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Adults with Spina bifida –

from health and living conditions to motor-cognitive performance

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ADULTS LIVING WITH SPINA BIFIDA –

FROM HEALTH AND LIVING CONDITIONS TO MOTOR-COGNITIVE PERFORMANCE

THESIS FOR DOCTORAL DEGREE (PhD)

By

Martina Bendt

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ABSTRACT

Spina bifida (SB) is a congenital spinal cord dysfunction often leading to physical, medical and cognitive challenges. The level and extent of the spinal involvement often affects both sensory and motor function and secondary complications are common. There is a knowledge gap regarding adults with SB. The first part of this thesis aimed to describe health and living conditions of adults with SB in different age groups. Also, to identify and describe ambulatory and cognitive function within different levels of muscular function (MF). The second part aimed to describe gait and balance in ambulatory adults and explore motor cognitive performance during walking while performing a cognitive task.

A cross-sectional study was performed on a near-total regional cohort of adults with SB. Participants were consecutively invited and interviews, questionnaires and assessments on physical, medical, social, and cognitive function were performed. A total of 196 participants were included (104 women 53%, 18-73 years, md 33 years [IQR 23]). Those with MF level 3 (hip flexion and knee extension grade 4–5) were further investigated for potential factors associated with ambulation.

In the second part, 41 were included (49% women, 19-59 years, mean 37 [SD 12]) with a regular daily walk distance >30 meters. A sensor-based gait analysis system was used to capture gait characteristics and dynamic balance was assessed with the Mini-BESTest. Motor and cognitive performance as well as the Timed up and go (TUG) was explored in both single task and dual task (DT) condition.

In the total cohort 54% were ambulators and 46% used a wheelchair. Mode of mobility and cognitive capacity varied substantially across the group. A linear association was seen for presence of HC, contractures, and scoliosis with a lower degree of MF. For those with MF level 3 ambulation was independently associated with BMI, scoliosis, and a higher cognitive capacity. The youngest participants had a higher prevalence of HC and tethered cord symptoms, and fewer had passed compulsory school.

For those included in the second part mean gait speed was 0.96 m/s (SD 0.2) and for the MiniBESTest 11 (SD 7). Participants with MF level 3 showed lower results ($p \leq .001$, $p \leq .05$ respectively) and a larger thoracic lateral sway ($p \leq .05$). A DT cost was seen for gait speed (4%). For cognition a small DT cost was seen in accuracy, but no difference was seen in reaction time ($p \leq .05$, $p = .14$ respectively). The largest DT cost was seen for TUG.

Adults with SB have a complex set of physical, medical and cognitive problems that must be addressed to increase health and living conditions. More extensive problems were seen in the younger persons, who will most probably need more interventions in the future. Adults with SB showed a significant DT cost on most of the analysed parameters of gait, possibly indicating a risk of falling. Tailored follow-ups are important to meet the differing needs. The results can improve health and living conditions for adults with SB and contribute to more targeted interventions and better care.

SAMMANFATTNING

Ryggmärgsbråck (RMB) är en medfödd ryggmärgsmissbildning. I nivån med bråcket syns ofta en kotmissbildning, bråcket kan vara öppet eller hudtäckt. Symptomen påverkas av nivån på ryggraden samt storleken på bråcket. Det finns de som har få symptom och de som har många och komplexa symptom av sitt RMB. Vanliga symptom är nedsatt muskelfunktion, felställningar och nedsatt känsel nedom bråcket, men också en påverkan på blås- och tarmfunktionen är vanligt förekommande. Gångförmågan är ofta påverkad, vissa går, några kombinerar att gå med att använda rullstols och andra förflyttar sig endast med rullstol. Det är också vanligt med hydrocephalus och kognitiva nedsättningar som kan påverka inlärningsförmågan och förmågan att hantera sin vardag och de medicinska utmaningarna. som ofta följer med den medfödda ryggmärgsmissbildningen.

Idag är RMB klassad som en sällsynt diagnos i Sverige, då det föds allt färre per år till följd av fosterdiagnostik och folsyraberikning av kosten. Det föds ca 10 personer/år i Sverige och idag överlever ca 75% till vuxen ålder på grund av den medicinska utvecklingen. Jämförelsevis så föddes ca 70 personer/år på 70-talet, och ca 25% nådde 5 års ålder på 60-talet.

Kunskapen kring vuxna med RMB har varit låg och därför var syftet med den här avhandlingen att förbättra kunskapsnivån kring vuxna som lever med RMB. Den första delens syfte var att kartlägga personernas hälsa ,vardagsliv och deras förflyttningsförmåga i relation till muskelfunktion. Den andra delen hade som syfte att identifiera och beskriva gång- och balansförmåga samt den eventuella påverkan som blir då två saker utförs samtidigt, dvs att gå samtidigt som en kognitiv utmaning utfördes (så kallad dual-tasking). I det dagliga livet är det vanligt att man gör två saker samtidigt men hur vuxna personer med RMB påverkas av det är okänt.

En nästan total regional prevalensgrupp med RMB blev tillfrågade om att deltaga i samband med sina ordinarie uppföljningsbesök på Spinalismottagningen, Aleris Rehab Station i Stockholm. Av de 219 som tillfrågades accepterade 196 personer (89%) att delta i den första kartläggande delen. I avhandlingens andra del inkluderades 41 personer varav 34 slutligen var med i analysen av gång med samtidig kognitiv uppgift.

Den första delen genomfördes i nära anslutning till det kliniska arbetet av det multiprofessionella teamet på Spinalismottagningen. Genom intervjuer, frågeformulär och kliniska undersökningar insamlades data kring patienterna. Vi undersökte och dokumenterade gruppens muskelfunktion, känsel, hjälpmedelsbehov, förflyttnings- och gångförmåga, hur deras vardagsliv fungerade, utbildningsnivå, behov av hjälp i vardagen samt medicinska aspekter.

