasticity reduction and functional benefits of SDR in combination with physiotherapy in children between the age of four and ten [74, 75]. A third randomized controlled trial researched the effects of SDR in children operated between the age range of 3 and 14 [76], and reported spasticity reduction benefits attributed to SDR (in combination with physiotherapy), but no enhanced functional mobility improvements in comparison to a group who only received physiotherapy. However, controversy exists with SDR performed in children over the age of ten years and in adults. At that age weakness and lower limb deformity are often more relevant than spasticity, and these children may have better outcomes with multi-level orthopedic surgery [77]. Some institutions perform SDR in adults with the aim to improve quality of life [78].

In addition, variations exist between institutions regarding the used preoperational screening tools. Some possible additional preoperative parameters to evaluate SDR candidacy may be selective botulinum toxin injection as part of the preoperative workup to

test the biomechanical hypothesis, gait observance and MRI (to confirm periventricular leukomalacia, which is often seen in spastic CP, and no involvement of basal ganglia, brainstem or cerebellum since they are associated with dystonia) [38, 68, 79]. These additional preoperational tools might not be available to all institutions or countries.

Current practice at Red Cross War Memorial Children's Hospital, Cape Town is to consider indications for SDR in two groups- those who are likely to walk if their spasticity is controlled, and those in whom SDR is a means to reduce lower limb tone to improve posture and facilitate care. In the former group, the goal is not improvement in gait alone, but a meaningful functional improvement [Dr JMN Enslin, personal communication].

The selection criteria which are currently used in Cape Town for ambulant children are described in Figure 1.6. These selection criteria are based on the initial criteria defined by Peacock and Arens [69, 70]. Over the years, the age range (ideally between the ages of five

I. History:

i. Bilateral lower limb spasticity with minimal upper limb involvement
ii. Supportive home environment with well-motivated patient and parents, committed to intensive rehabilitation pre-operatively and post-operatively
iii. Typically between the ages of five and ten
iv. Good response to botulinum toxin
v. Ideally perform SDR prior to orthopedic surgery

II. Examination:

i. Ambulation with or without assistive devices, typically GMFCS grade I, II or III
ii. Good lower extremity antigravity strength (kneeling test/ sitting to standing test)
iii. Good trunk control
iv. No dystonia, athetosis or chorea
v. Exclude progressive neuromuscular conditions associated with spasticity
vi. No moderate or severe spinal deformity
vii. No contra-indication to surgery
viii. Cognitive and emotional ability to cope with intensive rehabilitation

Figure 1.6 *Selection criteria for SDR used in Cape Town, South Africa [Credit: Dr JMN Enslin].*

and ten years), the response to botulinum toxin (as a diagnostic tool to assess functional improvement after botulinum toxin injection) and surgery order (ideally perform SDR prior to orthopedic surgery) were added to the selection criteria used for SDR in Cape Town.

International Classification of Functioning, Disability and Health (ICF) model

A common framework used to assess and understand outcomes of management in CP since 2001, is the International Classification of Functioning, Disability and Health (ICF) model from the World Health Organization (Figure 1.7) [80]. The framework has a biopsychosocial focus on functioning, disability and health [36]. It provides a perspective to describe functioning, disability and health from the interactions among anatomy and physiology (e.g. body structure and function); daily activities (e.g. walking, eating); participation (e.g. school, work); personal factors (e.g. age, gender, educational level, motivation, coping style) and environmental factors (e.g. family attitude, housing situation, laws, service availability).

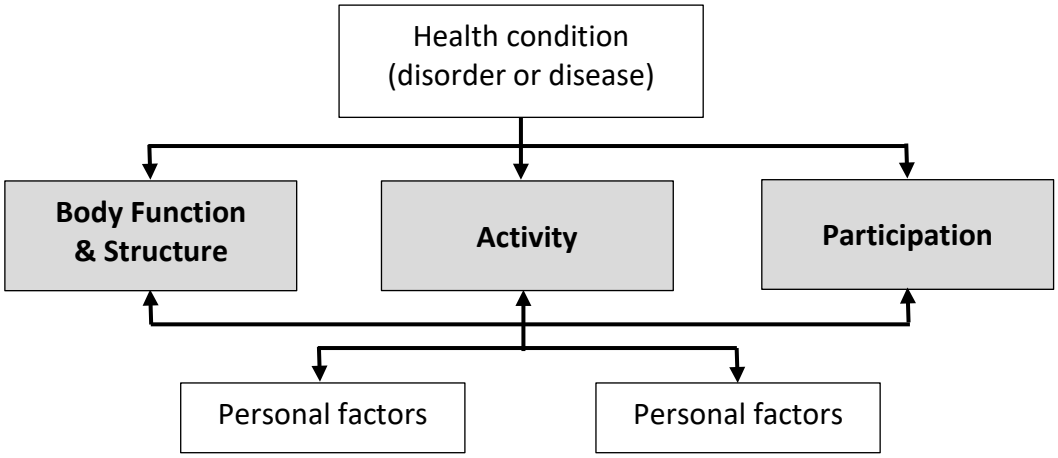

Figure 1.7 *International Classification of Functioning, Disability and Health (ICF) model as published by the World Health Organization [64]*

Change in any of these domains is hypothesized to affect other domains and influence the person's health. Disability may occur when one or more of these domains are limited. Although quality of life is not part of the ICF-model, McDougall *et al.* proposed an expanded ICF model where the overall dimension 'quality of life' is added since it is an essential concept to consider and it sums up many of the dimensions in the ICF-model [81].

Outcomes of SDR

Many studies have been published on the short-term outcomes of SDR (<5 years), including two reviews and a meta-analysis, consisting of three randomized controlled trials, showing that SDR has a positive impact on the ICF domains 'body structure and function' and 'activity' of children with spastic diplegia [82, 83, 84]. The invasive and non-reversible effects of SDR might possibly impact the child into their adolescence and adulthood. Therefore, long-term outcomes evaluations are imperative for clinicians and parents to make informed decisions. Although SDR has been performed since the 1980's, studies with a long term follow-up of minimal five years are limited [85]. Since CP is a condition that covers the lifespan, the evaluation of SDR outcomes influencing the ICF domain 'participation' and quality of life over the life course became particularly important.

The aim of this literature review is to summarize the outcomes of long-term studies after SDR based on the domains of the ICF-model and quality of life. From childhood to adolescence; 5 to 15 years post–SDR and from adolescence to early adulthood; ≥15 years post-SDR.

ICF-model domain: Body function and structure

5 -15 years post-SDR

Grunt *et al.* published a systematic review in 2011 based on 21 articles (published between 1998 and 2010), including 966 children, with a follow-up time of at least five years. The outcomes were based on evidence level in order to draw tentative conclusions about effects attributed to SDR and grouped in line with the ICF model. The final conclusion stated that SDR had a poor to moderate positive long-term effect on the ICF domain 'body function and structure' based on spasticity reduction, range of motion increase and gait improvements [85]. Similar findings regarding the long-lasting spasticity reduction effect of SDR were observed by research that was conducted in the last eight years [49, 51, 86, 87, 88]. For passive range of motion (ROM), latest studies showed different results in the long-term concluding improved [49], unchanged [51, 87] and some deterioration in ROM [51, 86]. Outcomes concerning muscle strength also varied, with Munger *et al.* [49] reporting no differences in muscle strength between baseline and 13 post-SDR and Ailon *et al.* [86] who

observed a sustained increase in strength (quadriceps muscles), more than 10 years following SDR. Munger *et al.* also reported no change in selectivity [49]. With regards to the gait pattern, based on 3 Dimensional Gait Analysis (3DGA), sustained improvements in respectively Gait Profile Score (GPS) and Gait Deviation Index (GDI) were observed [49, 89].

Concerning spinal deformities Grunt *et al.* concluded that these seem more common in children and adolescents who underwent SDR. Though, the authors also state that it remains unclear to what extent SDR is associated with spinal deformities, since this could also be due to the natural history in CP [85]. There is a high rate of some spinal deformities in the general population with CP and with the lack of control groups (patients who did not receive SDR) in the included studies; it is questionable what the cause is of the spinal deformities [85]. This hesitation was confirmed by Van Schie *et al.* [88], who reported a low percentage of spinal deformities (scoliosis and spondylolysis) six years after SDR.

A relation between spinal deformities and back pain has been observed 5 – 15 years after SDR [66, 90]. Grunt *et al.* reported that five – 29 % of patients who underwent SDR suffered from back pain at long-term follow-up [85]. However, besides spinal deformities, multiple other factors can cause pain in adolescents and young adults with CP such as comorbidities and persistent muscle spasticity [38, 51]. In addition, it's known that the prevalence of pain in adults with CP is higher than in the general population [91, 92]. A study of Tedroff *et al.* reported low pain severity and interference with daily tasks based on the The Brief Pain Inventory and suggested that SDR might have possible influenced this [51]. Munger *et al.* also reported similar results and stated that pain caused only minimal interference with activities. Although they attributed the result not to SDR but concluded that SDR and alternative treatment regimens equally prevent the onset of pain through early adulthood [49].

≥15 years post-SDR

The spasticity reduction effect of SDR seems relatively non-controversial. However, there is limited literature available in (young) adults with CP with a follow-up period of 15 years or more following SDR. Dudley *et al.* (15 years post-SDR) and a follow-up study of Langerak *et al.* (17 – 25 years post-SDR); confirmed sustained reduced muscle tone in early adulthood [48, 93]. This was also reflected in the gait pattern as Langerak *et al.* showed (17 – 25 years post-SDR) in their 3DGA study [94]. Despite the fact that the young adults walked with a mild crouch gait pattern, relatively good active joint ROM was shown. A 2DGA study of the same research group confirmed this finding in a 2DGA follow-up study conducted 1, 3, 10 and 20 years after SDR [95]. In addition, another study of Langerak *et al.* (1 and 20 years post-SDR) reported on passive ROM, muscle strength and voluntary movement (combination selectivity and muscle strength) and showed overall sustained improvements in these parameters [96].

Concerning spinal abnormalities there is only one study reporting on the spinal abnormalities in young adults with CP more than 15 years post-SDR. This study of the Cape Town research group observed incidences of scoliosis, hyperkyphosis, hyperlordosis, spondylolysis and spondylolisthesis and found that only the incidence of relatively mild scoliosis increased over time. However, it remained unclear to what extent these abnormalities were due to SDR or natural history of CP [93].

Chronic backpain was reported in (young) adults with CP 19 years (based on Pain Numerical Rating Scale) [97] and 22 years post-SDR (Patient Reported Outcome Measurement Information System and Pain) [98]. However, pain incidence, interference and location were similar for these adults as what has been reported in the literature for adults with CP [97] and to an age-matched control group (adults with CP who did not receive SDR) [98]. The long-term SDR follow-up study of Langerak *et al.* [93] focused on spinal abnormalities, but also reported on the incidences of pain in upper and lower extremities as well as on spinal level more than 17 years after SDR, though this pain had none or minimal influence on daily activities as indicated by the Oswestry Disability Index.

ICF-model domain: Activity and Participation

5 -15 years post-SDR

No evidence was found supporting the positive effect of SDR on the ICF-model 'activity' and 'participation' domains by the review of Grunt *et al.* [85]. Following this systematic review, a variety of articles has been published with divergent results. Van Schie *et al.*[88], Bolster *et al.*[99] and Josenby *et al.*[87] showed sustained improvement in Gross Motor Function Measure (GMFM) 6 to 10 years post-SDR. In contrast, Tedroff *et al.* reported a decline in GMFM ten years post-SDR [51] and Munger *et al.* showed no difference in function (based on Median Gillette Functional Assessment Questionnaire and Functional Mobility Scale (FMS)) between the SDR and control group, 10 – 17 years post-SDR [49].

There are very few long-term outcome studies addressing level of participation of children and adolescents in the community, especially as part of a SDR follow-up study. Grunt *et al.* reported none [85], and into our knowledge only Munger *et al.* included this domain in their 13 year SDR follow-up study. Based on the Frequency of Participation Questionnaire they concluded no differences in participation levels between a SDR and a non-SDR group [49].

≥15 years post-SDR

Positive results regarding functioning were reported for young adults more than 15 years post-SDR. Dudley *et al.* [36] observed sustained improvement in GMFM 15 years post-SDR. Langerak *et al.* [70] also described a sustained improvement in functioning based on the Berman scale, 20 years post-SDR [70] and high levels of functioning based on the FMS 17-25 years post-SDR [100]. Self-reported higher functional levels and fewer decline in motor function (based on GMFCS and MACS) in comparison to a control group were described by Hurvitz *et al.*, 19 years post-SDR [73].

Only one research group published a study with outcomes regarding participation more than 17 years post-SDR, showing that adults with CP experience high levels of accomplishment and satisfaction in daily activities and participation based on the Life-Habits questionnaire [100]. The vast majority of adults with CP were independent in the accomplishment of life habits such as personal care, participation in community life and employment. Some problems were found for mobility and recreation.

Quality of Life

5 -15 years post-SDR

More than 10 years after SDR adolescents with CP perceived to have a good health–related quality of life as concluded by Tedroff *et al.* (based on The Health-Related Quality of Life Health Survey (SF-36v2) [51]. The adolescents who underwent SDR perceived their mental health quality of life even better than the age norm. The overall level of satisfaction with life was also good (Diener Satisfaction with Life Scale), and did not differ from peers who did not undergo SDR in childhood [49].

≥15 years post-SDR

Limited information is available about the quality of life of adults with CP who underwent SDR. Hurvitz *et al.* [97] reported on satisfaction with life (Diener Satisfaction with Life Scale), in adults with CP more than 15 years post-SDR. They found that adults with CP perceived a high level of satisfaction with life, 19 years post-SDR. Langerak *et al.* observed high satisfaction levels with the accomplishment of daily life activities and participation 17 – 25 years post-SDR [100].

Complications

Complications of SDR may occur as a direct result of the operation [88]. Acute complications of the procedure may include infection, hemorrhage and leak of cerebrospinal fluid [89]. Perioperative complications like sensory changes and neurogenic bladder or bowel problems have been reported [101]. However, major complications occurred infrequently and were mostly addressed by change of protocols by neurosurgeons which reduced complication events [102].

Possible long-term suboptimal outcomes described in earlier studies are hypotonia, weakness, sensory change, spinal instability, hip subluxation and urinary incontinence [67, 101, 103]. These may occur due to poor patient selection but the percentage of rootlets cut and spinal levels involved are also variables that can cause suboptimal outcomes [12].

OUTLINE THESIS

Research questions and aims

Among the most compelling challenges for the twenty-first century in the rehabilitation field is the need to chart and understand the life course of adults who have grown up with a 'pediatric condition' like CP and the long-term effects of treatments they have received in childhood [25]. SDR is an effective non-reversible procedure to address spasticity in lower extremities of children with CP. Follow-up studies which describe the effects of SDR in adolescence (5 -15 years post-SDR) are available but there are very limited long-term studies (≥ 15 years post-SDR) addressing the effects of SDR in adults according all the domains of the ICF-model and quality of life. Therefore, the question remains: What is the status of adults with CP who underwent SDR in childhood and what challenges do they face while aging?

Currently the longest follow-up studies of adults who underwent SDR in childhood are those performed up to 25 years after surgery by our research group in Cape Town [77, 78, 84]. Since we have the longest track record in SDR studies we feel the need and responsibility to patients, parents and the clinical community to follow adults who underwent SDR during their life course in order to understand and address the long-term outcomes of SDR. We hope to provide important clinical insight to support parents, caregivers and clinicians in their decision process.

Therefore, the aim of this PhD thesis was to determine the status of adults with CP and spastic diplegia – related to all domains of the ICF-model and health related quality of life – more than 25 years after SDR. The second aim was to investigate the changes in gait pattern, spinal deformities and level of accomplishment and satisfaction in daily activities and participation in adults with CP over a nine-year period. The third and last aim was to explore associations between results in the different ICF-model domains along with personal and environmental context factors.

Study design and population

This PhD thesis forms part of a longitudinal investigation tracking the health and wellness of adults with CP. The original studies were performed in 2008 [93, 94, 100] and consequently

a recent follow-up was conducted in 2017 in the same CP cohort. All participants underwent SDR according to the Peacock method (laminectomies L2 – S1) at Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1981 and 1991. The cross-sectional studies of 2008 conducted by Dr. Langerak *et al.* [93, 94, 100] were based on 32 adults with CP more than 17 years after SDR. Inclusion criteria were a diagnosis of spastic diplegia, without dystonia, athetosis, ataxia and/or hypotonia. All participants underwent SDR with the aim to improve on functional level, had access to on-going physiotherapy before and after SDR, together with adequate care-taker support. In addition, participants were pre-operative classified as Gross Motor Function Classification System (GMFCS) level I, II or III.

For the 2017 studies, participants were excluded if they had developed other neuromuscular disorders. In addition, to address the results in a South African context a typically developing group (TD) was recruited, which matched for age, gender, SES and BMI with SDR cohort.

The studies were approved by the Human Research Ethics Committee of the University of Cape Town (HREC NO: 133/2016).

Chapters

This PhD thesis is based on four studies, with the first being a cross-sectional study conducted in 2017 (Chapter 2) and the other three are nine-year follow-up studies (2008 vs. 2017). Each study included a matched TD group, except for the spine study (Chapter 4).

Chapter 2 includes a study investigating the physical, mental and health-related quality of life status of adults with CP and spastic diplegia 25 – 35 years post-SDR. In addition, associations were investigated between the physical aspects, functional mobility and quality of life status in the SDR group. A study investigating the gait pattern and change in gait pattern in adults with CP 25 – 35 years post-SDR is presented in **Chapter 3**. Associations with personal and contextual factors were also explored. **Chapter 4** captures a study determining spinal deformities and pain as possible complications of SDR and the change in these factors over a nine-year period. In addition, associations with personal and contextual factors were presented**. Chapter 5** contains a study which describes the change in the functional mobility, level of accomplishment and satisfaction in daily activities and participation of

adults with CP while aging. Associations between functional mobility and level accomplishment and satisfaction in daily activities and participation were investigated. In **Chapter 6** the overall reported outcomes are summarized and discussed in the light of the ICF-model. In addition, a description of the implications for patients, clinical community, CP management and possible future research directions will be given.

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PHYSICAL STATUS, QUALITY OF LIFE AND LEVELS OF ANXIETY AND DEPRESSION IN ADULTS WITH CEREBRAL PALSY MORE THAN 25 YEARS AFTER SELECTIVE DORSAL RHIZOTOMY

INTRODUCTION

Cerebral palsy (CP) is defined as a persistent non-progressive disorder of posture or movement arising from damage to the immature brain [1]. Primary neuromuscular and musculoskeletal impairments of CP include spasticity, poor balance, loss of selective motor control, and muscle weakness [2], which can lead to secondary abnormalities of CP like contractures and bone deformities. Addressing these primary and secondary effects has been the main focus of CP management in children. Tracking of their physical development into adulthood is imperative since life expectancy of individuals with CP is now similar to that of typically developing (TD) adults [3]. Subsequently, the management of CP has shifted to a biopsychosocial lifespan approach, aligned with the International Classification of Function, Disability and Health (ICF) model [4]. Management plans now include several life and health components besides physical function such as social participation, mental health and quality of life (5-8).

Selective Dorsal Rhizotomy (SDR) is a well-established neurosurgical treatment option designed to reduce spasticity in the lower limbs, and that aims to improve motor function in children with CP [5]. Long-term follow-up studies up to 20 years after SDR have described positive benefits of this procedure for adults with CP on the ICF domain body structure and function [6]. However, less is known about the effects of spasticity reduction on other factors like functional mobility, balance, mental well-being and quality of life. Recently, several studies have evaluated aging in adults with CP, reporting challenges with functional mobility, quality of life and mental-wellbeing [7, 8, 9, 10, 11]. The status of adults with CP longer than 25 years post-SDR on these domains have not reported as well as not how these factors relate to the body structure and function domain.

Healthy aging is important for adults with CP, thus it is vital to establish the physical, mental and quality of life status and the relationship between those domains, in adults with CP more than 25 years after SDR. This could assist parents of children with CP and inform clinicians to make evidence based decisions regarding life span support and therapies for children with CP who underwent SDR [12].

Therefore, the first aim of this study was to determine the (i) physical status: lower extremity muscle tone, passive range of motion (ROM), strength and selectivity; (ii) functional mobility and dynamic balance; (iii) health-related quality of life and; (iv) anxiety

and depression levels in adults with CP who underwent SDR at least 25 years ago, compared to matched typically developing (TD) individuals. The second aim of the study was to determine the relationships between physical status and functional mobility, health-related quality of life, anxiety and depression levels within the CP population.

METHODS

Study design and participants

This is a cross-sectional study of adults with CP and spastic diplegia, who underwent SDR at Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1981 and 1991. For comparison, a group of TD adults was recruited and matched for age, gender, body mass index (BMI) and Social Economical Status (SES) with the CP cohort. Adults in the TD group were excluded if they had any neuromuscular disorders and/or other physical impairments. Before agreeing to participate in the study all participants signed a written informed consent. The study was approved by the Human Research Ethics Committee of the University of Cape Town (HREC NO:133/2016).

Participants' characteristics

Participants' characteristic information obtained included age, gender, SES, BMI, Gross Motor Function Classification System (GMFCS), current health status and previous orthopedic and other interventions received related to CP. Estimation of SES was determined by housing density, calculated as the number of people living in the house divided by the number of rooms in the house (excluding kitchen and bathroom). SES categories were defined as follows: < 1: 'high SES'; ≥1 and ≤1.5: 'normal SES'; and >1.5: 'low SES'[13]. The number of previous interventions received was determined by clinical record review, identifying scars and thoroughly asking the participants and/or parents/care-takers. In addition, participant level of GMFCS (age bracket 12 - 18 years) [14] was determined by observation and consultation with the participant.

Physical examination

The physical examination determined muscle tone, passive ROM, muscle strength and selectivity in the lower extremities. All assessments were conducted by the same physiotherapist (BEV) with an assistant and according to standard measures used for physical examination in people with CP as described by Novacheck *et al.* [15].

Muscle tone of the hip flexors, hip adductors, knee flexors, knee extensors and plantar flexors were assessed and rated according to the Ashworth scale [16]. The Ashworth scale categories are as follows 0: 'no increase in tone'; 1: 'slight increase in tone giving a catch when the limb is moved'; 2: 'more marked increase in tone but limb easily moved'; 3: 'considerable increase in tone, passive movement difficult' and 4: 'limb rigid during passive movement'.

Passive ROM was measured using a goniometer. Joints assessed included; Hip: flexion, extension, adduction, abduction, femoral anteversion, external and internal rotation; Knee: flexion, extension, popliteal angle (uni- and bi-lateral, with hamstring shift), thigh foot angle and bimalleolar axis; and Ankle/Foot: dorsiflexion (with knee flexed and extended) and plantar flexion.

Muscle strength (maximal isometric force) was measured with the use of a handheld dynamometer (HHD; MicroFet2, ProCare B.V., Groningen, NL). Muscle strength was determined for: Hip: flexion, extension, abduction and adduction; Knee: flexion and extension; and Ankle: dorsi- and plantar flexion. Assessments in standardized positions were followed according to the manufacturer's recommendations (Table 2.1).

Table 2.1 *Standardized position of the participant and hand-held dynamometer to assess muscle strength of eight muscle groups*

Muscle group	Position	Placement HHD
Hip flexors	Sitting	Anterior thigh, 3cm proximal to patella
Hip extensors	Prone	Posterior thigh, 5cm proximal to knee joint
Hip abductors	Side	Lateral thigh, 5cm proximal to knee joint
Hip adductors	Supine	Medial thigh, 5cm proximal to knee joint
Knee flexors	Sitting	Anterior tibia, 5cm proximal to malleoli
Knee extensors	Sitting	Posterior calf, 5cm proximal to malleoli
Ankle dorsiflexors	Supine	Dorsal surface of metatarsal heads
Ankle plantar flexors	Supine	Plantar surface of metatarsal heads

The isometric 'make' test, in which participants were instructed to increase muscle force gradually by pushing maximally for five seconds against the resistance given by the investigator, was used (16). Peak isometric force was determined as the mean force over three trials, and was normalized for bodyweight (17). In instances where the last value was the highest value, an additional trial was performed. Selectivity of movements (motor control) were determined for Hip: flexion, extension, abduction and adduction; Knee: flexion and extension; and Ankle: dorsi- and plantar flexion. These were ranked on the selectivity scale ranging from 0 – 2; 0: 'only patterned'; 1: 'partially isolated' and 2: 'completely isolated'. [15].

Functional mobility and balance

The Timed Up and Go test (TUG) is a measure of participants' level of functional mobility and dynamic balance (performance level). During the TUG test participants are asked to stand up from a chair (with back and arm rest), walk 3 meters up and down and sit down in the same chair again in the fastest possible time [17]. Each participant performed the test three times, with the fastest time used for data analysis. The TUG is a valid and reliable tool and is often used in CP research studies for the determination of functional mobility and balance [18, 19].

Health-related quality of life

Health-related quality of life (HRQoL) was assessed with the Short Form-36 Health Survey version 2 (SF-36) [20]. The SF-36 is 36-item questionnaire that assesses eight health concepts and their perceived impact on quality of life: (1) physical functioning; (2) limitations in usual role activities because of physical health problems (physical role functioning); (3) bodily pain; (4) general health; (5) vitality (energy and fatigue); (6) social functioning; (7) limitations in usual role activities because of emotional problems (emotional role functioning); and (8) general mental health (psychological distress and well-being). The SF-36 generates two summary scores: the Physical Health Component Score (PCS) and the Mental Health Component Score (MSC). These summary scales are used as a measure of participants' overall HRQoL. The eight health concepts and summary scores range from 0 to

100, with higher scores indicating a better HRQoL. The SF-36 surveys were processed through the Quality Metric Health Outcomes Scoring Software 4.0 (QualityMetric Incorporated, Lincoln, RI, USA). The SF-36 is a valid and reliable questionnaire used in a wide range of study populations including adults with CP [8, 10, 21].

Anxiety and Depression

The Hospital Anxiety and Depression Scale (HADS) is a questionnaire which screens for symptoms of anxiety and depression [22]. It is a self-rating scale consisting of 2 subscales: Anxiety and Depression. Each subscale includes seven questions with four options (score 0 – 3), resulting in a possible total score of 0 to 21. The total Anxiety and Depression scores were categorized as: 0 – 7: 'normal'; 8 – 10: 'mild case'; 11 – 14: 'moderate case'; and 15 – 21: 'severe case'. The HADS has shown to be a reliable and valid questionnaire in screening for the caseness of anxiety disorders and depression in ambulant populations [23].

Statistical analysis

Descriptive statistical analysis was used to summarize participants' characteristics. Normality of outcome measures was tested using the Shapiro-Wilk test to determine the use of parametric or non-parametric statistical analyses. Differences for gender, age, BMI and SES between adults with CP and TD adults were assessed with Chi-Square and Mann-Whitney U tests.

Muscle tone and selectivity assessments outcomes were presented as frequencies and Fishers' exact tests were performed to determine differences between adults with CP and TD adults. Non-parametric variables: Strength, ROM, TUG, HADS and SF-36 were presented as median [interquartile ranges (IQR)]. The difference in the non-parametric variables between adults with CP and TD adults were assessed using a Mann-Whitney U test. To compensate for multiple comparisons (ROM: 16, strength: 8, TUG: 1, HADS: 2 and SF-36: 10), a Bonferroni corrected alpha-level was applied: ROM: $p < 0.0031$; strength: $p < 0.0063$; TUG: $p < 0.05$; HADS: $p < 0.025$; and SF-36: $p < 0.005$.

To examine the associations between physical status domains (muscle tone, ROM, strength and selectivity) and TUG, HRQoL (PCS and MCS), anxiety and depression levels Spearman's

rank correlation analyses were used. As a threshold for statistical significance, to compensate for multiple comparisons (8), a Bonferroni corrected alpha-level of $p < 0.0063$ was applied. Statistical analyses were performed using SPSS version 25 (IBM SPSS Statistics, IBM Corporation, Chicago, IL, USA).

RESULTS

Participants' characteristics

Twenty-six adults with CP and 26 matched TD adults were recruited for this study. The general characteristics of the two groups are shown in Table 2.2.

Table 2.2 *Participants' characteristics of CP and TD cohorts (each cohort n=26).*

Variable	CP	TD
Gender, male	16 (60)	16 (60)
Current age (years)	35.8 [34.2 – 41.40]	35.7 [33.2 – 44.2]
SES	0.9 [0.7 – 1.3]	0.8 [0.6 – 1.3]
BMI (kg/m^2)	25.2 [21.6 – 31.2]	25.9 [24.1 – 28.2]

Abbreviations: IQR, interquartile range; SES, socio-economic status; and BMI, Body Mass Index.

No differences in gender, age, BMI and SES were found between the two cohorts. The median [IQR] age at SDR of the CP cohort was 4.9 [3.7 – 10.1] years, while the median follow-up time since SDR was 30.1 [27.5 to 32.7] years. At the time of current study, 13 adults with CP (50%) were classified as GMFCS level I, while 10 (38%) as level II and 3 (12%) as level III. In addition to the SDR, 14 of the CP participants (54%) received orthopedic interventions before SDR, while 15 (58%) received additional orthopedic surgery after SDR. None of the adults with CP received either intramuscular botulinum toxin injections or an intrathecal baclofen pump.

Physical status

No differences were found in muscle tone between the CP and TD groups (Figure 2.1). Increased muscle tone (Ashworth 1 or 2) was seen in a minimal number of muscle groups (up to 12%) in adults with CP ($p > 0.235$).

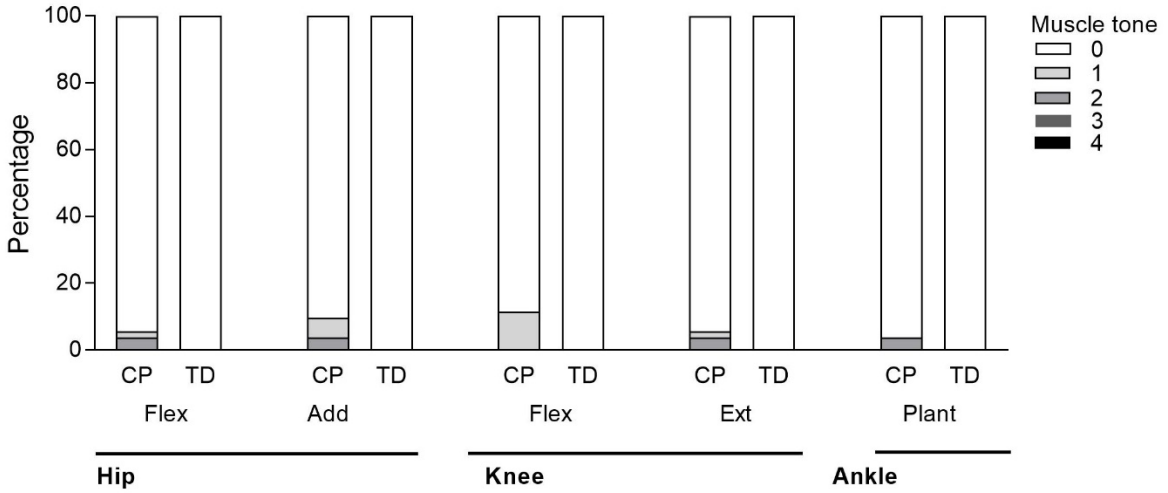

Figure 2.1 *Frequencies per Ashworth score for muscle tone assessment in lower extremities in CP and TD cohorts*

Differences between the CP and TD cohort in ROM were found for hip flexion, abduction, external rotation and femoral anteversion ($p < 0.001$). While at the knee, differences were found in knee extension and pop-angles (both bi- and uni-lateral) ($p < 0.001$). Ankle passive ROM differences in dorsiflexion with both a flexed and extended knee were found ($p < 0.001$) (Table 2.3)

Table 2.3 *Passive Range of Motion (ROM) of lower extremities for CP and TD cohorts*

Passive ROM (degrees)		**CP**	**TD**	***p***
		Median [IQR]	Median [IQR]	
Hip	Flexion	114 [108 – 123]	135 [125 – 140]	<0.001*
	Extension	18 [15 – 23]	21 [18 – 25]	0.032
	Abduction	38 [31 – 43]	63 [55 – 68]	<0.001*
	Adduction	25 [23 – 28]	24 [20 – 25]	0.419
	External rotation	37 [31 – 45]	49 [45 – 55]	<0.001*
	Internal rotation	54 [40 – 55]	50 [45 – 58]	0.582
	Femoral anteversion	23 [20 – 28]	15 [13 – 19]	<0.001*
Knee	Flexion	141 [125 – 148]	144 [140 – 148]	0.202
	Extension	4 [1 – 5]	7 [5 – 10]	<0.001*
	Pop-angle (uni-lateral)	47 [41 -53]	15 [10 – 15]	<0.001*
	Pop-angle (bi-lateral)	35 [30 – 38]	7 [0 – 15]	<0.001*
	Thigh foot angle	13 [8 – 16]	10 [8 – 14]	0.246
	Bi-malleolar axis	12 [7 – 25]	18 [13 – 23]	0.267
Ankle	Dorsiflexion - Flexed knee	8 [5 – 13]	23 [18 – 25]	<0.001*
	Dorsiflexion - Extended knee	0 [-4 – 5]	11 [8 – 15]	<0.001*
	Plantar flexion	44 [38 – 50]	46 [43 – 50]	0.236

**p < 0.0029 is significant*

Muscle strength in all muscle groups were lower in the CP cohort than in the TD cohort ($p < 0.001$) (Table 2.4). Muscle strength data of knee flexion of two adults was excluded due to contractures.

Table 2.4 *Strength of lower extremities muscles for CP and TD cohorts measured with hand-held dynamometer*

Force (N/kg)		**CP**	**TD**	***p***
		Median [IQR]	Median [IQR]	
Hip	Flexion	1.2 [1.0 – 1.8]	3.7 [2.4 – 4.3]	<0.001*
	Extension	1.3 [0.8 – 1.7]	3.6 [2.3 – 4.6]	<0.001*
	Abduction	1.3 [0.9 – 1.7]	4.5 [3.0 – 5.1]	<0.001*
	Adduction	1.8 [0.9 – 2.4]	3.3 [2.3 – 3.8]	<0.001*
Knee	Flexion**	0.8 [0.4 – 1.4]	2.8 [2.2 – 3.2]	<0.001*
	Extension	1.7 [1.2 – 2.8]	4.7 [4.1 – 6.5]	<0.001*
Ankle	Dorsiflexion	0.1 [0.0 – 0.1]	0.3 [0.2 – 0.4]	<0.001*
	Plantar flexion	0.1 [0.0 – 0.1]	0.5 [0.0 – 0.6]	<0.001*

** p < 0.0063 is significant; **n=24*

Selectivity in the CP cohort were poorer in comparison to the TD cohort, in all movement directions ($p < 0.023$) except for hip adduction (Figure 2.2). Minimal (up to 7%) 'only patterned' selectivity (selectivity score 0) was found for the different muscle groups in adults with CP.

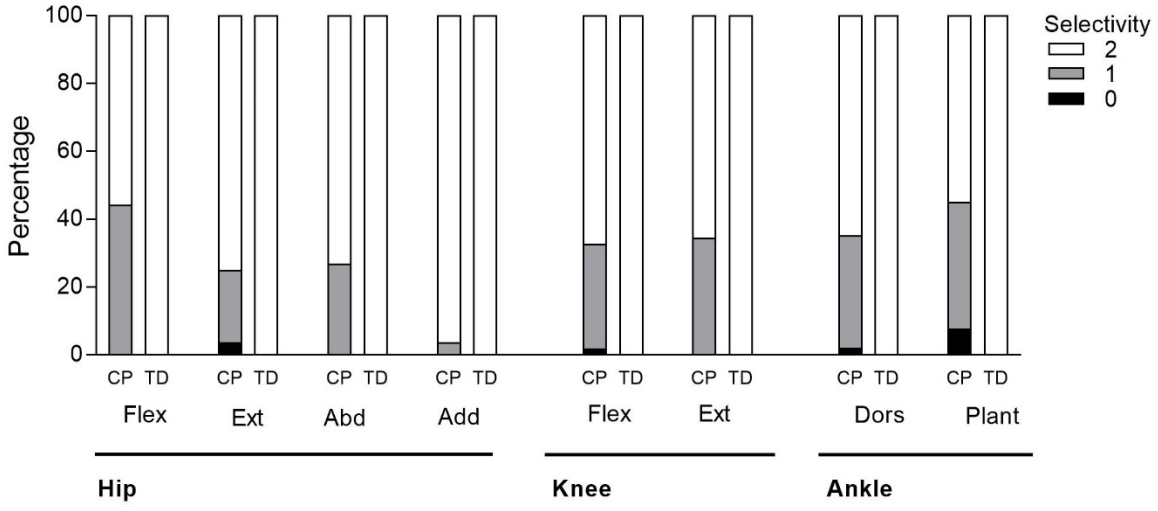

Figure 2.2 *Frequencies per selectivity score in lower extremities in CP and TD cohorts Functional mobility and balance*

Functional mobility and balance

Functional mobility and dynamic balance, measured by the TUG test, was poorer in the adults with CP than in TD adults ($p < 0.001$). In the CP cohort the median [IQR] time for the TUG was 7.9 [5.6 to 11.0] seconds, while the median time in the TD cohort was 3.5 [3.1 to 3.8] seconds.

Health-related quality of life

No differences between CP and TD groups for the eight health concepts, except for physical functioning ($p < 0.001$) (Table 2.5). Adults with CP perceived their physical functioning to be worse than the TD adults. A difference in the physical component summary score (PCS) was found ($p < 0.005$), with lower scores for adults with CP; while the mental component summary score (MCS) were similar between groups.

Table 2.5. *Health-related quality of life for CP and TD cohorts*

SF-36 (0 – 100)	**CP**	**TD**	***p***
	Median [IQR]	Median [IQR]	
Health concepts			
Physical functioning	78 [50 – 95]	100 [95 –100]	<0.001*
Physical role functioning	100 [75 –100]	100 [94 – 100]	0.468
Bodily pain	73 [51 – 100]	84 [74 – 100]	0.021
General Health	86 [72 – 100]	82 [67 – 87]	0.065
Vitality	75 [56 – 81]	75 [63 – 81]	0.941
Social functioning	100 [75 – 100]	100 [88 – 100]	0.815
Emotional role functioning	100 [100 – 100]	100 [83 – 100]	0.262
Mental Health	85 [70 – 90]	83 [75 – 90]	0.853
Summary scores			
Physical component (PCS)	52 [44 – 57]	57 [55 – 60]	<0.005*
Mental component (MCS)	58 [51 – 60]	53 [48 – 58]	0.176

**p < 0.005 is significant*

Anxiety and depression

No difference in levels of anxiety ($p = 0.713$) or depression ($p = 0.867$) were found between the adults with CP and TD adults (Figure 2.3). Mild to moderate levels of anxiety were experienced by 23% of the adults with CP and 15% of the TD adults. While no levels of

depression were observed in adults with CP and 8% of the TD adults reported a mild to moderate level of depression.

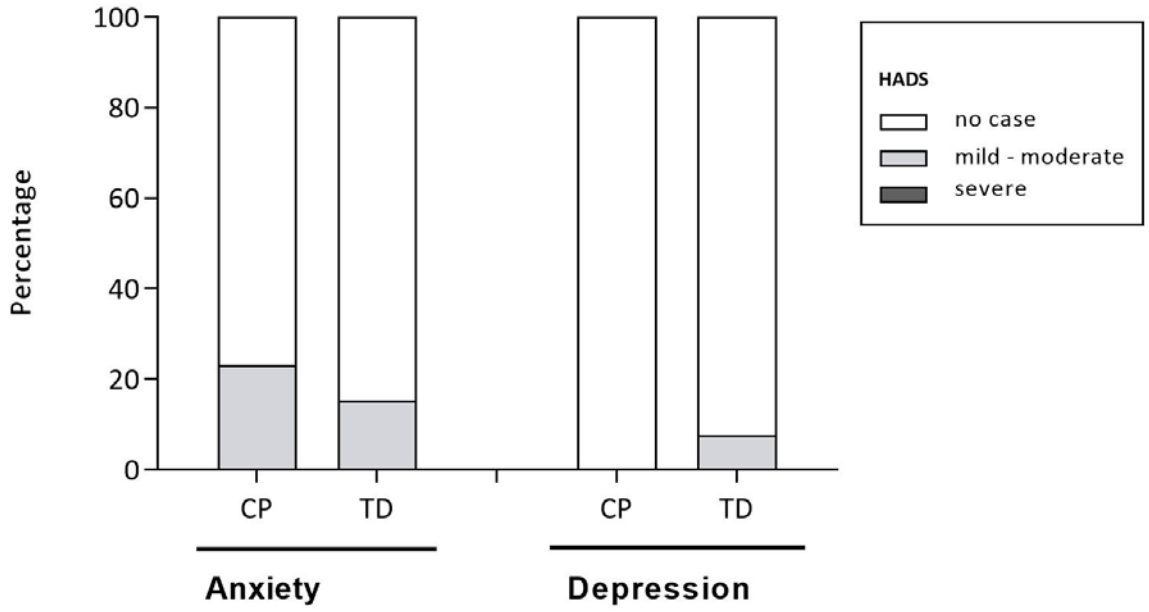

Figure 2.3. *Frequencies of Anxiety and Depression (HADS) scores for CP and TD cohorts*

Correlations

Muscle tone and depression data were not included in the statistical analyses as the number of abnormal muscle tone and depression levels were limited in the CP cohort. Correlations were found between strength measurements (muscle groups: hip extensors and abductors, knee flexors and extensors and ankle dorsiflexors) and TUG, with correlations ranging from -0.53 to -0.72. Except for a correlation between hip extensor strength and HRQOL PCS score ($r = 0.54$, $p = 0.005$), no other correlations with muscle strength were found (Table 2.6). No correlations were found for ROM (Table 2.7) and selectivity (Table 2.8) with the functional mobility and balance, HRQoL summary scores and anxiety.