I den andra delen användes ett sensorbaserat ganganalyssystem för att kunna analysera personernas gång i detalj. Sex små sensorer fästes utanpå kläderna som registrerade data om bland annat gånghastighet, steglängd och bålens rörelse under gången. Balansen undersöktes

med ett balanstest, MiniBESTest. För att undersöka gångens eventuella påverkan vid samtidig kognitiv uppgift användes samma gånganalyssystem samt en kognitiv uppgift som patienterna hörde i hörlurar. Båda uppgifterna gjordes först enskilt och därefter i kombination och den eventuella skillnaden räknades ut.

Vi fann att många vuxna med RMB lever med komplexa medicinska, fysiska och kognitiva problem som måste få uppmärksamhet för att kunna förbättra personernas hälsa. Många var överviktiga och ej fysiskt aktiva i sin vardag. I den totala gruppen var hälften gångare och hälften använde sig av rullstol i sin vardag. De med hydrocephalus hade en sämre kognitiv förmåga än de utan. Muskelfunktionen påverkade i hög grad förflyttningsförmågan och för de med en muskelfunktion som innebar i stort sett full funktion i höftböjarna och knästräckarna (MF3), var gångförmågan påverkad av BMI, skolios och kognitiv förmåga. De yngre verkade ha en mer komplex livssituation med flera associerade symptom. Eftersom de som lever med RMB lever längre idag måste framtida uppföljningar troligen i många fall anpassas till ett mer komplext och större behov.

Personer med RMB gick långsammare och med kortare steg än normalbefolkningen och deras balans var nedsatt. Vid dual-task påverkades gången men också hur "rätt" de svarade men inte hur snabbt de svarade. "Svaren var lika snabba men oftare fel". För personer med en muskelfunktion motsvarande MF3 var gången och balansen avsevärt sämre än för de med en bättre muskelfunktion och de uppvisade också en större rörelse av bålen vid gång.

Sammanfattningsvis så skulle den nedsatta balansförmågan i kombination med den försämrade gången vid dual-task kunna öka risken för fall och olyckor. Regelbunden livslång uppföljning är viktigt för att hjälpa dessa personer på bästa sätt och det är viktigt att individualisera uppföljningarna utifrån personernas behov. Ett multiprofessionellt team är önskvärt för att på bästa sätt hjälpa vuxna med RMB med deras multifacetterade problematik.

LIST OF SCIENTIFIC PAPERS

This thesis is based on the following papers, referred to in the text by their Roman numerals.

I. Bendt M*, Gabrielsson H*, Riedel D, Hagman G, Hultling C, Franzén E, Eriksson M, Seiger A.
Adults with spina bifida: A cross-sectional study of health issues and living conditions. Brain Behav. 2020;10(8):e01736. Doi: 10.1002/brb3.1736.
*Shared first authorship.

II. Bendt M, Seiger A, Hagman G, Hultling C, Franzén E, Forslund EB.
Adults with spina bifida: ambulatory performance and cognitive capacity in relation to muscle function. Spinal cord. 2022;60(2):122-8. Doi: 10.1038/s41393-021-00658-w

III. Bendt M, Forslund EB, Hagman G, Hultling C, Seiger A, Franzén E.
Gait and dynamic balance in adults with spina bifida. Gait & posture. 2022;96:343-50. Doi: 10.1016/j.gaitpost.2022.06.016

IV. Bendt M, Forslund EB, Hagman G, Hultling C, Ekman, U, Rydström A, H Johansson, L Bezuidenhout, Seiger A, Franzén E.
A Motor-Cognitive Task in adults with Spina bifida: Dual-Task Effects and patterns of prioritisation.
In manuscript.

CONTENTS

LIST OF ABBREVIATIONS

ADL	Activities of daily living
AFO	Ankle foot orthosis
AS	Auditory Stroop
BMI	Body mass index
CI	Confidence interval
D-KEFS	Delis-Kaplan Executive Function System
DT	Dual task
DTE	Dual task effect
GDPR	General Data Protection Regulation
HC	Hydrocephalus
IQR	Inter quartile range
KAFO	Knee-ankle-foot-orthosis
KI	Karolinska Institutet
MF	Muscle function
MMC	Myelomeningocele
MMCUP	Myelomeningocele follow up programme
NTD	Neural tube defect
OT	Occupational therapist
PT	Physiotherapist
RAVLT	Rey Auditory Verbal Learning test
ROCF	Rey–Osterrieth Complex Figure test
SB	Spina bifida
SCI	Spinal cord injury
SD	Standard deviation
SMO	Supra malleolar orthos
ST	Single task
TMT	Trail making test
WAIS-IV	Wechsler Adult Intelligence Scale, fourth edition

1 INTRODUCTION

This thesis has evolved from the daily clinical work at the Spinalis outpatient clinic, where for many years I have worked as a part of the multi-professional team focusing on the follow-up for adults with Spina bifida (SB). This follow-up has been carried out by the team at the Spinalis outpatient clinic, at Aleris Rehab Station, for over twenty years. The clinic is specialised in spinal cord disorders and has the outpatient responsibility, in the greater Stockholm area, for more than 1,400 patients, of whom almost 250 are adults with SB. This SB prevalence group is unique in Sweden and even in the world. Over the years we, as a team, gradually became aware of the need for another approach for persons with SB compared to those with spinal cord injury (SCI).

I am a physiotherapist (PT), a specialist in neurology, and my master's thesis was titled “Walking in adults with Spina bifida with respect to muscular function” [1]. That project left me with questions and a feeling of a knowledge gap when it came to mobility for this group as well as questions concerning health and daily living. To me it seemed that many of these individuals were severely challenged in their daily life and walked to a greater extent than those with an acquired SCI with a corresponding level of muscular function. Their assistive devices were often not optimised and in need of an update. Many had a high body mass index (BMI) [2] and did not carry out any regular physical activity. They often had a larger need for a team approach. Persons with SB are born with their spinal cord dysfunction and have lived their entire life with their challenges.