Table 2.6 *Spearman's rho correlations for strength vs. TUG, PCS, MCS and Anxiety of the CP cohort*

Strength		**TUG**		**PCS**		**MCS**		**Anxiety**	
		r	*p*	r	*p*	r	*p*	r	*p*
Hip	Flexion	-0.46	0.019	0.23	0.268	0.05	0.823	-0.10	0.636
	Extension	-0.72	<0.001*	0.54	0.005*	0.07	0.749	-0.18	0.373
	Abduction	-0.59	0.001*	0.38	0.053	-0.07	0.721	0.11	0.585
	Adduction	-0.36	0.073	0.29	0.159	-0.26	0.194	0.09	0.681
Knee	Flexion**	-0.55	0.005*	0.08	0.704	-0.03	0.875	0.12	0.576
	Extension	-0.53	0.005*	0.31	0.122	-0.14	0.506	0.02	0.935
Ankle	Dorsiflexion	-0.63	<0.001*	0.26	0.198	0.06	0.789	-0.18	0.373
	Plantar flexion	-0.48	0.014	0.16	0.442	-0.06	0.761	0.05	0.801

Abbreviations: TUG, Timed Up and Go test; PCS, Physical Component Summary score; and MCS, Mental Component Summary Score.
**p < 0.0063 is significant; ** n=24*

Table 2.7 *Spearman's rho correlations for ROM vs. TUG, PCS, MCS and Anxiety of the CP cohort*

ROM		**TUG**		**PCS**		**MCS**		**Anxiety**	
		r	*p*	r	*p*	r	*p*	r	*p*
Hip	Flexion	-0.36	0.072	0.27	0.176	-0.14	0.496	-0.16	0.426
	Extension	-0.24	0.229	0.06	0.783	-0.26	0.206	-0.11	0.601
	Abduction	-0.01	0.636	0.02	0.923	-0.39	0.051	0.29	0.148
	Adduction	0.16	0.940	-0.01	0.988	-0.07	0.731	0.15	0.477
Knee	Flexion**	-0.19	0.345	0.22	0.210	-0.20	0.336	-0.22	0.289
	Extension	-0.10	0.613	0.20	0.335	-0.18	0.375	0.46	0.017
Ankle	Dorsiflexion	-0.35	0.076	0.32	0.108	0.00	0.989	0.00	0.986
	Plantar flexion	-0.22	0.281	0.08	0.682	-0.36	0.076	-0.00	0.996

Abbreviations: TUG, Timed Up and Go test; PCS, Physical Component Summary score; and MCS, Mental Component Summary Score
**p < 0.0063 is significant; ** n=24*

Table 2.8 *Spearman's rho correlations for Selectivity vs. TUG, PCS, MCS and Anxiety of the CP cohort*

Selectivity		**TUG**		**PCS**		**MCS**		**Anxiety**	
		r	*p*	r	*p*	r	*p*	r	*p*
Hip	Flexion	0.03	0.896	0.21	0.313	0.23	0.255	-0.42	0.033
	Extension	-0.22	0.279	0.37	0.065	0.37	0.066	-0.24	0.237
	Abduction	-0.16	0.446	0.24	0.244	0.19	0.351	-0.11	0.593
	Adduction	-0.28	0.166	0.20	0.327	-0.33	0.096	0.11	0.597
Knee	Flexion**	0.10	0.629	-0.25	0.221	-0.22	0.272	0.04	0.834
	Extension	0.03	0.899	-0.03	0.877	0.05	0.799	0.04	0.834
Ankle	Dorsiflexion	-0.06	0.757	-0.11	0.588	-0.08	0.699	0.10	0.641
	Plantar flexion	-0.19	0.345	-0.05	0.823	-0.04	0.851	0.00	1.000

*Abbreviations: TUG, Timed Up and Go test; PCS, Physical Component Summary score; and MCS, Mental Component Summary Score. *p < 0.0063 is significant; ** n=24*

DISCUSSION

This is the first study to report physical, mental and quality of life status of adults with spastic diplegic CP more than 25 years after SDR. Insights in outcomes related to physical status will help to guide individuals in the long-term after SDR, promoting healthy aging.

Physical status

The prominent result found in this study was the normalized muscle tone in adults with CP more than 25 years post-SDR. It is known that SDR has a direct effect on spasticity [5, 24, 25], which proved to result in sustained decreased muscle tone through adolescence [12, 26], early adulthood [21, 27, 28, 29] and later in adulthood more than 25 years after SDR, as confirmed in this study. ROM of adults with CP was impaired when compared to TD adults despite, almost normal muscle tone and receiving additional orthopedic interventions before and after SDR (common practice) [30]. Interestingly, mobility in children with CP is different to what has been seen in typically developing children and adolescents [31, 32, 33], and with increasing age, a decrease in ROM, due to natural history of CP, can be expected [34]. Therefore, it is not surprising that the ROM of more than half of the assessments (9/16 assessments) were different between the adults with CP and their matched peers. Muscle strength and selectivity was reported to be lower in the adults with CP than their TD peers. The effect of SDR on muscle strength and motor control has been a

point of discussion. After SDR some studies have shown no changes [28, 29] or improvement [12] in strength, while there are also reports of deterioration [5] during first years after surgery. Generally, it is agreed that children, adolescents [35] and adults [36] with CP are weaker than the typically developing population, and also show impaired selectivity [37, 38]. This agrees with the findings of the current study, with overall muscle strength of the adults with CP being half of what has been assessed in the TD cohort.

Differences in ROM, muscle strength and selectivity appear to be influenced by differences in neurophysiology of muscles in individuals with CP compared to TD adults. Structural abnormalities in the muscle among individuals with CP, such as reduced muscle size (shorter and smaller) and abnormal composition, combined with altered neural control (e.g. increased co-contraction and selective activation) are seen and contribute to reduced muscle strength when compared with TD individuals [3, 7, 39] as well as the ability to rapidly produce force [40, 41, 42]. Lifelong exercise and training programs may assist in improving these outcome measures as customized traditional [43, 44] and high-velocity [41, 45] muscle resistance training programs have shown to be beneficial in CP populations, if specific methods and guidelines/training protocols are adhered.

Functional mobility and balance

The majority of adults with CP showed typical functional mobility with no higher risk for falls but took longer to complete the TUG compared to the TD adults. This might be due to the differences found in physical status, especially muscle strength appears to impact functional mobility, as a correlation was found between TUG and muscle strength. Many ambulant adults with CP experience functional mobility decline earlier than their non-disabled peers [7], with reduced balance performance and elevated falls risk evident. However, a study of Maanum *et al.* [19], who assessed adults with CP (age range 18 – 65 years, GMFCS I-III), found that most of their cohort completed the TUG within 13.5 seconds, which indicates a normal functional mobility an no higher risk for falls [46]. These results correspond with our findings, where 89% of the CP cohort also completed the TUG within this time frame. This suggest that adults with CP manage to function well despite being on the lower end of the normal scale attributed to their physical status.

Health-related quality of life

Surprisingly, the adults with CP perceived a relatively good HRQoL since, seven of the eight health concepts in the SF-36, physical role functioning, bodily pain, general health, vitality, social functioning, emotional role functioning and mental health did not differ between adults with CP and TD adults. Other studies reported challenges for adults with CP in most of these areas [9, 10, 11, 47], although, the adults with CP in this study perceived a lower HRQoL in physical functioning (concept and PCS score) than TD adults, which have been described previously [10, 21]. In addition, no difference in overall HRQoL mental score (MCS) was found that suggests that while adults with CP have ongoing physical challenges, this might not directly impact their mental health.

The mean HRQoL summary scores in current CP cohort (PCS and MCS score) were higher than reported in other studies including adults with CP where interventions in childhood were not specified [8, 10, 48]. A likely explanation for these differences might be that all studies included adults with higher GMFCS levels (lower functional level). Since the interventions in above studies were not specified, the positive impact of SDR due to spasticity reduction on level of functioning (4) could have also influenced the health-related quality of life in our cohort.

Anxiety and depression

Levels of anxiety and depression did not differ between adults with CP and TD adults. This is in contrast with the findings of Smith *et al.* who reported increased levels of anxiety and depression in an extensive group of adults with CP compared to the general population [9]. Only mild to moderate levels of anxiety were found (23%) in this study, while no increased depression levels were observed in the CP cohort. This is a very positive finding, where other studies with adults with CP reported anxiety in 26% of the cohort [49] and depression in 25% [11] and even 37% [49]. The findings of current study are adding to the good HRQoL MCS scores found in this study suggesting that mental health, including levels of anxiety and depression, might not be directly affected by the physical status of adults with CP more than 25 years following SDR.

Correlations

Physical characteristics of CP such as muscle tone, passive range of motion, muscle strength and selectivity appear to have limited impact on functional mobility, balance, quality of life, anxiety and depression in adults with CP more than 25 years post-SDR. Muscle strength however seems to strongly influence functional mobility and balance, since correlations between muscle strength and TUG were found. These findings indicate that stronger participants have better functional mobility and balance. However, other research groups found that the muscle ability to generate force quickly (power) has greater relationship to functional mobility than strength on its own [41, 45, 50]. This suggests that not only traditional muscle resistance training might have a positive impact on muscle function and walking ability in individuals with CP [43, 51], but high-velocity resistance training (power training) might also be beneficial for functional mobility and balance in adults with CP after SDR [41, 45, 50]. In addition, this might also benefit the HRQoL in adults with CP, which has been found to be related to functional walking ability [8].

Limitations

All physical examination outcome measures, were 'passive' assessments, that did not include active ROM (e.g. during gait analysis) and muscle strength in more functional movements such as climbing stairs. Other factors, like habitual physical activity and exercise programs of individual participants were not taken into account; these may have influenced the results of the physical examination in the adults with CP and TD adults.

Most of adults in the CP cohort received orthopedic interventions before and after the SDR, which is not uncommon due to secondary complications of CP [30] and these may have influenced certain functional outcomes. Future research should compare a cohort of adults with CP who underwent a combination of SDR and orthopedic surgery, to a true control group such as adults with CP who only received orthopedic interventions and determine the influence on functional level. In addition, it would also be of interest to investigate the effects of strength training (e.g. traditional versus high-velocity resistance training) on functional improvement in adults with CP, who underwent SDR or who only received orthopedic interventions.

In conclusion, adults with CP and spastic diplegia maintained decreased muscle tone more than 25 years after SDR when compared to TD adults. Collectively, passive ROM, muscle strength and selectivity were lower in adults with CP than the matched TD group but in line with what is reported for adults with CP. The adults with CP in this study perceived relatively good HRQoL on all domains, but scored lower for physical functioning when compared to TD peers. Mental health was reported to be similar as in TD peers and only limited symptoms of anxiety and depression were found. These results reveal that adults with CP more than 25 years after SDR experience good mental health regardless of physical challenges. The associations found between muscle strength and TUG suggest the importance of strength training in adults with CP after SDR, as would improve or maintain functional mobility and balance and contribute to healthy aging.

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WALKING PATTERNS OF ADULTS WITH CEREBRAL PALSY MORE THAN 25 YEARS AFTER SELECTIVE DORSAL RHIZOTOMY

A LONG-TERM FOLLOW-UP STUDY DURING ADULTHOOD

INTRODUCTION

Cerebral Palsy (CP) is no longer seen as just a pediatric disorder, but also as a lifelong condition that is associated with a variety of challenges [1, 2]. Health related quality of life in adults with CP is related to a decline in walking ability, a recognized problem with aging in CP [3]. Morgan and McGinley [4] conducted a systematic review and reported that >25% of ambulant adults with CP show a deterioration in their walking ability with aging. However, most studies included in this review conducted self-reported surveys to measure the change in walking ability rather than an objective gait measurement. In addition, a wide variety of CP diagnoses were included (e.g. spastic diplegia, hemiplegia, quadriplegia, dystonia and dyskinesia). The subjective nature of and high variety within the study populations, makes it hard to establish if this deterioration in walking ability can be referred to adults with CP in general.

The predominant indicator for walking decline with aging in adults with CP, is the level of walking ability in childhood or early adulthood. The deterioration in walking was most frequently seen in adults with spastic diplegia, and appear to be related to levels of pain, fatigue, balance problems, but also factors of spasticity and contractures [4].

Selective Dorsal Rhizotomy (SDR) is a neurosurgical procedure that addresses lower extremity muscle tone in children with spastic diplegia, with the main aim to improve functional mobility [5]. To determine whether a child is eligible for SDR, as well as to monitor the change in physical status after surgery, instrumented gait analysis is a preferred method as it is a comprehensive and objective measurement technique.[6]. A variety of short-term follow-up studies confirmed the benefits of SDR based on kinematic data [7]. There are also some studies based on adolescents or young adults with CP [8, 9], but less is known about the gait later in adulthood [10, 11].

Since SDR was first reintroduced in Cape Town, South Africa [12], we have the longest track record of research in this field. In the long-term, our research team has been privileged to monitor the aging process post-SDR and have published gait analyses studies before and one, three [13], ten [14], and twenty [15] years after SDR. Positive outcomes have been shown, however, it was acknowledged that the results were based on two-dimensional gait analyses (2DGA) as this was the only available technique at the time the first children underwent SDR in the 1980s. Since then three-dimensional gait analysis (3DGA) is preferred.

In 2008 a cross-sectional 3DGA study was conducted on adults with CP and spastic diplegia post-SDR. Based on this cohort a sustained influence of SDR was shown more than 17 years after surgery. Overall the gait pattern was described (in the sagittal plane) as a mild crouch gait, with an adequate loading response and range of motion. [16]. A follow-up of this cohort is helpful to provide insight of the stability of the gait pattern of adults with CP during adulthood in the long-term after SDR.

For clinical decision-making, it is important to understand what the long-term outcomes of SDR are and the associations with personal and environmental factors. Therefore, the aim of this study was to evaluate the gait pattern (kinematic data, spatiotemporal parameters and gait deviation index (GDI)) of adults with CP and spastic diplegia more than 25 years after SDR in perspective to a reference group (typically developing adults) and to the previous testing period in nine years ago. In addition, associations between GDI and age at SDR, follow-up time, current age (2017), gender, pre-SDR and current GMFCS levels, body mass index (BMI) and socio-economic-status (SES) were investigated.

METHODS

Study design and participants

This is a nine-year follow-up study of adults with CP and spastic diplegia, who underwent SDR at Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1981 and 1991. Thirty-one adults with CP participated in the original study conducted in 2008 [16] and investigators searched and re-invited them for the study in 2017. Before taking part in the follow-up study, participants were screened for not having received any medical interventions or developed a neuromuscular disorder (what had an influence on their physical status) since participating in the original study. Eligible participations completed the consenting procedure as approved by the Human Research Ethics Committee of the University of Cape Town (HREC NO: 133/2016).

Participants' characteristics

Participants' characteristics information obtained included age, gender, BMI, SES, GMFCS levels (age bracket 12 - 18 years) [17] and information about previous orthopedic surgeries

or other interventions received related to CP. BMI was based on height and weight. Estimation of SES was determined by housing density ratio, calculated as the 'number of people living in the house' divided by the 'number of rooms in the house' (excluding kitchen and bathroom). A high SES corresponded with a score < 1.0, while a low SES was indicated with a score > 1.5 [18]. The type and number of previous interventions received related to CP, as well as the pre-operative and GMFCS levels determined in 2008 were retrieved from the original study [16], while participants' current GMFCS levels (2017) were determined by observation and consultation with the participant.

For comparison purposes reference data was created based on gait analyses of 41 typically developing (TD) adults matched for age, gender and BMI. Before taking part in the study, the TD adults were screened for not having any neuromuscular or orthopedic abnormalities that could influence their gait pattern.

Gait analysis

Data were collected at Tygerberg, Neuromechanics Unit, Central Analytical Facilities (CAF) of Stellenbosch University. Similar to the original study [16], reflective markers were placed upon the participants' skin surface according to a modified Helen-Hayes marker set used for the lower body Plug-in Gait model (now known as the Conventional Gait Model). Marker trajectories were captured by a 10-camera (eight MXT20 and two Bonita 10 cameras) Vicon motion capture system (Vicon, Oxford Metrics, UK), sampling at 200 Hz.

Participants were asked to walk in their self-selected comfortable walking speed, barefoot, with or without assistive devices (representing their daily life situation) over a 20-meter walkway of which eight meters were captured for analysis. At least five good trials were captured per participant, where the data of the three best quality and consistent trials were selected. Per trial one gait cycle was used for further analysis, resulting in three gait cycles of left and right limbs per participant.

Data Analysis

These gait cycles were processed in Vicon Nexus, which included marker trajectory reconstruction, labeling of markers, gap filling of labelled trajectories where necessary,

running of the Plug-in Gait model, filtering of model outputs with standard fourth-order zero lag low-pass Butterworth filter with a cut-off frequency of 6 Hz and finally events were detected and inserted into the trial. Thereafter the trial kinematics were checked for validity and feasibility using the reference videos (sagittal and frontal plane). Subsequently, data were exported to MATLAB (MATLAB R2017a, The MathWorks, Inc., Natick, Massachusetts, United States) and custom code scripts were used to extract discrete points of the gait cycle but also to normalize the entire gait cycle (100%) to 101 continuous data points. Thereafter, continuous kinematic gait data were plotted for the pelvis, hip, knee and ankle in three planes in PRISM (GraphPad Prism version 7.02, GraphPad Software, San Diego, CA, USA)). In addition, spatiotemporal parameters and Gait Deviation Index (GDI) [19] were calculated.

Similar to the original study, the following discrete kinematic gait parameters were analyzed: Pelvis: mean tilt, range of motion (ROM) in sagittal and transverse planes; Hip: maximal extension and adduction, mean rotation, ROM in sagittal and frontal planes; Knee: initial contact (IC) flexion, ROM in sagittal plane, maximal extension and flexion; Ankle: IC and mean dorsi/plantar flexion, maximal plantar flexion and dorsiflexion, and mean foot progression. In addition, non-dimensional (ND) [20] spatiotemporal parameters were also reported, including ND walking speed, cadence and time to foot off (TFO). The last outcome measure used was the GDI. The GDI is a validated outcome measure to quantify participants' gait pattern. This index was calculated according to Schwartz and Rozumalski [19], with using the kinematic data of the TD as the reference (GDI mean ± standard deviation (SD) of 100 ± 10).

Statistical analysis

Most of the gait parameters were normally distributed according to Shapiro-Wilk normality test. Subsequently data are graphically displayed and tabulated as mean +/- SD. Parametric statistical analyses were performed, including paired t-tests to evaluate differences between the gait parameters and GDI of the studies conducted in 2008 and 2017, and unpaired t-tests to compare current outcomes of the CP cohort with reference data of TD adults. As a threshold for statistical significance, to compensate for multiple comparisons (2 x 20), a Bonferroni corrected alpha-level of $p \leq 0.001$ was applied for these comparisons. Spearman's rho correlations were used to examine associations between the 2017 GDI and

age at SDR, follow-up time, current age (2017), gender, pre-SDR and current GMFCS levels, BMI and SES. A Bonferroni corrected alpha-level of $p \leq 0.006$ was accepted to compensate for multiple comparisons (8). Statistical analyses were conducted with PRISM (GraphPad Prism version 7.02, GraphPad Software, San Diego, CA, USA).

RESULTS

Participants' characteristics

From the 31 adults with CP who participated in the 2008 study, five were not included in the follow-up. One adult was untraceable, two elected not to participate in the study, one participant suffered from physical disability due to a car accident and one was pregnant at time of data collection. This resulted in 26 participants of whom 10 were female and 16 male. The median [interquartile (IQR)] age was 26.8 [25.6 – 32.0] years at the 2008 study and 35.8 [34.2 – 41.4] years at follow-up. At time of SDR the participants had a median age of 4.9 [3.7 – 10.1] years, resulting in a median follow-up time of 21.4 [18.4 – 23.6] years in 2008 and 30.1 [27.5 – 32.7] in 2017. The adults with CP had a median BMI of 23.0 [20.3 – 29.9] and 25.2 [21.6 – 31.2] and SES ratio of 1.25 [0.8 – 1.7] and 0.9 [0.7 – 1.3], respectively in 2008 and 2017.

Pre-operative 18 (69%) adults were classified as GMFCS level II, and eight (31%) as level III. This distribution changed with an improvement of at least one level in two-third of the children who were pre-SDR classified as GMFCS level II, and half of the cohort who were classified as GMFCS level III (Figure 3.1)

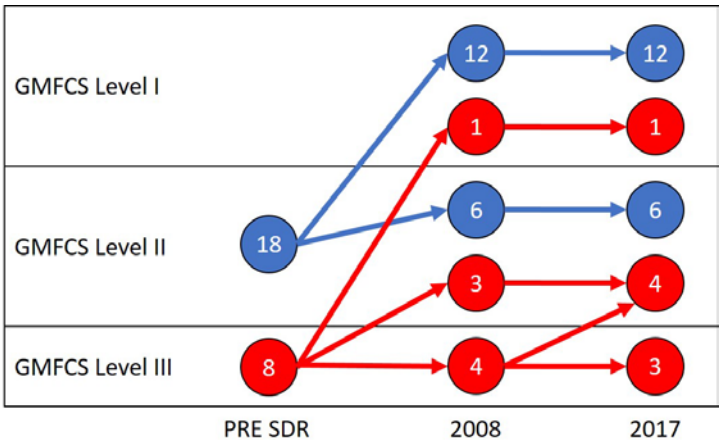

Figure 3.1. *Changes in GMFCS levels of CP cohort (n=26) over time*

In addition to the neurosurgical SDR procedure, most of the participants received also at least one orthopedic soft tissue and/or bony surgeries. Fourteen participants (54%) received surgery pre-SDR and 15 (58%) post-SDR (Table 3.1). In addition, none of the participants ever received other interventions like intramuscular botulinum toxin or intrathecal baclofen.

Table 3.1. Overview of orthopedic surgeries received by adults with CP before and/or after SDR

Interventions	**Number of participants (%)**	
	Pre-SDR	Post-SDR
Soft-tissue surgery		
Plantar flexors	12 (46)	12 (46)
Rectus Femoris	3 (12)	2 (8)
Hamstrings	7 (27)	13 (50)
Adductors	7 (27)	2 (8)
Iliopsoas	1 (4)	1 (4)
At least one soft-tissue surgery	14 (54)	14 (54)
Bony surgery		
Femoral derotation	2 (8)	1 (4)
Tibial derotation	0 (0)	0 (0)
Ankle/foot	0 (0)	4 (15)
Toe	0 (0)	4 (15)
At least one bony surgery	2 (8)	7 (27)

The reference data were based on a convenience sample of 41 adults, including 22 females and 19 males, with a median age of 35.5 [31.9 – 40.7] years and median BMI of 24.1 [22.4 – 26.6].

Gait analysis

Overall the gait pattern (GDI) did not change over the nine-year period (p=0.569), with a mean (SD) GDI of 67.0 (8.7) at the 2008 study and 68.0 (9.3) in 2017. However certain discrete gait parameters changed over time, including a decrease in hip and knee ROM, peak knee flexion, ND walking speed and swing phase time (increase in TFO) ($p < 0.0001$) (Table 3.2). Differences in gait pattern of adults with CP more 25 years after SDR (2017) were found when compared to reference data of TD adults (GDI: $p < 0.0001$). This was most apparent in the sagittal plane, where the adults with CP walked with a mild flexed gait pattern, including increased anterior pelvic tilt, reduced maximum hip and knee extension and plantar flexion ($p < 0.0001$) (Table 3.2 and Figure 3.2).

Table 3.2 *Overview of gait parameters for the adults with CP and Reference group.*

Parameters	**2008 CP**		**2017 CP**		**Reference**		**2008 vs**	**2017 CP vs**
	Mean	SD	Mean	SD	Mean	SD	**2017 CP**	**Reference**
Pelvis								
Mean tilt	22.4	7.6	25.9	7.0	9.5	5.8	3.5	-16.4#
ROM tilt	7.9	4.1	8.0	5.1	3.5	1.3	0.1	-4.5#
ROM rotation	17.9	7.2	16.2	6.6	10.9	4.1	-1.6	-5.3#
Hip								
Maximum extension	7.5	9.7	12.7	9.5	-8.6	8.0	5.2	-21.3#
ROM flexion/extension	51.4	8.1	44.2	8.1	42.5	5.0	-7.2*	-1.7
Maximum adduction	8.1	5.2	5.7	5.8	7.1	3.9	-2.4	1.4
ROM abduction/adduction	17.7	6.0	15.7	5.5	14.9	3.7	-2.1	-0.7
Mean rotation	4.9	13.5	-5.9	14.8	-5.7	6.2	-10.8	0.2
Knee								
IC flexion	27.2	10.6	23.6	12.6	5.1	5.8	-3.6	-18.6#
Maximum extension	15.0	12.2	11.2	15.0	0.5	5.3	-3.8	-10.7#
Maximum flexion	67.2	9.2	57.8	11.0	58.8	4.7	-9.3*	1.0
ROM flexion/extension	52.2	13.8	46.7	14.6	58.4	5.0	-5.5*	11.7#
Ankle/Foot								
Mean dorsi/plantarflexion	6.8	5.9	6.1	7.9	1.8	2.5	-0.7	-4.2#
Maximum plantarflexion	-10.3	8.7	-7.0	10.4	-16.5	5.5	3.2	-9.5#
Maximum dorsiflexion	19.5	7.1	17.3	7.8	14.2	3.4	-2.1	-3.1
IC dorsi/plantarflexion	2.6	7.0	1.0	7.2	-1.2	3.3	-1.6	-2.1
Mean foot progression	-15.8	14.6	-18.8	13.9	-9.6	6.4	-3.0	9.2#
Spatiotemporal parameters								
ND Speed	0.35	0.06	0.30	0.08	0.42	0.06	0.05*	0.12#
ND Cadence	0.52	0.08	0.51	0.14	0.57	0.04	-0.01	0.06#
TFO	60.9	3.6	66.0	6.1	62.0	1.8	5.2	-4.0#
GDI	22.4	7.6	67.6	9.6	99.2	9.7	0.6	31.6#

*Abbreviations: ROM: range of motion; IC: initial contact; ND: non-dimensional; TFO: Time to foot off; GDI: Gait deviation index; SD: standard deviation. Significant differences with Bonferroni corrected alpha-level of $p \leq 0.001$ between *2008 and 2017 CP studies and #2017 CP studies and Reference values.*

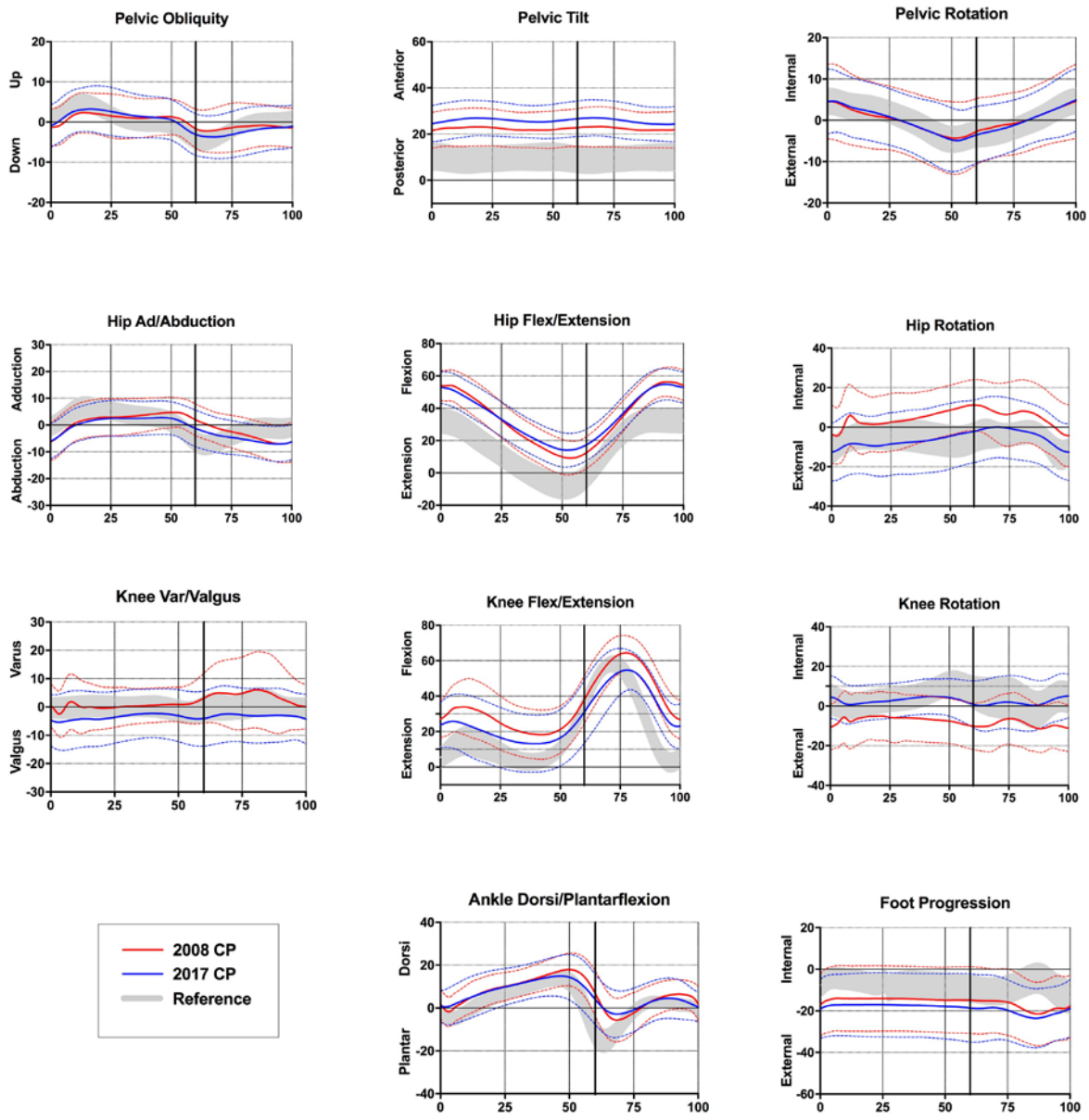

Figure 3.2. *Kinematic data (mean +/- 1 standard deviation) for the adults with CP assessed in 2008 and 2017 in relation to the Reference data*

Correlations

With respect to the associations, there were no correlations between GDI at 2017 and age pre-SDR, follow-up time, current age (2017), gender, pre-SDR GMFCS levels, BMI and SES. On the other hand, GDI was correlated to the GMFCS levels classified at the same time (2017) ($p < 0.0001$; r = -0.70) (Table 3.3).

Table 3.3. *Spearman's rho correlations between GDI (CP 2017) and contextual factors*

Contextual factors	**GDI**	***GDI***
	r	*p*
Age at SDR	0.313	0.120
Follow-up time	-0.084	0.683
Current age	0.257	0.205
Gender	-0.200	0.327
GMFCS Pre-SDR	-0.456	0.019
GMFCS 2017	-0.704	<0,0001*
BMI	-0.006	0.978
SES	-0.114	0.579

*Significant with Bonferroni corrected alpha-level of $p \leq 0.007$

DISCUSSION

This is the first 3DGA SDR follow-up study reporting on changes of gait pattern during adulthood in people with CP and spastic diplegia more 25 years after SDR. The data is based on a nine-year follow-up study (data collection in 2008 and 2017). Reference gait of typically developing adults was captured from carefully matched controls. In addition, to support clinical decision-making, the relationship between current status and certain contextual factors were investigated.

During the nine-year follow-up (median age of 26.8 to 35.8 years) in adulthood, the overall gait pattern of the adults with CP did not deteriorate. Although the GDI did not change over time, the values of the adults with CP were abnormal (more than 2 SD from TD mean) and discrete biomechanical changes were found especially in the sagittal plane. Hip ROM decreased with the average ROM shifting towards TD adult values, although this value is a result of reduced peak hip extension prior to toe-off. Knee flexion ROM also deteriorated but that was associated with a reduced peak knee flexion during swing. Despite these changes, the gait graphs (and GDI) of adults with CP more than 25 years post-SDR were still similar to the figures of the adolescents with CP 13 years after SDR as reported by Munger *et al.* [9].

More than 25 years after SDR, the walking pattern could be described as a mild crouch gait, principally contributed to by increased hip and knee flexion, and excessive ankle dorsiflexion especially during stance phase [21]. However, the adults with CP did not show knee stiffness

(knee ROM throughout gait cycle of less than 30degrees), a common CP gait characteristic seen with crouch gait [21], and normally caused by contractures and/or spasticity.

The current study confirmed that SDR has a long-lasting positive effect on the gait pattern by ameliorating spasticity. The gait waveforms of adults with CP show minimal signs of spasticity, although not the same as TD adults. This is reflected by absence of the following signs: a double bump in pelvic tilt (sign of Psoas or Hamstring spasticity), a combination of posterior tilt and decreased knee extension (Hamstring spasticity), delayed and/or impaired knee flexion during early swing (Rectus Femoris spasticity) and early plantar flexion in stance (Gastrocnemius spasticity) [11].

The overall gait pattern quantified by the GDI at the long-term follow-up (2017) was not associated with age pre-SDR, follow-up time, current age, gender, BMI or SES. GDI was also not associated with pre-SDR GMFCS levels, though it was correlated to the gross motor function (GFMCS levels) determined in 2017. This may be influenced by an improvement by at least one GMFCS level when compared to pre-operative levels by the majority of the cohort. We acknowledge that GMFCS is not an outcome measure [17], though we found this improvement of 65% of the CP cohort an important finding especially when seen in the light of possible expectations based on a big cohort registry study. Alriksson-Schmidt *et al.* reported that 25% of 297 children with spastic diplegia changed at least one GMFCS level over time, with 11% showing improvement, but also 14% reported deterioration (lower GMFCS level) [22].

When interpreting the results of current nine-year follow-up study, some methodology limitations and other important factors have to be taken into account. Unfortunately, no pre-SDR 3DGA data were available and the study was conducted with a limited sample size. These are methodological limitations, which could not be addressed. However, the study is of value with the longest follow-up results ever published. Another point of discussion could be that the majority of the participants received at least one orthopedic interventions before and/or after SDR, though this common practice with SDR [11]. A last point to acknowledge is that careful selection of children is imperative for positive results [11, 23]. Each of the participants fulfilled strict selection criteria, what probably contributed to positive outcomes of current study.

Conclusion

In conclusion, more than 25 years after SDR adults with CP and spastic diplegia walked with a mild crouch gait pattern, with minimal signs of spasticity. The concern about decline in walking ability with aging in CP [4] was not confirmed in adults after SDR. In long-term adults with CP were still ambulant and their walking pattern did not change over the nine-year follow-up period. The GDI of adults with CP was related to the GMFCS levels assessed during this study (2017), though pre-SDR GMFCS level (and other contextual factors) was not associated. The majority of the adults with CP had better gross motor function than pre-operative (lower GMFCS level) and none showed deterioration. However, it has to be acknowledged that additional orthopedic surgical interventions were common and very strict selection criteria are imperative to gain positive long-term outcomes after SDR.

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SPINAL ABNORMALITIES AND LEVELS OF PAIN IN ADULTS WITH CEREBRAL PALSY MORE THAN 25 YEARS AFTER SELECTIVE DORSAL RHIZOTOMY

A LONG-TERM FOLLOW-UP STUDY DURING ADULTHOOD

INTRODUCTION

Selective dorsal rhizotomy (SDR) is an effective neurosurgical treatment for reducing spasticity in a selected group of patients with cerebral palsy (CP) [1, 2]. This procedure was refined by Warwick Peacock in the 1980's and entails selective sectioning of dorsal rootlets in the lumbosacral area [3]. As a consequence, muscle spasticity is reduced through decreasing sensory input. Since then the procedure has gained worldwide popularity after Peacock relocated from Cape Town, South Africa to Los Angles, USA and the now known 'Peacock' method remains the most commonly used SDR technique in the world [4, 5].

Despite the fact that SDR succeeds in its aim of reducing spasticity, spinal abnormalities and back pain due to SDR, especially when laminectomy is performed as part of the surgical procedure remain a concern [6]. Several studies have documented the prevalence of spinal abnormalities (e.g. scoliosis, hyperkyphosis, hyperlordosis, spondylolysis and spondylolisthesis) after SDR [7, 8, 9, 10], and a higher frequency of spinal deformities has been reported in adults with CP when compared to typically developing (TD) adults [11]. However, no indisputable evidence has shown that this is a result of the SDR procedure, instead of general secondary complications associated with CP. Thus, spinal abnormalities appear to be a common complication in adults with CP regardless of interventions performed previously [12].

Typically, spinal abnormalities are associated with several other problems, such as pain and altered sensation [13]. While some studies report pain in adults with CP who underwent SDR [14, 15, 16], it is also known that the prevalence of pain in adults with CP mostly is higher than the general population [17, 18, 19, 20]. Remarkably, despite high pain prevalence in adults with CP the impact of pain on daily activities varies from minor to moderate [18, 21].

Given the improving life-expectancy of adults with CP, it is important to understand the impact of normal aging on various parameters in those adults with CP who have undergone SDR. Establishing whether or not spinal curvatures, spinal abnormalities and pain worsen during aging in this population, will provide important clinical insight in to possible prevention or improved management of these issues.

This study forms part of a longitudinal investigation tracking the health and wellness of adults with CP, who underwent SDR during childhood (> 25 years ago). The last follow-up was performed in 2008 and consequently a recent follow-up was conducted in 2017. Thus, the aim of this study was to determine if spinal curvatures (scoliosis, kyphosis, lordosis) and spinal abnormalities (spondylolysis and spondylolisthesis), as well as the perceived level of disability due to back (and leg) pain changed over the nine-year period (2008 – 2017) in adults with spastic diplegic CP, who underwent SDR more than 25 years ago. In addition, it was of interest to determine if there were associations between spinal curvatures as well as spinal abnormalities with participants' background factors and level of disability due to pain.

METHODS

Study design and participants

The current study is a follow-up of a study performed in 2008 which focused on evaluating spinal abnormalities in adults with CP more than 15 years after SDR [22]. Based on the original database, all patients were contacted and asked to participate in the current follow-up study. Similar to the 2008 study, all participants had a diagnosis of CP and spastic diplegia (with mild unilateral upper extremity involvement allowed) and underwent SDR at Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1981 and 1991. At the time of surgery, all participants had been ambulant with a Gross Motor Function Classification System (GMFCS) level I, II or III [23]. The aim of surgery was improvement on a functional level, and the children required access to on-going physiotherapy before and after SDR, together with adequate mental and physical support of a parent or care-taker. Adults were excluded from the follow-up study if they had any non-related CP injuries and/or accident, during the nine-year period, that may have resulted in and/or influenced their spinal abnormalities. The study was approved by the Human Research Ethics Committee of the University of Cape Town (HREC NO: 133/2016) and all participants provided written informed consent before enrolling in the study.

SDR procedure

All the participants underwent the SDR procedure as described by Peacock [3, 24]. Following a midline lumbar incision, laminectomies were performed from the second to the fifth

lumbar vertebra in order to open the dura to access the cauda equina [3]. Posterior rootlets were carefully separated from the anterior rootlets and stimulated with a 50-Hz train of stimuli at the threshold intensity of muscular contraction and the muscle response assessed with electromyography. Dorsal nerve rootlets associated with a normal response were left intact while rootlets associated with an abnormal response were divided, with up to 50-70% of the rootlets taken at each level [3, 24].

Participants' characteristics

Participant' characteristics including age, gender, GMFCS level (age bracket 12 - 18 years) [23], BMI [25] and Social Economical Status (SES) were obtained. SES was estimated by housing density, calculated as the number of people living in the house divided by the number of rooms in the house (excluding the kitchen and bathroom). SES score categories are as follows: < 1: 'high SES'; ≥1 and ≤1.5: 'normal SES' and >1.5: 'low SES' [26].

A qualified physiotherapist assessed the participants for sensory loss and abnormal proprioception in the lower extremities. Neurological examination included light touch, pin-prick and deep pressure in dermatomes L1 to S5 as described by Lee *et al.* [27], and proprioception of knee and big toe flexion-extension movements.

Using a semi-structured interview, participants were asked if they used pain medication and/or underwent surgical interventions related to spinal abnormalities. To gain insight into the participant's experience of the SDR, specific SDR related questions included: 1) Do you feel that SDR has been worthwhile? 2) What would you have done differently if you look back? 3) If you had to decide by yourself now, would you make the same decision as your parents to undergo SDR?

Radiographs

All radiographs were taken in a standing position and were reviewed by two clinical specialists, who were blinded for the participants' characteristics and former radiograph data (2008). If a clear judgment could not be made, a consensus meeting was held with both specialists. Scoliosis, defined as a spinal curvature in the coronal plane [28], was determined

with antero-posterior (AP) views and by Cobb angles [29]. An angle of 10 - 30˚degrees was considered as a mild scoliosis, an angle of 30 - 40˚ degrees as moderate scoliosis, and an angle above 40˚ degrees as severe scoliosis [11, 30]. Kyphosis describes the sagittal convexity of thoracic spine and was measured on a lateral view from inferior endplate of T3 to inferior endplate of T12 [29, 31]. When X-ray penetration, made visualization of T3 not possible the inferior endplate of T5 was used. The range of 20 – 50˚ described by Bernardt and Bridwell [32] was used as a reference for normal. Lumbar lordosis, the sagittal convexity of the lumbar spine [33], was measured on a lateral view from superior endplate of L1 to the inferior endplate of L5 [34]. Normal range values of 20 – 60˚ were used [32]. Examining radiographs were subject to the inherent inter- and intra-observer variability that exists in measuring spinal alignment. To correct for this and assess the clinical relevance of the found differences in spinal curvatures, a minimal clinically meaningful difference (MCID) of 10° was used [7, 10, 35].

The prevalence of spondylolysis (defect in pars articularis of vertebra) and spondylolisthesis (slip of vertebra) was examined by using the lateral and oblique radiographic views. Meyerding classification was used to ascertain the severity of spondylolisthesis, based on the percentage of displacement; 25%: ‘grade I’; 50%: ‘grade II’; 75%: ‘grade III’ and 100%: ‘grade IV’[36].