We wanted to expand the knowledge about adults with SB from a multi professional perspective. We found that previous research mostly had a focus on children and young adults [3-9] and often a focus on one part of the complex congenital dysfunction and without a holistic perspective. We found some research focusing on adults with SB and their complex life situation [10-16], but however we experienced a research gap.

Therefore, this thesis intended to expand the knowledge of ambulatory function and the potential interplay between gait and cognition as well as the knowledge regarding health and everyday living in adults with SB. All with the intention to improve the support and healthcare for adults with SB.

2 BACKGROUND

2.1 SPINA BIFIDA

Spina bifida (SB) is a congenital neural tube defect (NTD) frequently involving multiple systems in the body [17-21] and requiring multidisciplinary efforts and life-long follow-up [22-24]. Today, SB is considered a rare disorder in Sweden. However, the number of adults living with SB is still increasing since they live longer [25].

Spina bifida can be further subdivided into SB aperta and SB occulta. SB aperta, also termed open SB, including different forms; myelomeningocele (MMC), meningocele, and myelocele, as well as lipomyelomeningocele and lipomeningocele [19, 20].

- MMC is the most common type and is characterised by a dorsal cystic herniation of the spinal cord, meninges, and cerebrospinal fluid. At the level of the hernia the vertebrae has a dorsal defect.
- Meningocele involves protrusion of meninges and cerebrospinal fluid through a spinal defect and normally causes fewer symptoms than MMC.
- Lipomeningocele and lipomyelomeningocele are characterised by lipomatous tissue attached to the spinal cord or filum terminale.
- SB occulta, usually in the lower spinal region, is a malformation of the spine where some of the vertebrae are not fully closed. It is the mildest form of NTD.

2.1.1 Epidemiology and etiology

In Sweden, the incidence of newborns with SB was 6-8:10,000 before 1973 falling to 1.3:10,000 between 2008 - 2015 [22, 26, 27] and is today considered a rare disorder in Sweden [27]. There was a statistically significant ($p<.001$) decline in incidence between 1999 and 2016 [28].

There are international reports suggesting that provision of folic acid to women could reduce the risk of NTD [19, 21, 29]. Genetic factors are also of importance, as individuals with SB are more likely to have a child with SB [21, 30].

The frequency of reported children reported born with neural tube defects and foetuses with NTD has been studied in Sweden since 1999, when interrupted pregnancies based on this malformation also began to be registered on a national level [28]. Today the decline of children born with SB in Sweden appears to reflect an actual decreasing risk for this group of serious birth defects and cannot solely be explained by improved prenatal diagnosis.

Although fewer children are born with SB in Sweden, the prevalence group, of about 1,400 individuals [27] is not decreasing due to increasing life expectancy resulting from improved medical treatments [23]. Today 75% of those born with SB reach adulthood [31] compared to the 1960s, when only 20-25% reached the age of five [23]. However, in a study by Oakshott et al. [32] the mortality rate in those between 5 to 40-years-old was ten times the national average, and often sudden and unexpected.

2.1.2 Impaired motor and sensory function

Depending on the extent and level of spinal involvement, SB often leads to both impaired motor and sensory function below the malformation [20]. This leads to partial or complete paralysis often affecting ambulatory function and a muscular imbalance around the affected joints and/or partial or complete sensory loss that heightens the risk of pressure sores [20, 24].

2.1.3 Mode of mobility

Mobility is an important prerequisite for participation in the community and enables ways to be physical active and healthy [33]. For persons with SB mode of mobility is closely related to the neurological level and level of motor impairment [34-37]. Long-term functional outcomes in SB are difficult to predict as they are affected by many different factors; age, contractures, motivation, physical activity, body mass index (BMI), and cognitive status [33, 38]. Different modes of mobility are used [39], ranging from walking with or without orthoses and assistive devices, to the use of a manual or powered wheelchair [35, 40].

Ambulatory impairment is frequent in this population. In this thesis ambulation refers to the ability to walk [41] in line with the classification by Hoffer et al [33, 42]. Independent ambulation is strongly associated with the level of spinal involvement even though there are other factors of importance for ambulation as mentioned above. During childhood, persons with SB are provided a thorough multidisciplinary team approach with the intention to improve ambulatory function, prevent scoliosis and contractures and to improve health and performance of daily activities related to ambulation such as standing, transfers and walking [43].

From a clinical perspective ambulation has positive effects on contractures, cardiovascular status, and facilitates self-care, pressure relief and independent transfers [37]. Ambulation is therefore important for health, participation and living conditions. Ambulation into adulthood is common in persons with SB low lumbar SB while those with high lumbar SB often cease walking. Persons with a mid-lumbar SB often combine walking with wheelchair use [4, 23, 37, 39].

For many persons with SB assistive devices like orthoses and walking aids are important to facilitate, enable and improve ambulation [44, 45]. Orthoses, such as the most commonly used ankle-foot orthoses (AFOs), are used to avoid musculoskeletal deformities, protect the feet and improve gait and thereby decrease energy cost of walking [45]. Other orthoses commonly used are supra malleolar orthoses (SMO) and knee-ankle-foot-orthoses (KAFO) either open or locked. In many cases also insoles and orthopaedic shoes are also used. A review by Ivanyi et al. [45] concluded that both AFOs and crutches had beneficial effects for gait characteristics as well as on the oxygen cost of walking.

Both manual and powered wheelchairs are used for mobility. In some cases, a wheelchair is used as a complement and in some cases as the only way for mobility. A powered wheelchair is sometimes used for longer transfers in combination with both ambulation and an active manual wheelchair and sometimes as the only assistive device.

2.1.4 Gait and Balance

Gait abnormalities are common in individuals with SB leading to a characteristic movement pattern [46, 47], with an increased thoracic lateral sway, thoracic rotation, and pelvic movements. Also, a stance phase with flexed knees as a consequence of weakness of hip abductor and gluteal muscles, and ancle plantar and dorsal flexor muscles [3, 46, 47]. The hip abductor weakness contributes most to this typical pattern [47]. For children and adolescents there are several studies analysing and describing this gait characteristic [3, 4, 46-49] but only one study characterising gait in adults [50], focusing on adults over 50 years.