Pain questionnaires

The Oswestry Disability Index (ODI) is a valid an reliable questionnaire to identify how back and leg pain affect daily activities [37]. It addresses 10 sections including: pain intensity, personal care, lifting, sitting, standing, walking, sleeping, sex life, social life and travelling, with a score ranging from 0 (no pain problems) to 5 (severe pain problems affecting the daily activities) and an option to mark questions as not applicable. A percentage score indicates the level of disability experienced due to pain in daily life; 0 – 20%: ‘minimal disability’; 21 – 40%: ‘moderate disability’; 41 – 60%: ‘severe disability’; 61 – 80%: ‘house bound’ and 81 – 100%: ‘bed bound’. In addition, participants completed a self-developed questionnaire to indicate the frequency (‘never’, ‘occasionally’, ‘weekly’ and ‘daily’) and location of pain (spinal level, upper and lower extremities).

Statistical analysis

Outcome measures were tested for normality distribution by using the Shapiro-Wilk's test. As a substantial amount of the outcome parameters were not normally distributed, data was expressed as median and interquartile ranges. Descriptive statistical analysis was used to summarize participants´ background information and results of the pain questionnaire (frequency and location). Changes in spinal curvatures (scoliosis, kyphosis and lordosis), spinal abnormalities (spondylolysis and spondylolisthesis) and the frequency of pain (ODI) over time were analyzed with a Wilcoxon rank test, with significance accepted at $p < 0.05$. In addition, Cohen's-d effect sizes were calculated, using descriptors of trivial (<0.2), small (≥0.2 to <0.5), moderate (≥0.5 to <0.8), or large (≥0.8) [38]. In addition, based on the MCID of 10˚, likelihood levels were calculated if changes over time were clinically relevant or not.

Spearman's rho correlations were conducted to determine associations between spinal curvatures, spinal abnormalities and participants' background information (age at SDR, follow-up time, current age, upper limb involvement, gender, GMFCS, SES and BMI, sensory abnormalities) and pain (ODI). In the case of two binary variables, a Phi Coefficient was used as a measure of association (spondylolysis and spondylolisthesis with upper limb involvement, gender and sensation variables). To compensate for multiple comparisons (12), a Bonferroni corrected alpha-level of $p \leq 0.004$ was applied for the correlations.

RESULTS

Participants' characteristics

Of the 31 participants who took part in the 2008 follow-up study [22], six were not included in the current 2017 follow-up study. One participant was pregnant, one had been injured in a motor vehicle accident, one was lost to follow-up and three elected not to participate.

Descriptive characteristics of the remaining 25 participants are shown in Table 4.1. The current cohort consisted of 15 males (60%) and 10 females (40%), with four participants (16%) diagnosed with mild unilateral upper limb involvement. The median (interquartile (IQR)) age at SDR was 5.2 (3.7 – 10.6) years, while at the moment of the follow-up assessment participants were 25.5 to 35.1 years post-SDR.

Table 4.1. *Participants' characteristics (each cohort n=25).*

Variable	2008 CP n (%) / median [IQR]	2017 CP n (%) / median [IQR]
Current age (years)	26.8 [25.6 – 32.7]	35.9 [34.3 – 41.5]
Follow-up time (years)	21.5 [18.3 – 23.8]	30.2 [27.2 – 32.8]
SES	1.3 [0.8 – 1.7]	0.8 [0.6 – 1.1]
BMI (kg/m^2)	23.2 [20.5 – 30.0]	25.6 [22.1 – 31.3]
GMFCS		
Level I	13 (52)	13 (52)
Level II	8 (32)	9 (36)
Level III	4 (16)	3 (12)

Abbreviations: IQR, Interquartile Range; SDR, selective dorsal rhizotomy; SES, socio-economic status, BMI, Body Mass Index; and GMFCS, Gross Motor Function Classification System.

Nine participants (36%) had decreased touch sensation in at least one of the dermatomes (L2 – S2). Eleven participants (44%), including the nine who had decreased touch sensation, experienced decreased pin-prick sensation. No problems were reported for deep-touch sensation and knee flexion - extension proprioception test, while four (16%) participants had difficulties with proprioception assessment of the big toe. Three of these four participants indicated also touch and pin-prick sensation problems in the dermatome related to the big toe (L5) (Figure 4.1).

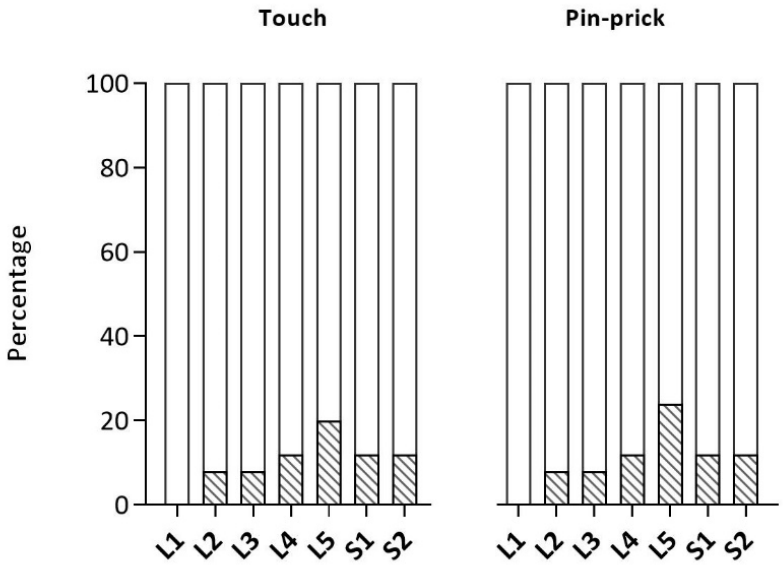

Figure 4.1. *Outcomes of sensation assessments (touch and pin-prick) per dermatomes. Normal sense* (*blank), decreased sense (dashed).*

Three participants were using medication to relieve back pain, while none of the participants to date needed or received surgical intervention on the spine.

In answering the question 'Do you feel that SDR has been worthwhile?', seven adults (28%) indicated that they were not able to answer this question as they were either too young at time of the operation (so they could not remember how it was before the operation) or they found it difficult to judge what results of other treatment options would have led to.

Of the eighteen adults that could answer the first question, seventeen (94%) responded positively to the question, indicating that they found SDR worthwhile because of mobility and/or quality of life benefits. One (6%) participant felt the operation was not worthwhile due to the experience of pain.

With respect to the question 'What would you have done differently if you look back?', five (20%) participants indicated they would have exercised more in the past years to maintain their fitness levels.

In response to the third question 'If you had to decide by yourself now, would you make the same decision as your parents to undergo SDR?', four (16%) participants felt that they could not answer this question since they found it difficult to judge what results of other treatment options would have led to.

Of the remaining twenty-one adults with CP, nineteen (90%) participants indicated that they would undergo the operation if they themselves had to decide based on the mobility and functional walking benefits, they experienced, while two (10%) participants would not undergo the operation because of the pain they experienced.

Radiographs

More than 25 years after SDR, five adults (20%) were diagnosed with a mild scoliosis (curvature; 10 – 30˚), one (4%) was diagnosed with a hyperkyphosis (curvature >50˚), while eight adults (32%) were diagnosed with a hyperlordosis (curvature >60˚). No changes over time were found in the scoliosis or lordosis curvatures, while an increase in kyphosis curvature was observed (p = 0.032) (Table 4.2 and Figure 4.2).

Table 4.2. *Changes in Scoliosis, lordosis and kyphosis curvatures (degrees) during a nine-year adult aging period.*

Variable	**2008 CP**	**2017 CP**	***p***
	Median [IQR]	Median [IQR]	
Scoliosis	7.0 [3.0-10.2]	5.5 [2.5-9.3]	0.649
Kyphosis	30.0 [24.0-37.0]	31.5 [23.0-38.8]	0.032
Lordosis	50.0 [46.0-59.5]	54.0 [44.5-62.4]	0.126

Abbreviations: IQR, Interquartile Range: As a threshold for statistical significance an alpha-level of $p < 0.05$ was applied for all parameter

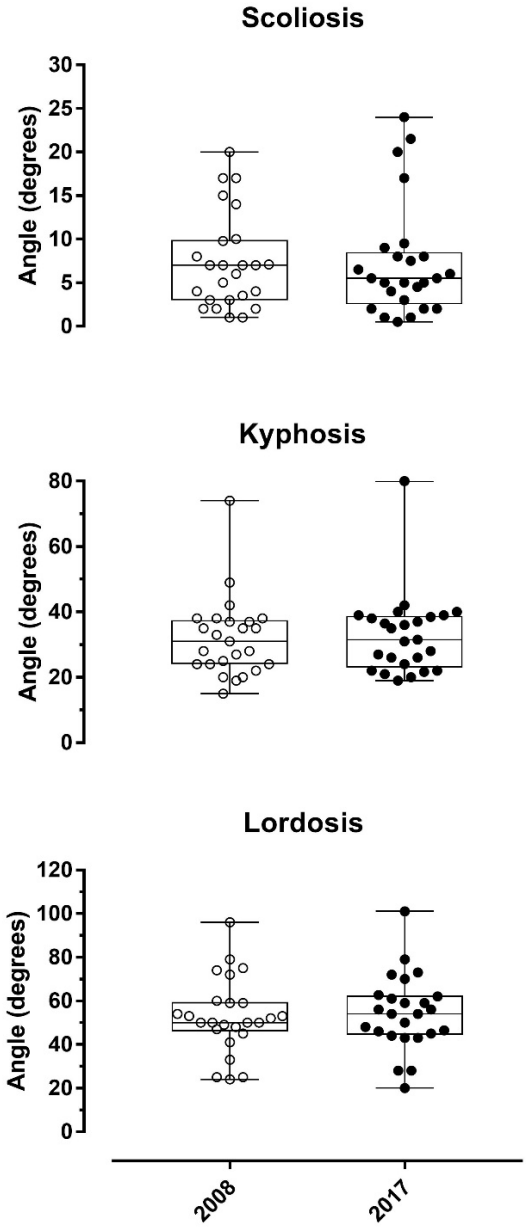

Figure 4.2. *Scoliosis, kyphosis and lordosis curves (degrees) in 2008 (open circles) and 2017 (closed circles) (n = 25).*

Cohen effect sizes indicated that the changes in all curvatures (lordosis, kyphosis and scoliosis) could be classified as 'trivial', indicating neither a decrease of increase in any of the curvatures was clinically meaningful (Figure 4.3). In line with this (based on a MCID of 10˚), 100% likelihoods were found that no clinically relevant change in curvatures were observed over the nine-year follow-up period.

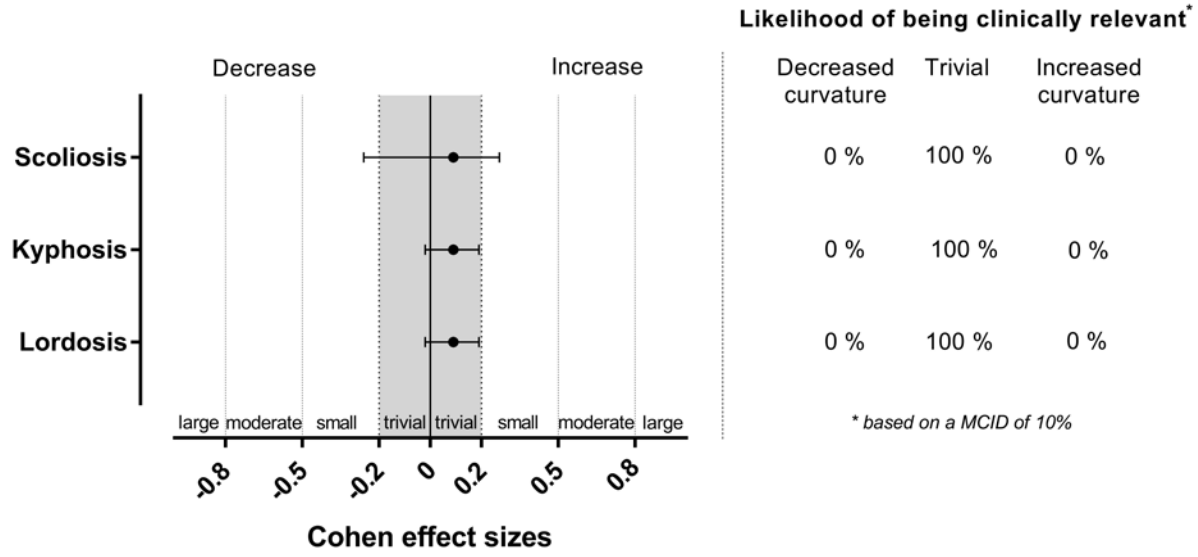

Figure 4.3. *Changes in scoliosis, kyphosis and lordosis curvatures, Cohen effect sizes and the likelihood of changes being clinically relevant.*

Although spondylolysis was observed in 11 adults (42%) and spondylolisthesis in five adults (20%), the prevalence of these spinal abnormalities did not change over time (p = 0.564 and p = 0.317, respectively). Worsening of spondylolisthesis from Grade I to grade II was only observed in one person.

Pain

The most common site for pain was the lumbosacral area as twenty-one (84%) participants reported lower back pain. Seven (28%) of these participants experienced lower back pain on a daily basis and three (12%) on a weekly basis (Table 4.3).

Table 4.3. *Frequency of experiencing pain at the time of the follow-up study.*

Location of the pain		Never		Occasionally		Weekly		Daily	
		n	%	n	%	n	%	n	%
Spinal Level	Cervical	21	84	1	4	1	4	2	8
	Thoracic	22	88	3	12	0	0	0	0
	Lumbosacral	4	16	11	44	3	12	7	28
Upper extremity	Arm	23	92	1	4	1	4	0	0
	Shoulder	20	80	2	8	2	8	1	4
Lower extremity	Leg	18	72	5	20	0	0	2	8
	Hip	17	68	4	16	2	8	2	8
	Knee	18	72	2	8	3	12	2	8

Abbreviations: IQR, interquartile range; SDR, selective dorsal rhizotomy; SES, socio-economic status, BMI, Body Mass Index and GMFCS, Gross Motor Function Classification System.

The median [IQR] ODI score at the time of the follow-up study was 2.00 [0.00 – 18.00]. Based on the ODI score, twenty adults (80%) were experiencing 'none to minimal disability' level; four adults (16%) were experiencing a 'moderate disability' level, while one adult (4%) was experiencing a 'severe disability' level. However, no changes in the overall ODI scores were found over time (p = 0.747). The three most common activities where participants experienced problems due to back (and leg) pain were lifting (48%), standing (44%) and sleeping (40%) (Figure 4.4).

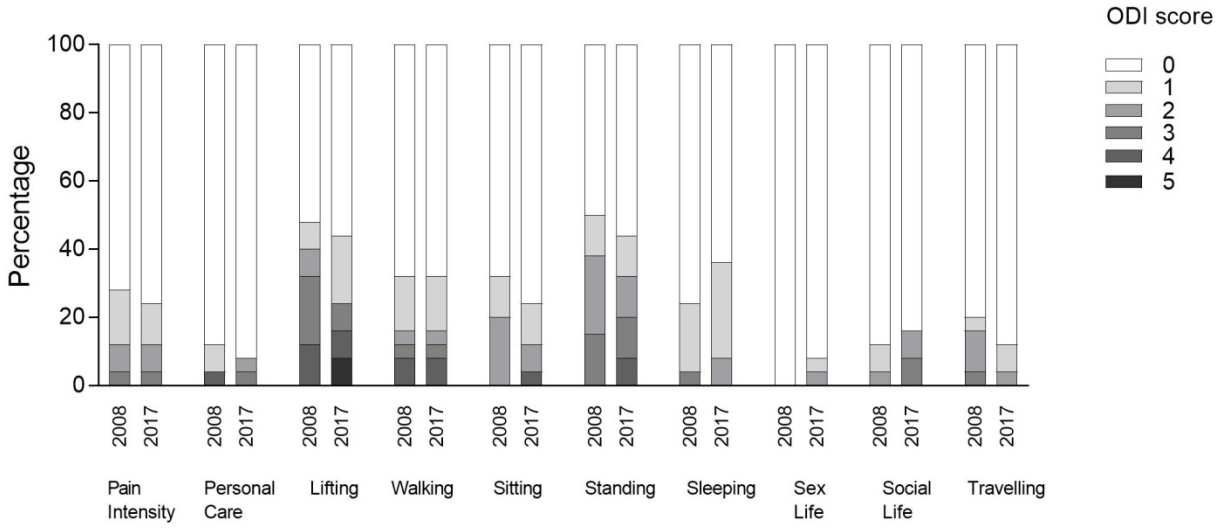

Figure 4.4. *Overview of the ODI scores at the time of the follow-up study.*

Correlations

Except for a correlation between the level of kyphosis and gender ($p < 0.001$, r = 0.75) no other correlation were found between the spinal curvature and/or deformities and patient characteristics and/ levels of disability due to pain (Table 4.4).

Table 4.4. *Correlations (Spearman's rho or Phi coefficient) between spinal abnormalities, participants' characteristics information and disability experienced due to back (and leg) pain*

Variable	Scoliosis		Kyphosis		Lordosis		Spondylolysis		Spondylolisthesis	
	r	*p*	r	*p*	r	*p*	r/ ϕ	*p*	r/ ϕ	*p*
Participants' characteristics										
Age at SDR	-0.02	0.912	-0.03	0.905	-0.35	0.089	-0.12	0.576	0.15	0.487
Follow-up time	0.13	0.536	-0.37	0.067	0.21	0.326	0.35	0.090	0.12	0.575
Current age	-0.03	0.880	-0.28	0.172	-0.23	0.263	0.07	0.750	0.17	0.407
Mild upper limb involvement	0.54	0.006	-0.28	0.175	0.12	0.564	0.05	0.792	0.06	0.785
Gender	-0.27	0.188	**0.75**	**0.001***	0.47	0.018	-0.07	0.742	0.00	1.000
GMFCS	-0.09	0.688	0.27	0.193	0.29	0.164	-0.06	0.768	-0.12	0.558
BMI	-0.03	0.140	-0.11	0.613	0.09	0.668	0.07	0.750	0.04	0.843
SES	-0.03	0.905	0.10	0.653	-0.01	0.958	0.00	0.979	0.01	0.947
Touch sensation	0.24	0.253	-0.31	0.129	-0.12	0.582	0.18	0.383	0.46	0.022
Pin-Prick sensation	0.21	0.321	-0.31	0.127	-0.11	0.613	0.03	0.897	0.36	0.070
Proprioception big toe	-0.36	0.081	0.12	0.564	-0.17	0.405	0.01	0.943	0.31	0.119
Disability due to pain										
Pain (ODI)	-0.91	0.665	-0.03	0.887	-0.21	0.304	-0.26	0.217	-0.07	0.737

*Abbreviations: SDR, selective dorsal rhizotomy; SES, socio-economic status, BMI, Body Mass Index and GMFCS, Gross Motor Function Classification System. As a threshold for statistical significance an alpha-level of p < 0.004 was applied for all scores. *p<0.004*

DISCUSSION

Growing awareness of the secondary complications facing the aging CP population oblige clinicians to understand the long-term outcomes of interventions performed in childhood. The present study is the first to report on changes in spinal abnormalities and pain during adulthood in adults with spastic diplegia who underwent SDR more than 25 years ago.

Scoliosis

Spinal abnormalities, specifically scoliosis, have a higher prevalence in individuals with CP (21 – 64%) [39, 40, 41, 42] compared to the general population (1 – 2%) [11]. Despite concerns based on the laminectomies performed [6], this prevalence has not been reported to be higher after SDR. Follow-up studies (2.8 – 21.4 years) reported a prevalence of 10 – 44% after SDR [7, 10, 16, 22, 43], similar to the 20% observed in the current study with a follow-up time of 30.2 years. The absence of severe scoliosis and stability in the long-term shown in current study is remarkable. Given that spasticity has been described as a risk factor for developing scoliosis [11, 30], the decreased muscle tone as a result of SDR may have contributed to this positive outcome. In addition, correlations have previously been described between age [44, 45] as well as participants' functional level (GMFCS) [41, 44, 45] and progression of scoliosis in CP populations, no association was found in the current study.

Kyphosis

Hyperkyphosis occurs in 5% of the general population [46], and 4.4 – 7% of individuals with CP [13, 41]. This prevalence is similar to the 1.9 – 9% previously reported in SDR (4.2 – 21.4 years) follow-up studies [9, 16, 22, 43], and 4% in the current long-term follow-up study. A change in the curvature of hyperkyphosis was found in this study, however, this was not clinically meaningful for the study since it fell within the 10˚ degrees measurement error (MCID) and the Cohen effect size was trivial. In the general population the kyphotic curve seems to increase after 40 years of age [47]. The median age of current study cohort was 35.9 years, which might explain why no clinically relevant changes in curvature of kyphosis have been found. On the other hand, the current study didn't show any correlation between

age and kyphosis curvature. The only association that was determined was greater kyphosis curve in women compared to men, which has also been reported in the general population [47].

Lordosis

There is limited information about the prevalence of hyperlordosis in CP as well as the general population, though it has been reported that children with CP are more likely to develop hyperlordosis [48] and progresses over time when compare to TD adults [49].

The prevalence of hyperlordosis (4.2 – 21.4 years) after SDR in this study was 32% and falls within the range of those previously reported (27 – 50%) [9, 16, 22, 43]. No change was observed between the previous 2008 and current 2017 follow-up study, despite that this is an expected change with aging in individuals with CP [10, 49]. There was no correlation between age and lordosis curves, as well as no associations were found with back and/or leg pain scores as has been described in the literature [13].

Spondylolysis

The estimated prevalence of spondylolysis in patients with CP has been reported as 21 – 30%, which is almost four times that of the general population [1, 49, 50, 51, 52]. Despite the concerns of spinal deformities due to laminectomies, a prevalence of 12% has been reported in the short-term (5.8 years) post-SDR [7]. However, a prevalence of 42% was found in this 2017 study, although no change was found between the current 2017 and previous 2008 follow-up study. The relatively high incidence reported, could be related to the laminectomy [8], but also to an observational error in other studies, where no oblique radiographs were obtained resulting in a likely underestimation of spondylolysis prevalence [53]. A hyperlordotic lumbar spine is a risk factor for developing spondylolysis, where it was reported that the prevalence was higher in participants with a lumbar lordosis exceeding 50° [49]. This was the case in five of the 11 participants diagnosed with spondylolysis in the current study.

Spondylolisthesis

The prevalence of spondylolisthesis in general population appears to be similar in the CP population (2 – 4%) but limited data is available [49, 50, 54, 55]. This number has been reported to be higher with 12 – 24% in short-term (4.2 – 8.6 years years) follow-up studies after SDR [16, 43]. The prevalence of slip in this study was 20% of the participant group, this is within the range of previously published short-term follow-up studies and was not different to prevalence of the 2008 follow-up study. Change was expected as aging is a risk factor for degeneration reported in the general population [56]. Each of the participants who were diagnosed spondylolisthesis, had slips up to Grade II which are classified as stable and asymptomatic [57] and no correlation was found between prevalence of spondylolisthesis and pain (ODI scores).

Pain

Almost one third of the general population has reported to have low back pain [58], while the prevalence of pain (with lower back pain as most common side) is almost double as high in adults with CP [18, 19, 20]. This frequency is similar to what has been shown in SDR long-term follow-up studies where a 34% prevalence of low back pain in the past week [14] and a prevalence of 51% chronic low back pain were reported [15, 16]. The current study also reported pain most commonly located at lumbosacral region, with 28% of the participants experiencing daily and 12% experiencing weekly pain. However, the overall finding of the ODI questionnaire showed that only 20% of the participants experienced limitations in daily activities due to low back (or leg) pain. Another interesting point is that two participants mentioned the experience of pain as a consequence of the SDR procedure, while the vast majority was happy with SDR experience reporting mobility and functional walking benefits.

Limitations

The sample size of the current study was relatively small. However, as this is the first follow-up study documenting adults with CP more than a quarter of a century after SDR (25 – 35 years post-SDR), the outcomes should be seen as an important indication of long-term outcomes of SDR. Unfortunately, limited studies report about the natural history of CP and the influence on spinal deformities that made it difficult to distinguish the independent

effects of SDR. It would also be of interest to compare the incidence of spinal abnormalities of a cohort of adults with CP who underwent SDR to a matched control group of adults with CP who only received orthopedic interventions in childhood. There is a need for further studies to address this topic in-depth. In addition, future studies should include computed tomography (CT) to describe the prevalence of spondylolysis. In this study, oblique radiograph views were used, which is standard practice, but CT is currently considered the most accurate imaging modality for the identification of spondylolysis [59]. We would also like to acknowledge that lumbar lordosis was measured from superior endplate of L1 to the inferior endplate of L5, similar to the 2008 study. The current standard to measure lumbar lordosis is from superior endplate of L1 to the superior endplate of S1 [60].

Conclusion

At follow up more than 25 years after SDR, spinal abnormalities like scoliosis, hyperkyphosis and hyperlordosis had no higher prevalence than those found in other CP populations and were remarkably stable over a nine-year period. Spondylolysis and spondylolisthesis prevalence also did not change over time but appear to occur more often than would be expected in adults with CP. However, found spinal abnormalities appeared not to result in disability experienced due to back pain. The prevalence of pain more than 25 years after SDR was comparable to what is expected for adults with CP, with the lower back as the most common site. In the majority of the cohort (80%), pain did not result in disabilities in daily life. Spinal abnormalities were not related to contextual factors, level of disability and sensory abnormalities, except for the levels of kyphosis and being female. Overall participants were satisfied with the SDR procedure based on experienced mobility and functional walking benefits. Despite the positive outcomes, there is a need for further studies, since limited studies report about the natural history of CP and the influence on spinal abnormalities which made it difficult to distinguish the independent effects of SDR.

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DAILY ACTIVITIES, PARTICIPATION, SATISFACTION AND FUNCTIONAL MOBILITY OF ADULTS WITH CEREBRAL PALSY MORE THAN 25 YEARS AFTER SELECTIVE DORSAL RHIZOTOMY

A LONG-TERM FOLLOW-UP STUDY DURING ADULTHOOD

INTRODUCTION

Until recently, the primary focus of cerebral palsy (CP) treatment and research has focused on children and less on adults. As life expectancy of individuals with CP have become similar to that of typically developing (TD) adults, adults with CP are now considered one of the world's largest populations with a physical impairment [1]. Therefore, the importance of healthy aging in individuals living with CP is imperative. Subsequently, CP management has shifted, according to the current International Classification of Function, Disability and Health (ICF) model [2], to emphasize a biopsychosocial approach. This means that in addition to the treatment of 'body structure and function' impairments, the level of 'activity and participation' is acknowledged as an important factor within the lifelong management plan for people with CP [3].

One of the biggest challenges with healthy aging is to prevent or minimize the secondary effects of CP on the musculoskeletal system (e.g. bone deformities and pain) and to improve functional status and quality of life throughout one's life span [4]. Spasticity is one of the main contributors to the development of secondary complications and is estimated to be present in approximately 80% of people with CP [5].

An effective treatment regime to reduce spasticity is a neurosurgical procedure known as Selective Dorsal Rhizotomy (SDR) [4, 6, 7]. SDR reduces spasticity by transecting a percentage of lumbar rootlets which disrupts the reflex arc at spinal cord level. First described by Foerster in 1913, SDR only gained popularity after Professor Warrick Peacock re-introduced an adapted technique of this procedure in Cape Town, South Africa in the early 1980's and in the United States of America from 1986 [8]. If strict selection criteria are adhered to, SDR has shown to be an effective treatment to reduce spasticity and improve functionality in children with CP. This has found to have a positive effect on the child's participation in the community [4, 9], however, less is known about the activity, participation and satisfaction levels of adults with CP who received SDR in childhood.

A study by Langerak *et al.* [10], interviewed a group of adults more than 17 years after SDR, reported that the majority of the cohort were independent in accomplishing daily activities and participation with high satisfaction levels. Similarly, Munger *et al.* [11] reported similar levels of participation in their SDR and control group (adults with CP who did not undergo SDR) based on the Frequency of Participation Questionnaire, more than 10 years post-SDR.

A study by van der Slot *et al.* [12], reported slightly poorer outcomes with perceptions of a low health-related quality of life in a group of adults with CP and spastic diplegia (though not indicating what treatment was received in childhood). In addition, Benner *et al.* [13], who also did not report of childhood interventions performed, observed increased health concerns (functional deterioration, pain and severe fatigue) and an impact of these health concerns on activities over a ten-year period in adults with CP. Studies reporting on level of accomplishment and satisfaction in daily activities and participation in adults with CP in developing countries are limited and longitudinal studies documenting on this subject more than 25 years following SDR do not exist.

Therefore, as part of a longitudinal study following the healthy aging in adults living with CP, we aimed to perform a nine-year follow-up (2008 - 2017) in the changes in functional mobility, level of accomplishment and satisfaction in daily activities and participation, in a group of adults with CP and spastic diplegia who underwent SDR more than 25 years ago. A secondary aim was to compare these outcomes of the adults with CP to a matched group of TD adults. Thirdly, associations between the participants' current level of accomplishment and satisfaction in daily activities and participation and (i) participants' characteristics; and (ii) level of functional mobility were studied.

METHODS

Study design and participants

This study forms part of a longitudinal investigation tracking the health and wellness of adults with CP, who underwent SDR during childhood (> 25 years ago). The last follow-up was performed in 2008 and was based on 32 adults with CP, who underwent SDR at Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1981 and 1991. Inclusion criteria were a diagnosis of spastic diplegia, without dystonia, athetosis, ataxia and/or hypotonia. All participants underwent SDR with the aim to improve on functional level. They had access to on-going physiotherapy before and after SDR and adequate care-taker support. In addition, participants were pre-operatively classified according to the ~~as~~ Gross Motor Function Classification System (GMFCS, age bracket 12 - 18 years), as GMFCS level I, II or III [14].

Participants from this 2008 study were contacted and asked if they were willing to participate in the current study (2017). In addition, a group of TD adults from similar backgrounds were matched for gender, body mass index (BMI) and Social Economical Status (SES) and recruited. Adults in the TD group were not included if they had any neuromuscular disorders and/or other physical impairments. Before enrolling into the study all participants signed a written informed consent. The study was approved by the Human Research Ethics Committee of the University of Cape Town (HREC NO: 133/2016).

All the assessments (interview, measurements, observations and questionnaire) were conducted by one of the two investigators (BEV and NGL), who were both familiar with the different assessments. If a clear judgment could not be made by the one investigator the other investigator was consulted.

Participants' characteristics

Participants' socio-demographic information and indicators of participation in daily life were obtained by a semi-structured interview. Age, gender, SES, marital status, children, living situation, highest level of education attained, employment status, main source of income and current health status were captured as part of this interview. SES was estimated based on housing density, as suggested by Micklesfield *et al.* [15], which is calculated by dividing the 'number of people living in the house' by the 'number of rooms in the house' (excluding kitchen and bathroom). Score categories are as follows < 1: 'high SES'; ≥1 and ≤1.5: 'normal SES'; and >1.5: 'low SES' [15]. In addition, to the interview, participants GMFCS level and BMI (based on height and weight) were determined.

Life Habits questionnaire

The Life Habits (LIFE-H 3.1) questionnaire was used to evaluate participants' level of accomplishment in daily activities and participation, as well as how satisfied they were to accomplish these life habits [16]. The LIFE-H questionnaire consists of 77 life habits, which are divided into 12 subscales related to Daily Activities and Social Roles. Daily Activities includes the following six subscales: 'Nutrition', 'Fitness', 'Personal care', 'Communication', 'Housing' and 'Mobility', while Social Roles includes the subscales of 'Responsibilities',

'Interpersonal relationships', 'Community life', 'Education', 'Employment' and 'Recreation'. For each of the Daily Activities and Social Roles subscales, a weighted Accomplishment and Satisfaction score was calculated [16, 17].

The Accomplishment scores range from 0 (not accomplished or achieved) to 9 (accomplished without difficulty and without assistance) and are based on the degree of difficulty and the type of assistance required to accomplish a task, while the Satisfaction scores range from 'very unsatisfied' (score -10) to 'very satisfied' (score 10) [17]. The LIFE-H questionnaire has shown to be reliable and valid [16, 17] and has been used in different cohort studies in adults with CP [10, 12, 18, 19, 20]. In line with previous study of Langerak *et al.* [10], the subscale of 'Education' was excluded from the analyses.

Functional Mobility Scale

The Functional Mobility Scale (FMS) was used to determine participants' level of mobility in their daily environment (performance level). The FMS is based on a 6-level ordinal grading system, rating the mobility for three different distances, namely 5, 50 and 500 meters, while taking the use of an assistive device in consideration. The FMS scores range from using a wheelchair (score 1) to being totally independent on all surfaces (score 6) [21]. The FMS has been used before in adults with CP [22, 23] and has shown to be a valid and reliable scale to determine functional mobility [21, 24].

Statistical analysis

Statistical analyses were performed by PPV, who is a statistician and also performed the statistical analysis for the 2008 study [10]. Descriptive statistical analysis was used to summarize participants´ characteristics and indicators of participation. A Chi-Square and analysis of variance (ANOVA) were used to determine if adults with CP in the 2017 study were matched to the TD adults for gender, age, BMI and SES.

LIFE-H data was categorized for interpretation purposes. Similar as in the 2008 study, the weighted accomplishment scores of the LIFE-H questionnaire were divided into 3 categories: (I) score ≥8.0: independent with no difficulties (with or without assistance); (II) score 5-8:

independent with difficulties (with or without assistance); (III) score ≤5.0: dependent, as this life habit is not performed by the participant or carried out with human assistance. The results of the weighted satisfaction scores were categorized into 2 levels: (I) score <0.0: dissatisfied; and (II) score ≥0.0: satisfied.

For statistical analysis the numerative (non-categorized) scores were used and reported by using non-parametric descriptives (median and interquartile ranges (IQR)). The Wilcoxon rank tests were used for the comparison of the subscales and total scores of accomplishment and satisfaction levels in daily activities and participation between the 2008 and the 2017 CP cohorts. To determine differences between the current CP and TD cohort, Mann-Whitney U tests were used. As a threshold for statistical significance, to compensate for multiple comparisons (48), a Bonferroni corrected alpha-level of $p \leq 0.001$ was applied for both analyses.

In line with the 2008 study, FMS scores were categorized for interpretation purposes, to: (I) independent / able to walk without walking aids (FMS level 5 and 6); (II) need to use walking aids (FMS level 2, 3 and 4); and (III) wheelchair dependent (FMS level 1). For statistical analysis the non-categorized scores were used. Wilcoxon rank tests were applied to compare the FMS scores between the 2008 and the 2017 CP cohorts. As a threshold for statistical significance, to compensate for multiple comparisons (3), a Bonferroni corrected alpha-level of $p \leq 0.0167$ was applied.

Spearman's rank correlation analyses were used to examine the associations between LIFE-H scores (i.e. total accomplishment and satisfaction scores), participant characteristics values (age at SDR, current age, SES, BMI) and FMS scores of the adults with CP. As a threshold for statistical significance, to compensate for multiple comparisons (8 and 6), a Bonferroni corrected alpha-level of respectively $p \leq 0.006$ and $p \leq 0.008$ was applied.

RESULTS

Participants' characteristics

From the 32 participants who participated in the 2008 study [10] six participants were not included in the 2017 study. One participant was pregnant, one had been injured in a motor vehicle accident, three elected not to participate and one was lost to follow-up. The

characteristics of the remaining 26 participants are shown in Table 5.1. In addition, similar information is also provided for the adults with CP at the 2008 study and 26 TD adults.

Table 5.1. *Participants' characteristics of CP (n=26) and TD cohorts (n=26).*

Variable		2008 CP	2017 CP	2017 TD
		n (%) / median [IQR]	n (%) / median [IQR]	n (%) / median [IQR]
Gender, male		16 (60)	16 (60)	16 (60)
Age (years)		26.8 [25.4 – 32.5]	35.8 [34.2 – 41.4]	35.7 [33.2 – 44.2]
SES		1.25 [0.8 – 1.7]	0.9 [0.7 – 1.3]	0.8 [0.6 – 1.3]
BMI (kg/m^2)		23.0 [20.3 – 29.9]	25.2 [21.6 – 31.2]	25.9 [24.1 – 28.2]
Age at SDR (years)		4.9 [3.7 – 10.1]	4.9 [3.7 – 10.1]	
Follow-up time (years)		21.4 [18.4 – 23.8]	30.1 [27.5 – 32.7]	
GMFCS	Level I	13 (50)	13 (50)	
	Level II	9 (35)	10 (38)	
	Level III	4 (15)	3 (12)	

Abbreviations: IQR, interquartile range; SDR, selective dorsal rhizotomy; SES, socio-economic status; BMI, Body Mass Index; and GMFCS, Gross Motor Function Classification System.

At a follow-up time ranging from 25 to 35 years after SDR, GMFCS levels of adults with CP were stable, except for one participant who improved one level (from GMFCS level III to GMFCS level II). No differences between the adults with CP in current study and TD adults were found for age, gender, SES and BMI. The median age of the adults with CP and TD adults was 35 years, while 60% of the participants was male and 40% female. The SES within both cohorts was similar, with 4% (CP) and 11% (TD) being classified as having a low SES, 46% (CP) and 35% (TD) a normal SES and 50% (CP) and 54% (TD) a high SES. Both cohorts also showed a comparable distribution of participants' BMI with 3.8% (CP) and 0% (TD) underweight, 50% (CP) and 42% (TD) normal BMI, and 50% (CP) and 58% (TD) overweight.

The majority of the CP study cohort had no other diagnosis influencing their medical status. Health issues reported were hypertension (n=4), Crohn's disease (n=1), Graves' disease (n=1), asthma (n=1), mental health conditions (e.g. depression, anxiety) (n=3). Incontinence was reported in three participants, all of whom had urge incontinence; a male participant had incontinence preceding SDR which remained unchanged, and two females reported incontinence following pregnancy and delivery.

Indicators of participation

The indicators of participation of the adults with CP (2008 and 2017 study) and the TD adults are shown in Table 5.2. With aging, more adults with CP moved out the house of (grand)

parents (35% versus 62%), were in a relationship or married (46% versus 65%) and had children (19% versus 42%). This number of adults with CP being in a relationship was similar to TD adults (61%), while it was more common for TD adults (of similar age) to be a parent (77%) and not living with (grand) parents (89%). Also, more TD adults were employed (89%) compared to the adults with CP in both studies (69% and 73%), while the difference was not that apparent regarding the proportion that completed higher education (TD: 77% versus CP: 61% and 69%).

Table 5.2. *Participants' indicators of participation for CP and TD cohorts.*

Variable	**2008 CP** n (%)	**2017 CP** n (%)	**2017 TD** n (%)
Marital status			
Single	14 (54)	9 (35)	9 (35)
Divorced/ widow	0 (0)	0 (0)	1 (4)
Relationship	7 (27)	5 (19)	2 (7)
Married	5 (19)	12 (46)	14 (54)
Children			
0	21 (81)	15 (58)	6 (23)
1	3 (11)	6 (23)	8 (31)
≥2	2 (8)	5 (19)	12 (46)
Living Situation			
Living on own	2 (8)	2 (8)	7 (27)
With (grand) parents	17 (65)	10 (38)	3 (11)
With partners	6 (23)	14 (54)	15 (58)
With others (e.g. family, friends)	1 (4)	0 (0)	1 (4)
Educational attainment			
Primary	1 (4)	1 (4)	0 (0)
Secondary	9 (35)	7 (27)	6 (23)
Higher education	16 (61)	18 (69)	20 (77)
Employment			
Paid employed	17 (65)	17 (65)	21 (81)
Self employed	1 (4)	2 (8)	2 (8)
Unemployment (health reason)	5 (19)	0 (0)	0 (0)
Unemployment (other reason)	2 (8)	7 (27)	3 (11)
Student	1(4)	0 (0)	0 (0)
Main Income			
Paid job	19 (73)	17 (65)	23 (89)
Disability grant	6 (23)	9 (35)	0 (0)
Family income & other	1 (4)	0 (0)	3 (11)

Life Habits questionnaire

The accomplishment and satisfaction levels, based on the LIFE-H questionnaire, of each cohort are shown in Figure 5.1^{A} and 5.1^{B}, respectively. Overall adults with CP in the current

study were independent and satisfied with accomplishing daily activities and social roles. However, 19% of the adults with CP scored being dependent for 'Mobility' activities, while 12% scored to be dependent for 'Community Life', 15% for 'Employment' and 12% for 'Recreation'. In line with this, 8% of the participants with CP were dissatisfied with their 'Mobility', 4% with their 'Community Life', 12% with their 'Employment' status and 4% with their 'Recreation' activities.