Balance in ambulatory children with high sacral level SB has been found to be affected, mainly due to weakness of the plantar and dorsal flexor muscles [51]. No study has to our knowledge analysed balance performance in adults with SB.

Both independent gait and dynamic balance are complex activities requiring cognitive input affected by neuropsychological capacity and complex interactions by the spinal cord and the brain [52-54]. Both are also dependent on postural control, the ability to stabilise body position [51], motor control and proprioceptive, visual and vestibular information [55]. Therefore, in this thesis they are discussed together, according to the model of balance control suggested by Horak et al [56], illustrated in Figure 1.

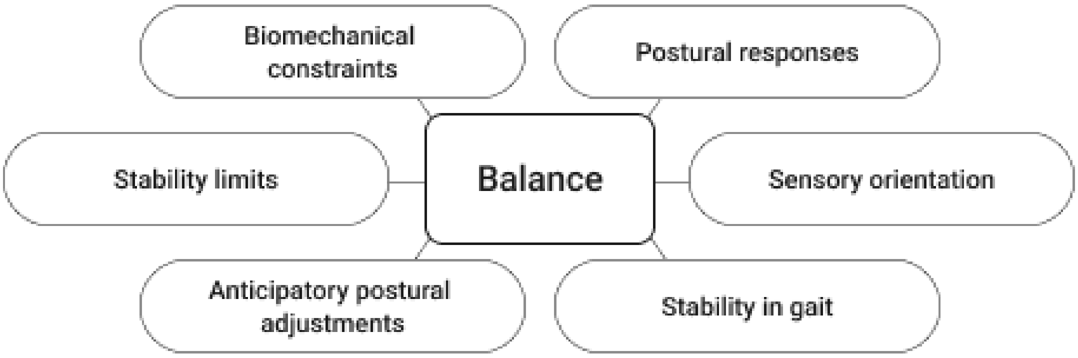


Figure 1. Subdomains of balance control according to Horak et al [56].

- Biomechanical constraints. Limits such as muscle weakness in lower limbs, as well as flexed posture. Leading to compensatory steps, and the use of ankle strategy for balance recovering.
- Postural responses. Adjustments in movement in response to pushes.
- Sensory orientation. Ability to process sensory information.
- Stability in gait. Stability during gait, involving dynamic control and challenges by speed or obstacles as well as cognitive control.
- Anticipatory postural adjustments. Small adjustments in posture prior to a movement.
- Stability limits. Movement of centre of mass, leading to body tilt or inflexible postural alignment.

2.1.5 Cognitive impairments

The neurocognitive pattern associated with open SB is highly variable [20] and often have an impact on everyday activities, participation, educational achievement and also the ability to take responsibility for medical complications [57, 58]. Cognitive impairments affecting executive function, time management, timing and prospective memory are common [16, 59-62].

Executive functions are crucial to most daily activities and affect the experience of problems [65], everyday life, and handling social interactions [64, 66]. Executive function is important for creativity, flexibility, self-control, discipline and unexpected challenges; as well as resisting temptations and staying focused [63, 64], to think before acting.

Cognitive difficulties, in persons with SB, usually become more evident during adolescence and adulthood, when demands for independence increase, with responsibility for housing, higher education, work, and relationships [67].

Individuals with other SB subtypes (other than open SB) often lack the neuroanatomical development associated with open SB and most often have more normal cognitive development [68, 69].

2.1.6 Other Spina bifida related complications

2.1.6.1 Brain related

Higher lesion levels are correlated with more complex malformations of the brain and higher levels of intellectual disability [68].

Most individuals born with open SB/MMC develop hydrocephalus (HC). Almost all with a thoracic level of lesion require a shunt, compared to lumbar (85%) and sacral level lesion (70%) [70]. HC associated negatively with cognitive function and in that way influences independence in everyday life [25, 59, 67, 69, 71, 72].

Migration abnormalities of the central nervous system are also common, as well as syringomyelia (a fluid-filled cyst in the spinal cord) and Chiari II malformation [20, 73-75]. The latter is located at the lower back part of the brain, often leading to a herniation of the cerebellum down through the foramen magnum. Chiari II affects up to 30% of individuals with SB [20] and can manifest as aspirations, apnoea, neck pain, and weakness or altered sensation in the arms [30].

2.1.6.2 Bladder and bowel

Most adults with SB have, as a consequence of the impaired neurology, a need for urological care and functional bowel management [76, 77]. A neurogenic bladder often implies voiding difficulties, recurrent urinary tract infections and risk of renal dysfunction [77, 78]. The bowel dysfunction often causes constipation and/or faecal incontinence [79]. Bladder and bowel incontinence problems are reported by over 50% [79].

A structured, customised programme for follow-up is necessary to improve health status by reducing urinary leakage, infections, renal deterioration and avoiding constipation and faecal leakage [37, 80].

2.1.7 Secondary complications

Secondary complications are to some extent preventable if they are treated in time. Such complications from SB are seen in many systems of the body; musculoskeletal related, overweight, pain, and pressure ulcers [17, 81], and affect health and the person's level of activity and participation. Secondary complications, although preventable, are unfortunately frequent causes of death in adults with SB [23, 82, 83].

Compared to the general population overweight and obesity are more frequent in persons with SB [84]. Overweight and obesity are negatively associated metabolic syndrome, cardiovascular disease, and type II diabetes [85]. All contributing to negative health outcomes. Overweight might also affect the ability to move and thereby impose the risk of an inactive lifestyle [14] and also increase the risk of pressure ulcers [86].

Tethered cord syndrome is frequently reported in people with SB, both in childhood during the growth spurt of adolescence, and in adulthood, often leading to sensory and motor changes, pain, and deterioration of bowel and bladder function [87].

Further, contractures in the lower limbs and hip dislocations (associated with muscular imbalance) are secondary complications affecting ambulation and thereby also health and living conditions. Scoliosis and kyphosis are secondary orthopaedic abnormalities associated with more severe deformities of the spinal cord [20, 37].