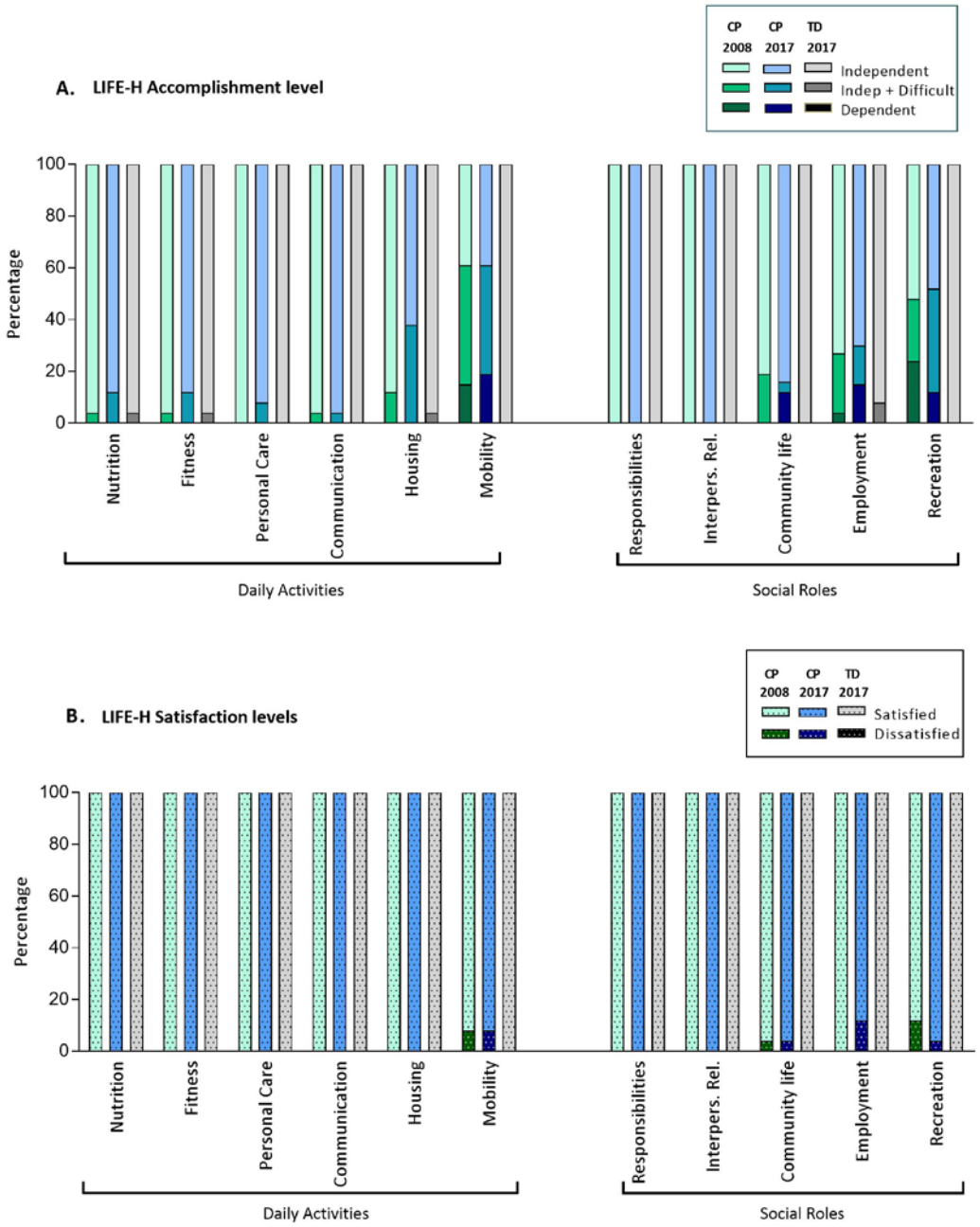

Figure 5.1. *Outcomes of LIFE-H categorized for CP (2008 and 2017 and TD cohorts).* ***A.*** *Accomplishment levels weighted > ≥8.0 independent and no difficulties; 5-8 independent with difficulties; and cores ≤5.0: dependent or not able to accomplish.* ***B.*** *Satisfaction levels with score ≥0.0: satisfied; and score<0.0: dissatisfied*

Table 5.3. *Outcomes of the LIFE-H questionnaire for the CP and TD cohorts*

LIFE-H item	Accomplishment			Satisfaction		
	2008 CP	**2017 CP**	**2017 TD**	**2008 CP**	**2017 CP**	**2017 TD**
	Median [IQR]	Median [IQR]	Median [IQR]	Median [IQR]	Median [IQR]	Median [IQR]
Daily activities						
Nutrition	10.0 [10.0 – 10.0]	10.0 [9.7 – 10.0]	10.0 [10.0 – 10.0]	10.0 [8.4 – 10.00]	10.0 [8.8 – 10.00]	10.0 [8.8 – 10.0]
Fitness	9.6 [7.5 – 10.0]	9.4 [7.5 – 10.0]$^{\#}$	10.0 [10.0 –10.0]$^{\#}$	7.5 [5.0 – 10.0]	7.5 [5.4 – 9.4]	9.4 [5.0 – 10.0]
Personal Care	10.0 [9.7 – 10.0]	9.9 [9.5 – 10.0]$^{\#}$	10.0 [10.0 –10.0]$^{\#}$	10.0 [6.4 – 10.0]	9.3 [6.8 – 10.0]	10.0 [9.8 – 10.0]
Communication	10.0 [9.7 – 10.0]	10.0 [10.0 – 10.0]	10.0 [9.9 – 10.0]	10.0 [8.6 – 10.0]	10.0 [10.0 – 10.0]	10.0 [10.0 – 10.0]
Housing	9.8 [9.3 – 10.0]*	8.3 [7.3 – 9.8]*$^{\#}$	10.0 [8.9 – 10.0]$^{\#}$	10.0 [5.8 – 10.0]	9.1 [5.0 – 10.0]	10.0 [9.0 – 10.0]
Mobility	6.8 [5.5 – 9.0]	7.0 [5.7 – 9.3]$^{\#}$	10.0 [10.0 –10.0]$^{\#}$	6.1 [3.3 – 8.0]	6.0 [1.2 – 8.5]$^{\#}$	10.0 [8.6 – 10.0]$^{\#}$
Total daily activities	9.2 [8.9 – 9.7]	9.0 [8.4 – 9.6]$^{\#}$	9.9 [9.7 – 10.0]$^{\#}$	8.7 [5.8 – 9.5]	8.1 [6.1 – 9.4]	9.5 [8.6 – 10.0]
Social roles						
Responsibilities	10.0 [10.0 – 10.0]	10.0 [10.0 – 10.0]	10.0 [10.0 – 10.0]	10.0 [9.3 – 10.0]	10.0 [9.8 – 10.0]	10.0 [9.8 – 10.0]
Interpersonal	10.0 [10.0 – 10.0]	10.0 [10.0 –10.0]	10.0 [10.0 – 10.0]	10.0 [8.3 – 10.0]	10.0 [7.9 – 10.0]	10.0 [8.4– 10.0]
Community life	10.0 [8.5 – 10.0]	10.0 [8.9 –10.0]	10.0 [10.0 – 10.0]	8.0 [5.0 – 10.0]	10.0 [5.5 – 10.0]	10.0 [9.7– 10.0]
Employment	9.0 [7.7 – 10.0]	9.3 [7.2 – 10.0]	10.0 [9.9 – 10.0]	7.1 [5.0 – 10.0]	7.2 [5.0 – 10.0]	10.0 [8.8– 10.0]
Recreation	8.6 [5.2 – 10.0]	7.4 [6.4 – 10.0]$^{\#}$	10.0 [10.0 –10.0]$^{\#}$	6.4 [4.3 – 8.6]	7.1 [4.8 – 10.0]	10.0 [8.5 – 10.0]
Total social roles	9.1 [8.1 – 9.8]	8.9 [8.1 – 9.6]$^{\#}$	10.0 [9.8 – 10.0]$^{\#}$	7.8 [6.3 – 9.6]	8.5 [5.5 – 9.5]	9.7 [8.5 – 10.0]

Abbreviations: IQR, Interquartile Range; As a threshold for statistical significance a Bonferroni corrected alpha-level of $p \leq 0.001$ was applied for all scores.
**Significant difference between 2008 and 2017 CP; # Significant difference between 2017 CP and 2017 TD.*

No differences in the Total Accomplishments and Satisfaction level scores were found between the 2008 and the current study in the adults with CP. However, when analyzing the different subscales between the 2008 and the 2017 study, adults with CP were more dependent in accomplishing 'Housing' activities ($p < 0.001$) (Table 5.3).

In comparison to adults with CP, the TD adults had overall better accomplishment levels for daily activities ($p < 0.001$), as a result of better scores for subscales 'Fitness', 'Personal care', 'Housing' and 'Mobility' ($p < 0.001$). In line with this, TD adults also had overall better social role accomplishment levels ($p < 0.001$), with TD adults scoring better for 'Recreation'. In contrast to accomplishment, satisfaction levels were the same between adults with CP and the TD adults, except for the 'Mobility' subscale ($p < 0.001$) (Table 5.3).

Functional mobility scale

Walking performance over 5, 50 and 500meter determined by the FMS in adults with CP at the 2008 study and at the 2017 study are shown in Figure 5.2. No changes in the FMS scores were found between the 2008 study and the current study.

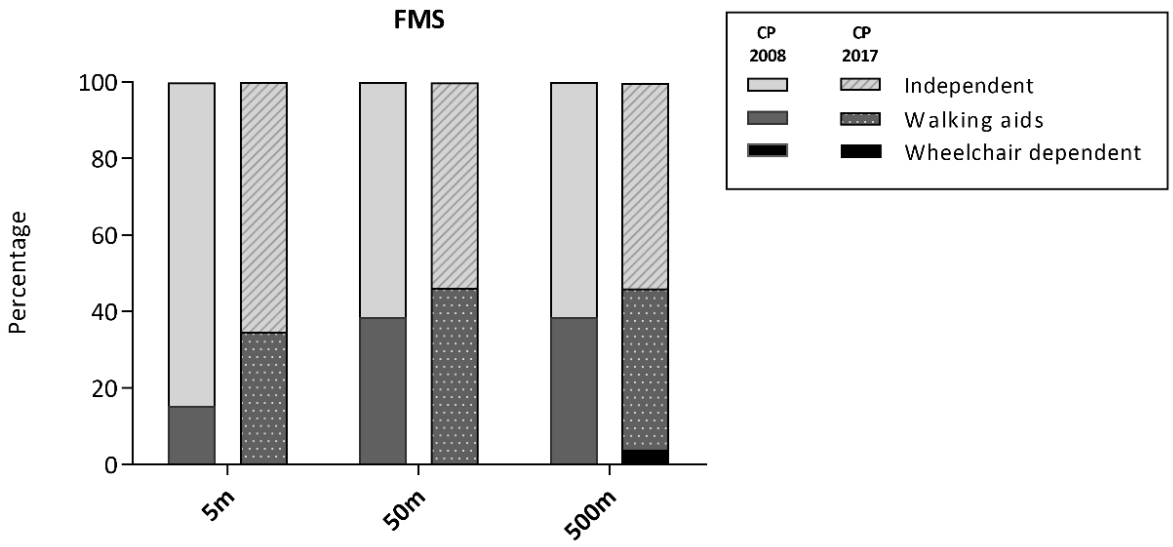

Figure 5.2. *Functional Mobility Scores for CP cohorts. Categorized FMS scores: (I) independent / able to walk without walking aids (FMS level 5 and 6); (II) need to use walking aids (FMS level 2,3 and 4); and (III) wheelchair dependent (FMS level 1)*

Within the current study, 65% of the participants was able to walk independently (FMS score 5 or 6) over 5 meters with 54% being able to walk independently over 50 and 500

meters. Walking aids were used (FMS score 2, 3 or 4) by 35% of the participants over a 5-meter distance, while 46% used it over a 50-meter distance and 42% needed a walking aid for a 500-meter walking distance. One adult with CP (4%) needed a wheelchair (FMS score 1) to cover 500 meters at the moment of the current study.

Correlations

The estimated rank correlation coefficients between the LIFE-H questionnaire, accomplishment and satisfactions levels, and participant characteristics are shown in Table 5.4. No relationships between participant characteristics and the level of accomplishment and satisfaction were found.

Table 5.4. *Correlations (Spearman's rho) between LIFE-H and participants' characteristic variables for 2017 CP cohort*

LIFE- H Total scores	Age at SDR		Current age		SES		BMI	
	r	*p*	r	*p*	r	*p*	r	*p*
Accomplishment	-0.040	*0.846*	-0.225	*0.27*	-0.309	*0.12*	-0.171	*0.40*
Satisfaction	-0.086	*0.678*	-0.236	*0.24*	-0.175	*0.39*	-0.114	*0.58*

Abbreviations: SDR, selective dorsal rhizotomy; SES, socio-economic status; and BMI, Body Mass Index. As a threshold for statistical significance a Bonferroni corrected alpha-level of p ≤ 0.006 was applied.

The estimated rank correlation coefficients between the LIFE-H questionnaire and FMS scores are shown in Table 5.5. Strong correlations were found between the LIFE-H accomplishment levels and FMS scores, with correlations ranging from 0.85 to 0.89. In line with this, strong correlations were also found between the LIFE-H level of satisfaction and FMS scores, with correlations ranging from 0.73 to 0.79.

Table 5.5. *Correlations (Spearman's rho) between LIFE-H and FMS scores for 2017 CP cohort (n = 26)*

LIFE-H Total scores		FMS – 5m		FMS – 50m		FMS – 500m	
		r	*p*	r	*p*	r	*p*
Accomplishment	25yr FU	0.85	*<0.001*	0.89	*<0.001*	0.87	*<0.001*
Satisfaction	25yr FU	0.79	*<0.001*	0.73	*<0.001*	0.76	*<0.001*

Abbreviations: FMS, Functional Mobility Scale; As a threshold for statistical significance a Bonferroni corrected alpha-level of p ≤ 0.008 was applied.

DISCUSSION

With the knowledge of secondary problems occurring with age in CP [1], there is an importance to understand the long-term outcomes of interventions performed in childhood like SDR. This is the first long-term follow-up study reporting the level of accomplishment and satisfaction in daily activities and participation as well functional mobility for adults with CP and spastic diplegia more than 15 and 25 years after SDR.

Level of accomplishment and satisfaction in daily activities and social roles

More than 25 years after SDR most of the adults with CP were independent in and satisfied with accomplishing the specific daily activities and social roles. No change was found between the 2008 [10] and the 2017 study regarding the overall level of accomplishment and satisfaction in daily activities and social roles. For the subdomains the only change was found in the Housing subscale (accomplishment). The change in this score over years was mainly attributed to a higher percentage of 'major household tasks' and 'maintaining the grounds of their home' were performed by a proxy. This may be explained by the fact that more adults in the 2017 study were married and living with their partners instead of their (grand) parents. Another reason could be, with the increase of SES, that participants were possibly able to pay a third party to complete these laborious tasks. Interestingly, none of the participants were dissatisfied with the level of accomplishment for this subscale, which suggests that they were happy to pay others or happy with a proxy to complete the task.

The perceived stability in level of accomplishment in daily activities and participation in current study is in contrast with the literature, where functional decline is shown for individuals with CP as they age [25, 26, 27]. The mean age at which functional deterioration has been reported is approximately 37 years [28, 29], while the median age of our study cohort was 36 years (mean age: 38 years). Participants' characteristics and remarkably current age of the CP cohort, were not related to the overall level of accomplishment and satisfaction in daily activities and participation in the 2017 study. This contributes to our findings that there seems to be no deterioration in the accomplishment of daily activities and participation regardless the aging of the adults in the CP cohort. A reason for absence of functional deterioration in our CP cohort, might be that all participants underwent a SDR

(where strict selection criteria have been adhered). The SDR may assist in avoiding secondary complications associated with spasticity reduction, and has been found to have a positive effect on level of functioning [9].

Despite not many changes over time in adults with CP some differences between daily activities and social role subscales were found when compared to their TD peers. The participants were more dependent and faced more difficulties with Fitness, Personal Care, Mobility and Recreation subscales than TD adults. Greater dependence and reduced subscale factors may be inherent to their GMFCS level, as 50% of our participants with CP were classified as GMFCS level II or III. However, the 61% of the adults with CP that experienced difficulties with Mobility in our study is lower than the 77% previously found by van der Slot *et al.* [12], in adults with spastic diplegia aged 25 – 45 years (no report of childhood interventions performed).

Another interesting element in this study was the difference in percentage of adults with CP involved in competitive employment between this study (developing country) and other studies in adults with CP living in Western societies (developed countries). In the 2017 study 73% of the CP cohort were employed, while in developed countries this ranged between 29 – 54% [12, 30, 31, 32]. This was also reflected in the LIFE-H outcomes (subscale Employment) with 70% of the adults living in Cape Town, South Africa, being independent (score <8) and 56% of the adults with CP living in the Netherlands [12]. This disparity appears to be due to differences in social security systems and the value of disability grants between developing and developed countries.

Remarkably, despite these obstacles adults with CP were as satisfied as their TD peers for all subscales, except for mobility. This is relevant information for clinicians to guide their therapies, adults with CP do feel restricted in movement but does not imply a feeling of dissatisfaction.

Functional mobility

The majority (54%) of the adults with CP in the current study were able to walk independently without walking aids. Andersson & Mattsson [25] and Ando & Ueda [26] reported similarly with 49% and 57%, respectively where interventions in childhood were

not specified. However, Maanum *et al.* [33] reported 70% of the study cohort was able to walk independently although their study included participants that were younger (age range: 18 – 65 years) and diagnosed with unilateral CP (almost 50% of their study population).

No change was found in FMS scores of the adults with CP between the 2008 and 2017 study. This is remarkable since most literature reports functional walking decline in participants with CP while aging, starting in their 20s and 30s [34]. A correlation between functional mobility (FMS score) and the level of accomplishment and satisfaction in daily activities and social participation was found. The fact that there was no change in FMS levels of adults with CP in the 2008 and the 2017 study, might be a contributing factor to the fact that there was also no significant change in level of accomplishment and satisfaction in daily activities and participation. FMS performance can explain 72 to 80% of variance in overall accomplishment levels, while it can explain 54 to 63% of the variance in overall satisfaction levels. These findings highlight the importance for adults with CP to maintain their walking function and mobility in order to enable daily activities and social participation. Clinicians and therapists should therefore inform adults with CP about the importance of an active lifestyle.

Limiting factors

The sample size of the study was moderate. However, as a first follow-up study more than a quarter of a century after SDR (25 – 35 years post-SDR), the conclusion should be seen as an important indication of long-term outcomes of SDR. The current study was conducted in South Africa, while results of similar studies from other research groups were based on study populations from developed countries. We should be aware that the health services in South Africa are not as well established as in Western countries [35], to limit the influence of this factor, a reference cohort consisting of South African TD adults was included in this study. However, for comparison purposes, it would be interesting for future studies to include a reference cohort of South-African adults with CP who did not receive SDR, but only orthopedic interventions or conservative treatment for example. It would particularly compelling to investigate the differences in functional mobility (use of assisted mobility) between the proposed cohorts. The last point to address is that this study only focused on a

few factors that could have been related to the daily activities and participation levels. Insight into other factors associated with level of accomplishment and satisfaction in daily activities and social participation (e.g. pain, fitness levels, depression) are essential to guide future therapies.

In conclusion, with this unique study reporting on the change in level of accomplishment and satisfaction in daily activities and participation as well as the change in functional mobility more than 25 years after SDR, we found that adults with CP and spastic diplegia have stable and lasting high levels of functioning within the Activity and Participation components of the ICF model. In addition, they are overall satisfied with accomplishing daily activities and participation in the community. This is relevant information for parents, care-givers and clinicians when they consider SDR as a treatment option for a child with CP. In addition, the strong correlation between functional mobility and the LIFE-H scores highlights the importance of focusing therapies and rehabilitation in adults with CP on maintaining their walking function and mobility in order to enable daily activities and social participation.

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SUMMARY AND CONCLUSIONS

RATIONALE

Cerebral palsy (CP) is the most common cause of physical disability in childhood. Almost all children with CP survive into adulthood with life expectancies similar to that of typically developing (TD) adults [1]. CP describes a group of permanent disorders of development of movement and posture, attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. While limitation of activity may be the main concern, the motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication and behavior, by epilepsy, and by secondary musculoskeletal problems [2]. Although the brain injury that initially causes CP is not progressive, the clinical manifestations may change throughout the life span [3], as secondary conditions develop over time [4, 5].

One of the biggest challenges is to prevent or minimize these secondary effects of CP on the musculoskeletal system (e.g. contractures due to spasticity) and to improve or maintain functional status and quality of life in the face of healthy aging [6]. There is currently no treatment that is able to cure the brain damage which causes CP, but a variety of options exist to address spasticity, the most prevalent primary condition which is estimated to be present in 80% of people with CP [7]. One of these options is the neurosurgical procedure of Selective Dorsal Rhizotomy (SDR) [8]. Originally described in *Gynecology and Obstetrics* by Foerster and refined by Warwick Peacock in the 1980's, this procedure entails selective sectioning of dorsal rootlets in the lumbosacral area. As a consequence, abnormal muscle tone is reduced through decreasing sensory input [9]. Following Peacock's relocation from Cape Town, South Africa, to Los Angles, USA, the procedure gained worldwide popularity [10, 11].

Although a large number of studies have demonstrated the benefits of this procedure, they largely comprise relatively short-term follow-up assessments in children and adolescents [12, 13, 14]. As stated by Colver *et al*. in a recent review in *The Lancet,* one of the most compelling challenges for the twenty-first century is the need to chart and understand the life course of adults who have grown up with a 'pediatric condition', like CP and the long-term effects of treatments they have received in childhood (such as SDR) [4]. This requires long-term follow-up studies focused on all facets of daily living and the International Classification of Functioning, Disability and Health (ICF) model with the domains of body

structure and function, activity and participation provides a suitable framework for doing this. Currently the longest follow-up studies of adults who underwent SDR in childhood are those performed up to 25 years after surgery by our research group in Cape Town [15, 16, 17]. This established track record gives us the opportunity to continue to follow this cohort of adults in order to understand the long-term outcomes of SDR on all domains of the ICF-model and quality of life. This will provide important clinical insight to support parents, caregivers and clinicians in their clinical decision-making process for their child with CP.

RESEARCH AIMS

The aim of this PhD thesis was to determine the status of adults with CP and spastic diplegia – related to all domains of the ICF-model and health-related quality of life – more than 25 years after SDR. The second aim was to investigate the changes in gait pattern, spinal deformities and level of accomplishment and satisfaction in daily activities and participation in adults with CP over a nine-year period. The third and last aim was to explore associations between results in the different ICF-model domains along with personal and environmental context factors.

ICF MODEL

The ICF model developed by the World Health Organization provides a clear overview of the level of 'Functioning, Disability, Health and Quality of Life in adults with CP more than 25 years after Selective Dorsal Rhizotomy' [18]. Figure 6.1 provides an overview of all outcome measurements used in this PhD thesis, with reference to the chapters where the results are described.

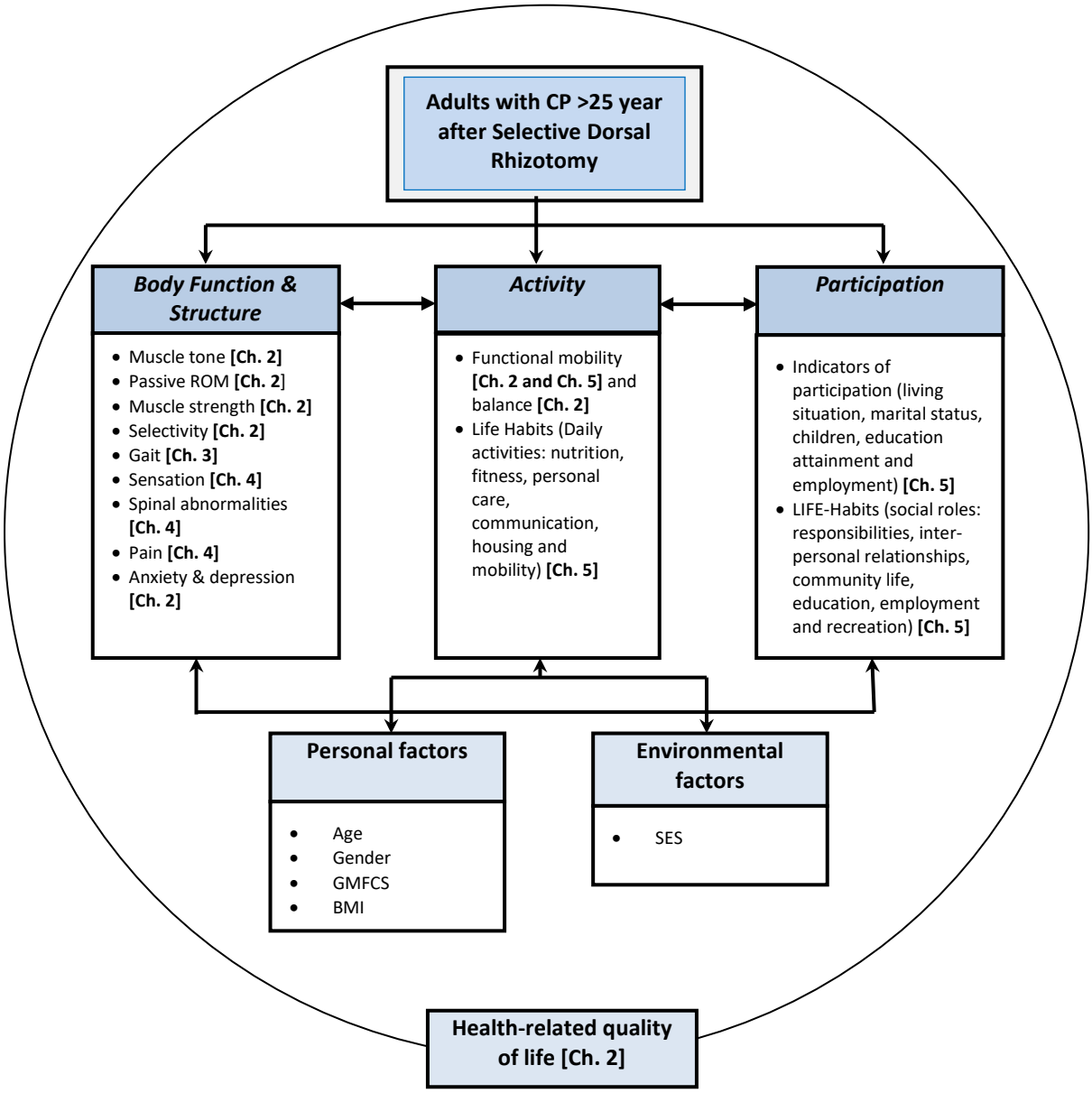

Figure 6.1. *Overview of all outcome measures used in this thesis in light of the ICF-model. Abbreviations: Ch., Chapter.; ROM, range of motion; GMFCS, gross motor function classification system; BMI, body mass index; and SES, socio-economic status.*

Health status and contextual factors

The CP cohort described in this thesis forms part of a longitudinal investigation tracking the health and wellness of adults with CP. The original studies were performed in 2008 [15, 16, 17] and consequently a recent follow-up was conducted in 2017. Of the 32 adults in the original cohort, 26 participated in current study. All underwent SDR according to the 'Peacock' method (laminectomies L2 – S1) at Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1981 and 1991. At the time of follow-up, ranging from 25 to 35 years after SDR, half of the cohort was classified as GMFCS level I, while 38% as level II and 12% as level III. The majority (65%) of the adults with CP had better gross motor function than pre-operative (lower GMFCS level) and none showed deterioration (Chapter 3). However, it has to be acknowledged that additional orthopedic surgical interventions were common and strict SDR selection criteria were adhered. The median age of the participants was 35 years, and 60% were male. The majority of the CP study cohort had no other diagnosis influencing their medical status. Health issues reported were hypertension (n=4), Crohn's disease (n=1), Graves' disease (n=1), asthma (n=1), mental health conditions (e.g. depression, anxiety) (n=3). Incontinence was reported in three participants, all of whom had urge incontinence; a male participant had incontinence preceding SDR which remained unchanged, and two females reported incontinence following pregnancy and delivery.

Body function and structure

The physical status of adults with CP and spastic diplegia is determined by the interaction of lower extremity muscle tone, passive ROM, muscle strength and selectivity. A prominent result found was the normalized muscle tone in adults with CP more than 25 years post-SDR (Chapter 2). It is well-established that SDR reduces spasticity [12, 19, 20], and sustained reduction in muscle tone has been reported through adolescence [21, 22], into early adulthood [23, 24, 25, 26] and later in adulthood, as confirmed in this study more than 25 years after SDR. The lower scores found for passive ROM, muscle strength and selectivity in comparison with the TD cohort (Chapter 2), are in line with what is expected in adults with CP. These differences could be explained by differences in neurophysiology of muscles in individuals with CP compared to their peers [1, 27, 28].

The reduction in muscle tone as a result of SDR had also long-lasting positive effects on the gait pattern of adults with CP (Chapter 3). More than 25 years after SDR, adults with CP and spastic diplegia walked with a mild crouch gait pattern, with minimal signs of spasticity. Their walking pattern didn't change over the nine-year follow-up period and was related to the GMFCS levels assessed at the same time (2017).

Although SDR reduces spasticity, the possibility of spinal complications such as deformity and back pain (due to laminectomy) remains a concern [14, 29]. At follow up more than 25 years after SDR, spinal abnormalities (e.g. scoliosis, hyperkyphosis and hyperlordosis) were found but appear not to occur more often than what has been reported in adults with CP. This was not the case for spondylolysis and spondylolisthesis, which appear to occur more often than has been reported for adolescents with CP. Overall spinal abnormalities did not change during the nine-year follow-up period (Chapter 4). However, there is limited data on the natural history of CP and the influence on spinal abnormalities, which makes it difficult to distinguish independently the effects of SDR [13]. The spinal abnormalities were not related to contextual factors (except for hyperkyphosis and females), abnormality in sensation, and the level of disability due to back pain. Participant's experienced minimal disability, which did not progress over time and did not restrict them in activities of daily living.

Activity

The concern about a decline in walking ability with aging in CP [27], starting in their 20s and 30s [30], was not confirmed in our cohort more than 25 years after SDR. No increased risk for falls was found in the majority of the cohort based on the timed up and go (TUG) test (Chapter 2). The majority (54%) of the adults with CP were able to walk independently without walking aids and no decline was found in functional mobility scores (FMS) of adults with CP over a nine-year period (Chapter 5).

These positive findings were reflected in high and stable levels of functioning regarding accomplishment of the daily activities that comprise the Life-Habit questionnaire (LIFE-H) domains of nutrition, fitness, personal care, communication, housing and mobility (Chapter 5). Despite the fact that adults with CP were more dependent and faced more difficulties

with fitness, personal care and mobility than TD adults, their level of satisfaction was similar (except for the domain of mobility). The correlations found between accomplishment levels and functional mobility highlights the importance of maintaining walking function and mobility while aging in order to enable daily activities. The finding that stronger participants have better functional mobility and balance (Chapter 2), suggests that muscle resistance training might be beneficial for functional mobility and balance in adults with CP after SDR.

Participation

At more than 25-year follow-up, more of the adults with CP were married or living with partners, and more had children in comparison to nine years ago, while there were fewer changes in education and employment over this time period. This number of adults with CP currently in a relationship was similar to TD adults (61%), although it was more common for TD adults (of similar age) to be a parent (77% vs. 42%) and not living with (grand) parents (89% vs. 62%). Also, more TD adults were employed (89%) compared to the adults with CP in both studies (69% and 73%). However, there is a remarkable difference in the percentage of adults with CP involved in competitive employment when comparing the current study with studies of adults with CP living in Western societies. In our South African cohort, 73% of adults with CP was employed, while this ranged between 29% - 54% in more developed countries [31, 32, 33, 34]. This also reflected in the LIFE-H outcomes (subscale Employment) with 70% of the adults living in Cape Town, South Africa, being independent in comparison to 56% of the adults with CP living in the Netherlands [37]. An explanation for this might be the need to work due to differences in social security systems and the availability and value of disability grants between African and Western countries.

Based on the LIFE-H scale, the adults with CP were more dependent and faced more difficulties for recreation activities compared to the TD adults, though the levels remained stable over the nine-year follow-up period (Chapter 5). The difference between the CP and TD cohorts can be explained by the fact that 50% of our participants with CP were classified as GMFCS level II or III.

Health-related quality of life – physical and mental health

Another striking finding was that the adults with CP reported a relatively good health-related quality of life (HRQoL). Seven of the eight health concepts from the short form-36 health survey (SF-36) (physical role functioning, bodily pain, general health, vitality, social functioning, emotional role functioning and mental health), did not differ between adults with CP and TD adults (Chapter 2). This was in contrast to other studies, where challenges in most of these areas were reported for adults with CP [33, 35, 36, 37]. The only health concept that the adults with CP in this study perceived a lower HRQoL compared to their peers, was related to physical functioning.

HRQoL mental score and levels of anxiety and depression were similar for the adults with CP and TD adults, which suggest that while adults with CP have on-going physical challenges, this might not directly impact their mental health. The levels of anxiety and depression found in current study are also lower than reported in other studies. Only mild to moderate levels of anxiety were found (15%), while no increased depression levels were observed in the CP cohort (Chapter 2).

ADVERSE EFFECTS

No serious adverse effects were found in this long-term follow-up study of SDR. Although decreased touch and pin-prick sensation was found in some patients, this was less than half of the CP cohort and was not troublesome (Chapter 4). Three participants reported bladder and bowel problems, but this appeared not to be related to SDR. While two participants reported pain as a consequence of the SDR, the prevalence of pain more than 25 years after SDR (28% daily pain and 12% weekly pain) was comparable to what is expected for adults with CP, with the lower back as the most common site. Therefore, we did not consider this an adverse effect of SDR since identifying the independent effect of SDR on pain is difficult is pain is a common problem and can have different causes in adults with CP [26, 38, 39, 40].

SUBJECTIVE IMPRESSION OF SDR

Most of the adults with CP (94%) viewed the SDR they had undergone as worthwhile based on the mobility and/or quality of life benefits experienced. From the 21 participants who answered the following question 'If you had to decide by yourself now, would you make the same decision as your parents to undergo SDR?', 90% responded positively based on the increased level of functioning, while 10% provided negative feedback due to experiencing pain. In addition, 20% of the participants indicated that if they could have done something different, they wished they had exercised more in the past years.

CLINICAL IMPLICATIONS

SDR effectively decreases lower limb spasticity in appropriately selected children with CP and this reduction in muscle tone is sustained in adulthood for at least 25 years after the procedure with no serious adverse effects. Adults with CP who underwent SDR in childhood report good health-related quality of life and most were satisfied with the treatment. Anxiety and depression were not prominent in this group who reported overall levels of satisfaction similar to their TD peers in accomplishing daily activities and participation. The reduction in spasticity appeared to impact positively on functional outcomes during aging in adulthood since no overall decline in functional mobility, gait and accomplishment of daily activities and participation was found, which might have been expected in aging adults with CP. This information should be of value to clinicians and caregivers wishing to make evidence-based decisions regarding management options for a child with CP.

In contrast to these positive outcomes, differences with TD adults were found in ROM, strength, selectivity, gait, functional mobility and balance. However, these outcomes could be explained by differences in neurophysiology of muscles in individuals with CP compared to their TD peers, and it does not mean that some of these parameters cannot improve. Fitness and muscle strength programs have shown to be beneficial in individuals with CP [41, 42, 43]. The correlations found between strength and functional mobility as well as between functional mobility and level of accomplishment and satisfaction in daily activities and participation emphasize the clinical importance of training programs for adults with CP who underwent SDR to support healthy aging. Based on the findings of Chapter 2 strength

training programs should focus on all the different muscle groups of the lower extremity, while attention should also be given on how exercises are performed as this can stimulate and possibly also improve the selectivity and maintain the ROM in the hip, knee and ankle. Programs should focus on improving strength in a functional way and incorporate balance aspects rather than focusing on muscle hypertrophy [44]. These types of programs are likely to prevent a reduction of range of motion due to hypertrophy and expected to improve functional strength and mobility in adults with CP. This is also reflected in the finding of Chapter 3 and 5, which shows that increased range of motion can possibly lead to better walking patterns and that functional mobility levels are associated with better accomplishment and satisfaction of daily activities and participation scores. However, the above-mentioned hypotheses should be tested in future research.

Spinal abnormalities appear not to worsen during aging in adulthood and seem not to negatively impact the daily activities of adults with CP more than 25 years post-SDR. This finding is particularly noteworthy as this cohort underwent SDR via a laminectomy, as opposed to the less invasive approach of laminotomy, which has replaced laminectomy in most centers as well as at Red Cross War Memorial Children's Hospital. The important clinical implication of this is that rather a conservative approach should be followed when treating spinal abnormalities in adults with CP who underwent SDR in childhood. As the general assumption might be that spinal deformities worsen with aging, especially in CP populations, the findings of Chapter 4 suggest that changes in spinal deformities remain rather stable during the adult aging period. In addition, and although a relatively large group of adults reported back pain issues the impact of this pain on disabilities levels seems to be relatively low. Although we advocate a conservative approach, surgical interventions might not always be preventable especially in cases of progressive deformity or instability.

OVERALL CONCLUSION

This thesis is the first to provide a comprehensive overview of the level of 'Functioning, Disability, Health and Quality of Life in adults with CP more than 25 years after Selective Dorsal Rhizotomy'. Based on the ICF-model framework we found positive outcomes for adults with CP and spastic diplegia who underwent SDR (strict selection criteria were adhered) in all the domains (*Body Function and Structure, Activity and Participation)* as well as HRQoL.

With respect to the ICF-model ***Body Function and Structure*** domain, adults with CP showed sustained improvement in muscle tone, a gait pattern with minimal spasticity signs, no increased prevalence of scoliosis, hyperkyphosis or hyperlordosis and level of pain that hardly did influence their daily activities. Some challenges were found regarding back pain, passive ROM, muscle strength and selectivity, but they were comparable for what is expected in adults with CP. Spondylolysis and spondylolisthesis appear to occur more often than would be expected in adults with CP, however limited data is available on the natural history of CP and the influence on spinal abnormalities which makes it difficult to distinguish independently the effects of SDR [13].

Concerning, the ***Activity*** domain the majority of the cohort was independent in functional mobility and the accomplishment of daily activities with no increased risk for falls, despite the fact that they reported lower levels of satisfaction with their mobility in comparison to TD adults.

Regarding ***Participation*** domain*,* the adults with CP more than 25 years post-SDR were independent and satisfied with their accomplishment of social roles. Most were married or had a relationship, lived independently (with or without partner), finished higher education and were engaged in paid employment.

The ***health-related quality of life*** was similar to that of TD adults in most of the health concepts (physical role functioning, bodily pain, general health, vitality, social functioning, emotional role functioning and mental health), except for physical functioning. No increased prevalence of anxiety and depression was found, which was in line with the mental health findings of the SF-36. This suggests that while adults with CP have on-going physical

challenges following SDR, this might not directly impact their mental health and levels of anxiety and depression.

The majority of the cohort viewed the SDR they had undergone as worthwhile due to mobility and functional walking gains.

Over a nine-year follow-up period no changes were found in gait, functional mobility, spinal deformities, pain and level of accomplishment and satisfaction in daily activities and participation. This indicates stability of function while aging, which is remarkable since functional decline might be expected.

Correlations were found between functional mobility (FMS) and the level of accomplishment in daily activities and participation as well as between functional mobility and balance (TUG) and muscle strength. This highlights the possible importance of maintaining walking ability and strength training in order to enable daily activities and social participation and prevent functional deterioration in the future.

RECOMMENDATIONS FOR FUTURE RESEARCH

To determine the independent effects of SDR, we ideally would have compared the results of our studies to a 'true' control group. By a true control group, we mean adults with CP and spastic diplegia with the same participant characteristics who did not undergo SDR, but underwent other interventions to improve functional mobility in childhood. Unfortunately, this was not possible within the scope of this PhD thesis. Overall, systematic, large-scale follow-up studies with a true control group, describing the natural history of CP over the life course are lacking and while this data would be very valuable for comparing outcomes of different treatment approaches.

Research on topics related to healthy aging as described in the general population, would also be of interest in this CP cohort. For example, it would be valuable to determine bone mineral density, effect of nutrition deficiency and levels of habitual physical activity and fitness. In addition, studies exploring the correlation of factors related to aging, HRQoL and mental status will add to the growing database of understanding aging with CP and might reveal possible predictors for challenges with healthy aging. In line with this, programs which could support healthy aging should be evaluated.

In addition, intervention studies with the focus on resistance training in adults with CP who underwent SDR in childhood would be of great value. We found a correlation between functional mobility and strength and functional mobility and level of accomplishment in daily activities and participation. However, despite improvements in strength, traditional strength (resistance) training programs for children with CP showed inconclusive evidence for improved walking function [41, 45]. On the other hand, high-velocity resistance training (power training) has shown promising benefits in walking function and gait speed. It would be valuable to further investigate if and which resistance training programs could benefit adults with CP more than 25 years post-SDR to maintain functional mobility.

The studies described in this PhD thesis were performed in South Africa. The findings of this thesis should therefore be interpreted in an African country context. Health care, environment (e.g. government support, accessibility of public spaces) and culture (e.g. coping strategies) are different to those in other continents [46]. In addition, no transition programs are available for children with CP to adult orientated care in Africa [47]. To control for these differences a matched TD group was added to the studies. However, it would be useful to compare outcomes of long-term SDR follow-up studies of adults with CP living in South Africa to different countries that are different socio-culturally, economically and politically.

Strict selection criteria are essential for successful SDR outcomes in children with CP, since SDR is an irreversible procedure that can also negatively influence motor function. While it is clear that a minimum set of selection criteria [48] should be adhered to in order to ensure success, there is a lack of uniformity of these criteria around the world [49], and international consensus for standardized selection criteria might be helpful.

The aging process is also a factor that inevitably interacts with the motor disorder associated with CP. Continuous follow-up remains important to monitor development and challenges during the full life-span of adults with CP after SDR. This will provide the appropriate long-term information which will assist parents of children with spastic diplegia, clinicians and the international community in making evidence-based decisions. In addition, it will help to develop the right management programs in order to support healthy aging, independence and management of new challenges that may arise as well as to inform these adults in the best way possible during their life-course living with CP.

WHAT THIS PHD ADDS TO THE BODY OF KNOWLEDGE ON AGING WITH CP IN ADULTS WHO UNDERWENT SDR IN CHILDHOOD:

- SDR in childhood has a striking and long-lasting effect in normalizing muscle tone well into adulthood if strict selection criteria are adhered
- Adults with CP who underwent SDR in childhood reported good health-related quality of life and the vast majority was satisfied with the SDR treatment
- Levels of anxiety and depression of adults with CP were similar to that of TD adults, and adults with CP were as satisfied with their overall accomplishment of daily activities and participation as their TD peers
- During aging no deterioration was found in functional mobility, gait (GDI) and overall level of accomplishment and satisfaction in daily activities and participation
- Spinal abnormalities did not change further during aging in adulthood and appeared not to result in disability experienced due to back pain.
- A conservative approach with respect to treating spinal abnormalities in adults with CP who underwent SDR in childhood may be appropriate
- During aging small changes were observed in active hip and knee ranges of motion and walking speed
- Strength, selectivity, ROM and functional mobility and balance of adults with CP were poorer than those of TD adults
- Strength appeared to correlate with functional mobility and balance. Functional mobility and balance were on the other hand correlated with level of accomplishment and satisfaction in daily activities and participation
- Management programs which focus on maintaining walking ability and resistance training may prevent functional deterioration and enable daily activities and participation in adults with CP while aging

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