2.1.8 Living conditions

Today, adults with SB live longer but as they have a variety of physical disabilities, health and cognitive impairments their living conditions differ. This affects activities and social participation and affect their chance of being employed and live independently [11, 88]. To access services and utilise emergency and inpatient healthcare can be a challenge [11]. Demanding environments with broken elevators and unreliable transportation are daily challenges for many, giving a feeling of poorer prerequisites for social participation [89]. Altogether many adults with SB have major challenges for a healthy, independent, and productive life [11, 88].

2.1.9 Follow-up programmes

Adults with SB have a continued need for follow-up of their complex medical and psychosocial problems [37, 90, 91]. A multidisciplinary approach focusing on both physical impairments and cognitive disabilities is necessary for this group, in order to prevent and treat secondary complications [18, 21, 37, 91, 92]. Bakketun et al. [92] concluded that multidisciplinary follow-up is crucial for "*optimal function, satisfaction with life, and for long-term survival*". Unfortunately, only a minority of the adults with SB are offered continued regular follow-up like that for children and adolescents with SB [32, 90, 92]. Consequently, many lose contact with healthcare providers with knowledge about this rare condition [11].

2.2 DUAL TASK AND RELATED TERMINOLOGY

Activities in daily life often require that attention is assigned to multiple tasks simultaneously ("dual" or "multi-tasking"), such as walking around a grocery store full of people while trying to remember what to buy or walking across a street when there are multiple distractions (traffic, children, mobile phones).

As a consequence of a neurological disorder, performing two or more tasks simultaneously can be more challenging since each task needs more attention. Thereby combining tasks may give a functional compromise [93-95]. Assessing dual task (DT) performance during gait in populations with neurological dysfunction has revealed walking difficulties that are not present during ordinary walking, single task (ST) gait [96-98]. Problems targeting both tasks or prioritising tasks may have serious consequences such as falls and injuries [99]. Also, if handling two things at once is a challenge, this can have an impact on autonomy in daily life.

This thesis uses the definition of DT by McIsaac et al. [93] as *"The concurrent performance of two tasks that can be performed independently, measured separately and have distinct, goals".* The DT can be motor-motor, motor-cognitive or cognitive-cognitive as long as the tasks are performed simultaneously and have individual goals [93]. The tasks are also performed as ST and the difference between DT and ST performance is the DT effect (DTE).

Plummer et al. [100] have described different results of the motor-cognitive performance in DT as compared to ST as a model [101], Figure 2 shows a modified version. Depending on where in the model the DTE (expressed in percent) is located, it can be interpreted as a DT cost or a DT benefit, and if one task was prioritised over the other, a posture-second or a posture-first strategy. If there is a prioritisation for one of the tasks it may have a clinical implication and give an indication of which task to prioritise in rehabilitation. It is believed that individuals may be able to control which task to prioritise [104].

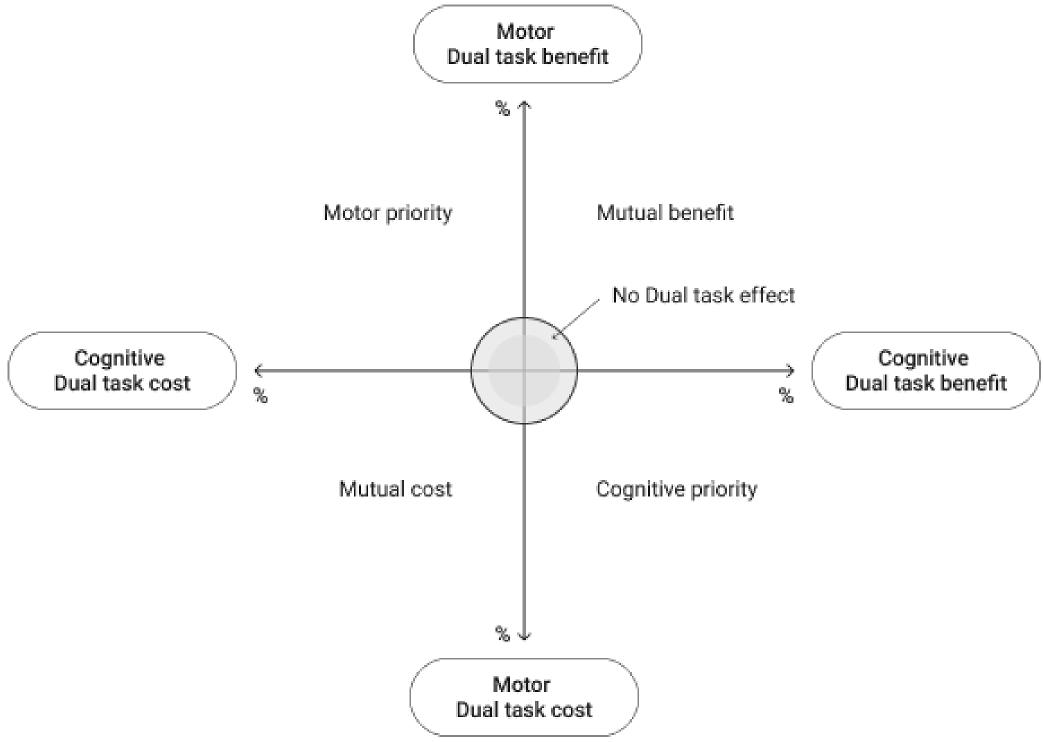


Figure 2. Presents different results of motor-cognitive performance. Figure modified from Plummer et al. [102] and the thesis by H Johansson [103].

It is well known that adults with SB have impaired gait function [1, 34, 38, 39, 47] and that cognitive impairments are common [16, 60], but how gait and balance are affected by simultaneous cognitive activity in persons with SB is unexplored. The impact of DT on both the ambulatory function and cognition in adults with SB is therefore also unexplored.

2.3 THEORETICAL CONSIDERATIONS

This thesis used a multi-professional approach and, a holistic perspective when describing adults with SB. The International Classification of Functioning, Disability and Health (ICF) [105], is a relevant framework to understand the health and living conditions for adults with SB. The ICF framework considers health to be influenced by different factors such as *Body Structure and Function (*physiology and anatomy), *Activity* (how a task or an action is executed) and *Participation* (involvement in life situations) and has also included *Contextual factors* (environmental and personal). For adults with SB all these factors are important and are considered in this thesis.

The last part of the thesis analyses gait and uses the biomechanical model of gait, the framework by Horak et al. [56] and also the theories of DT by Plummer et al. [100].

2.4 RATIONALE

This thesis has a close connection to the daily clinical work and describes the adult persons living with SB in the greater Stockholm area. We found that there was a lack of knowledge of the growing adult population living with this rare complex congenital disorder with multiple and severe medical needs, regarding such things as motor function, mode of mobility, gait and dynamic balance, as well as cognitive function, health, and daily life.

This thesis contributes to increased knowledge regarding this heterogeneous adult population, increased quality of life and the care for this population. Increased knowledge can lead to targeted interventions and better care, thereby reducing secondary complications, increasing health and living conditions for persons with SB and lowering costs for society. The possible interaction between cognitive function and physical factors associated with muscle function and learning more about dual-task ability in adults with SB can provide us with new insights into their physical performance, activity, and participation. Also, in can facilitate rehabilitation programmes and provide a better follow-up structure and improve the care of adults with SB.

3 RESEARCH AIMS

The overall aim of the first part of this thesis, Part I, was to describe the health and living conditions for adults with SB, and also to identify and describe ambulatory and cognitive function with different levels of MF. In the second part of the thesis, Part II we further aimed to describe spatiotemporal gait parameters and balance performance in ambulatory adults with SB and to explore motor cognitive DTE and potential differences in patterns of prioritisation according to gait speed and level of cognitive functioning.

3.1 SPECIFIC AIMS

Paper I

Describe health issues and living conditions in a cohort of adults living with SB.

Paper II

Describe and compare ambulatory performance and cognitive capacity in relation to MF in an adult cohort with SB. A second aim was to explore factors associated with ambulation in adults with MF level 3.

Paper III

Describe gait and balance performance in adults with SB, with focus on spatiotemporal gait parameters and secondly to characterise these parameters in adults with MF3.

Paper IV

Explore DTE, and potential patterns and differences in prioritisation with regards to gait and cognition in adults with SB.

4 MATERIAL AND METHODS

This thesis consists of two parts (data collections), Part 1 described in Papers I and II and Part 2 described in Papers III and IV. An overview of design, methods and the study population for Papers I-IV is found in Table 1.

Table 1. Overview of design, methods, and study population for the included papers.

	Paper I	**Paper II**	**Paper III**	**Paper IV**
Design	Cross-sectional population based design with a multiprofessional perspective.	Cross-sectional population based design.	Cross-sectional design.	Cross-sectional experimental design with observational and explorative elevmets included.
Data collection	Structured interviews based on questionnaires and clinical assessments.	Structured interviews based on questionnaires and clinical assessments.	Structured interviews based on questionnaires and clinical assessments and an instrumented gait analysis.	Structured interviews based on questionnaires and clinical assessments, an instrumented gait analysis and laboratory assessments.
Setting	Specialised outpatient clinic (Aleris Rehab Station in Stockholm, Sweden) for persons with spinal cord dysfunction, the Spinalis outpatient clinic.	Specialised outpatient clinic (Aleris Rehab Station in Stockholm, Sweden) for persons with spinal cord dysfunction, the Spinalis outpatient clinic.	Specialised outpatient clinic (Aleris Rehab Station in Stockholm, Sweden) for persons with spinal cord dysfunction, the Spinalis outpatient clinic.	Specialised outpatient clinic (Aleris Rehab Station in Stockholm, Sweden) for persons with spinal cord dysfunction, the Spinalis outpatient clinic.
Data analysis*	Descriptive, inferential.	Descriptive, inferential.	Descriptive, inferential.	Descriptive, inferential.
Outcome Measures	Presented according to different age groups as recommended by Devivo et al [106]; 18-30 years, 31-45 years, 46-60 years and ≥61 years to illustrate differences by age. For the cognitive subtests results are also presented for participants with and without HC.	Presented according to levels of MF (MF0 – MF5) as the aim of the paper was to describe and compare ambulatory performance and cognitive capacity in relation to level of MF.	Presented according to levels of MF (MF1, MF2 and MF3).	Presented divided into those included in the DTE analysis and those not included in the DTE analysis.
Study population				
Participants, n	196	196	41	41
Sex, Women (%)	53%	53%	49%	49%
Age, mean (SD)	33 (23) **	33 (23) **	37 (12)	37 (12)
- Min-max	18-71	18-71	19-59	19-59
Length/height (cm), mean (SD	158 (14)	158 (14)	162 (10)	162 (10)
- Min-max	120-193	120-193	141-185	141-185
Weight (kg), mean (SD)	67 (25) **	67 (25) **	68 (32) **	68 (32) **
- Min-max	34-155	34-155	47-145	47-145
BMI, Md (IQR)	27 (8)	27 (8)	27 (8)	27 (8)
Min-max	16-59	16-59	19-44	19-44

* For detailed information on the descriptive and statistical methods applied across Paper I-IV see Table 5. ** Presented with md, IQR.

4.1 STUDY DESIGN

The design of Part 1 was elaborated by the multi professional team (including PT, Occupational therapist (OT), Nurse, Social Worker, and a Neurologist) in close collaboration with the Research and Development Unit at Aleris Rehab Station. It was important to include the whole team in this part to ensure a holistic approach to health issues and living conditions.

The design of Part 2 was based on an idea by the main supervisor and the development of the design and experimental set-up were made by the doctoral student in collaboration with supervisors and co-authors.

4.2 PARTICIPANTS

In Part 1, all adults with SB attending the Spinalis outpatient clinic (n=219) were consecutively invited to participate in conjunction with their regular follow-up visit at the clinic. In Part 2, those matching the criteria from Part 1 were asked to participate. In addition, individuals attending the Spinalis outpatient clinic after the data collection for Part 1 were screened for the inclusion criteria at the time of their scheduled follow-up (or at their first attendance at the clinic). The inclusion criteria for Part 2 were adults with SB (age 18 - 65 years), regularly walking a minimum of 30 metres (community or household ambulators as defined by Hoffer et al. [22]) with a level of MF 1 to 3 [38]. As in Part 2 wanted to explore motor cognitive DT effect in adults with SB we had 65 years as a limit to avoid age- related changes in cognition [107]. Flow charts of eligible and the finally included participants in Parts 1 and 2 is presented in Figure 3a and 3b.

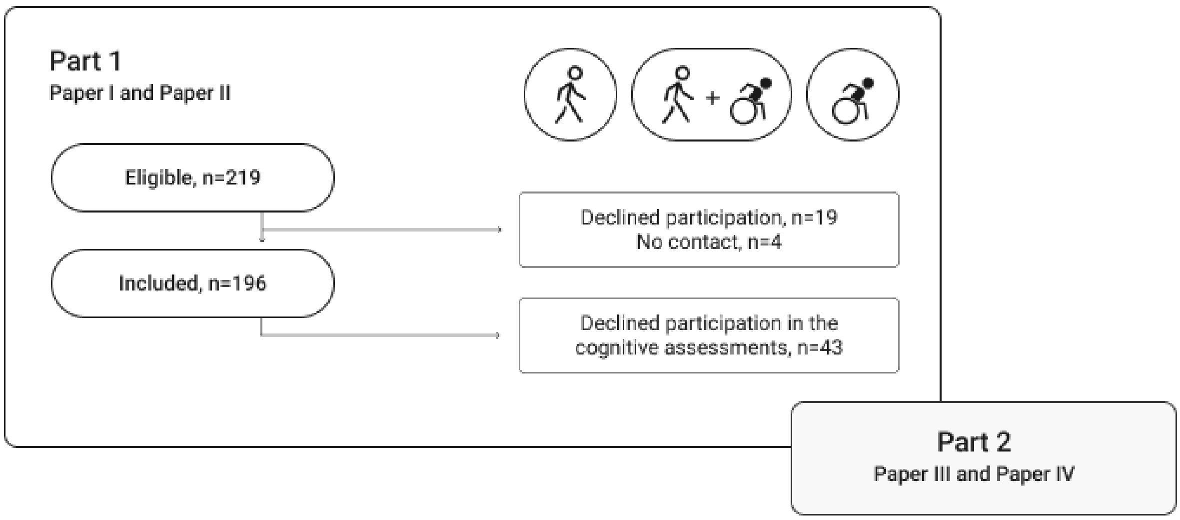
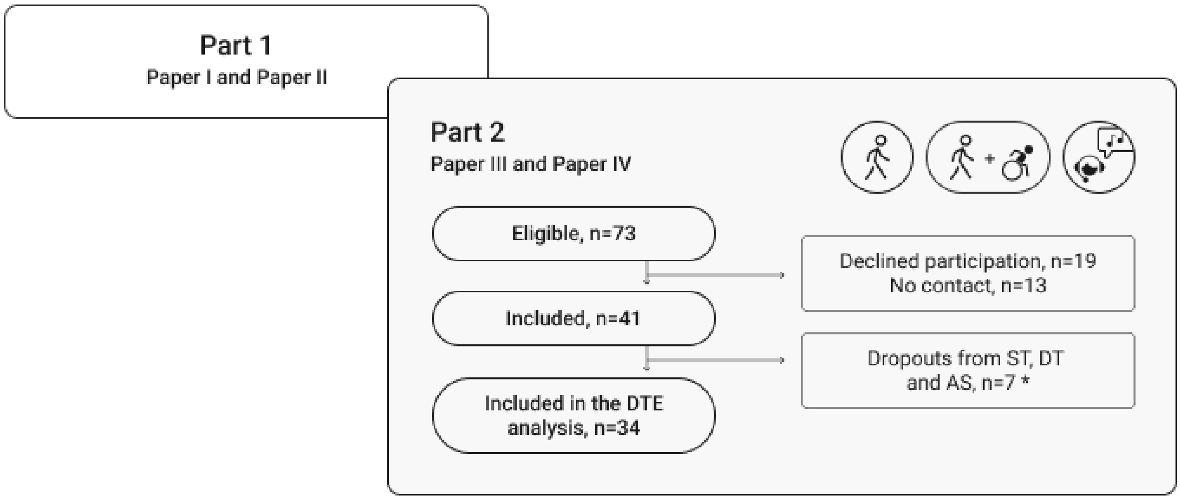


Figure 3a. Flow chart of eligible and ultimately included participants in Part 1.



Abbreviations: single task (ST), dual task, (DT), audio Stroop (AS), dual task effect (DTE). * One participant was excluded from the DTE analysis as the gait analysis system did not register enough gait cycles in ST. Further six participants were excluded from the DTE analysis as they did not manage to perform the AS (had <60% accurate answers in most cases they did not answer the pitch in the DT situation but the word) for four of those the gait analysis system did not register enough gait cycles in DT.

Figure 3b. Flow chart of eligible and ultimately included participants in Part 2.

4.3 DATA COLLECTION

Both in Part 1 and Part 2 data were collected through individual face-to-face sessions with semi-structured interviews as well as clinical and cognitive assessments. Questionnaires were used to guide the sessions and comprehensive databases were constructed including all collected data; patient-reported data (verified by control questions), objective data and data collected with clinical assessments. The medical records were used to confirm some data (related to medical issues, for example type of SB) including records from the children's hospital and paper records depending on availability. In Part 2 an instrumented gait analysis with and without a concurrent cognitive task, the auditory Stroop (AS), was performed.

In Part 1, data were collected by a PT, a Nurse and a OT (all with over 10 years of experience of working with adults with SB). Data collections were performed on two occasions to prevent fatigue. The cognitive assessments were performed at the second occasion. No significant differences were seen in age, sex, prevalence of hydrocephalus, muscle or ambulatory function between those persons who participated in the cognitive assessment and those who declined.

In Part 2 data were collected on one occasion by a PT and the cognitive assessments were performed by a Neuropsychologist or a Psychologist. An overview of both self-rated, clinically assessed outcome measures and instruments, for both Parts 1 and 2 (Papers I - IV) are presented in Table 2.

Table 2. Overview of outcomes reported in paper I – IV.

Outcome	Instrument	Paper			
Demographic		I	II	III	IV
Age	Interview (years).	●	●	●	●
Sex	Interview (women, men).	●	●	●	●
Length/height	Assessment (cm).	●	●	●	●
Weight	Assessment (kg). Standing or in a wheelchair.	●	●	●	●
Type of SB	Interview, medical record (MMC, Lipomeningocele, SB occulta).	●	●	●	●
Structural characteristics					
Hydrocephalus - Shunt, >2 revisions	Interview, medical record. Interview, medical record.	● ●	●	●	●
Muscle strength	Assessment, motor score, 0–5 graded scale [108].	●	●	●	●
Motor function	AIS [109, 110].	●	●	●	●
Sensory function	Light touch (ISNCSCI) [109, 110]	●	●	●	●
Bladder symptoms	Interview, medical record. NSCIR (method, voiding frequency, continence, use of incontinence pads, size, complications) [111].	●			
Bowel symptoms	Interview, medical record. NSCIR (method, frequency, continence, use of incontinence pads, size, complications) [111].	●			
Secondary complications					
- Pressure ulcer	Assessment (on examination day, presence and location).	●			
- Pain	Interview (on examination day and location). (Part1). ISCOS pain questionnaire (Part 2) [112].	●	●	● ●	
- Sleep pattern	Basic Nordic Sleep Questionnaire [113].	●			
- Ortopedic surgery related to SB	Interview, medical record.	●			
- Tethered cord symptoms	Interview, medical record (earlier in life and/or last year).	●		●	
Spine characteristics	Inspection, medical record (scoliosis, kyphosis, spine surgery).		●		
Contractures in lower limbs	Assessment [114] , goniometer (> 20 degrees in hip, knee or > 15 degrees ankle joints (including ankle arthrodesis)).	●	●	●	●
Use of prothesis	Inspection.		●		
Functional characteristics					
Mode of mobility	Community, household, non-functional ambulation or non-ambulators [42].	●	●	●	●
Spatial and temporal gait characteristics	Mobility lab (Opal, APDM Inc.) [115].			●	●
Dynamic balance	Mini-BESTest [116].			●	
Functional mobility	Timed up and go (TUG) and TUGcog [117].				●
Maximal walking distance	Interview with control questions. >1000 m, ≤1000 m, ≤100 m, ≤10 m, 0 m.		●	●	
Falls					
- Fear of falling	Interview.			●	
- Falls last year	Interview.			●	
- Concerns	Falls Efficacy Scale International (FES-I) [118, 119].			●	
Transfers	Assessment. Chair/wheelchair to bed. Independent, with support or with lift.	●			
Dexterity	Nine-Hole Peg Test [120].	●			
Hand strength	Grippit [121].	●			
Assistive devices					
Walking aids	Interview, inspection.	●	●	●	●
Orthoses	Insole, SMO, AFO, KAFO (open or closed), prosthesis.	●	●	●	●
Wheelchair	Interview. Manual/powered or both manual and powered.	●	●		
Cognitive function					
Psychomotor speed and executive functioning	- Coding test [122] (number of symbols in 120 s). - TMTa. (trail making test, number-sequencing) [123]. - TMTb (trail making test, number-letter switching conditions) [123].	●	●		● ● ●
Spatial visualisation and motor skill	Block Design test [122].	●	●		●
Episodic memory test	- RAVLT Learning (Rey auditory verbal learning test, words learned over 5 trials) [124]. - RAVLT Delayed (words recalled after 30inutes delay) .				● ●

	- ROCF Copy (non-verbal Rey–Osterrieth complex figure test) [125]. - ROCF Delayed Recall.				● ●
Verbal executive ability, mental speed	- FAS (verbal fluency test from the Delis-Kaplan executive function system (D-KEFS) test battery [123]. - The vocabulary subtest from Wechsler adult intelligence scale® fourth edition (WAIS-IV) [122].	●	●		● ●
Verbal reasoning	Similarities test (similarities correctly explained) [122].				●
Non-verbal problem solving	Matrix reasoning test [122].				●
Cognitive task	Assessment. Auditory Stroop test [126].				●
Medical characteristics					
Epilepsy	Interview, medical record.	●			
Blood pressure	Assessment. (nmHg).	●			
Latex allergy	Interview, medical record.	●			
Drug treatment	Interview, medical record.	●			
Psychological diagnoses	Interview, medical record. Depression, anxiety and intellectual disability.	●			
Neuro-psychiatric diagnoses	Interview, medical record. Asperger syndrome, attention deficit disorder, attention deficit hyperactivity disorder.	●			
Social independence, Support and Activities					
Housing and adjustments	Interview.	●			
Biological children	Interview.	●			
Main occupation	Interview.	●			
Grades in compulsory school*	Interview.	●			
Driver's license	Interview.	●			
Level of independence	FIM, the motor function part [127].	●			
Independence, support in daily life	Interview. Personal care, household activities, and/ or reminders.	●			
Finances	Interview (supply and guidance).	●			
Assistance provider	Interview. Municipality/state and/ or family members.	●			
Alternative healthcare providers	Interview.	●			
Transportation services	Interview.	●			
Weekly physical exercise habits	Interview. Categorised as no physical exercise, moderate exercise (minimum 30 min, 1–2 times per week) and vigorous physical exercise (minimum 30 minutes at least three times weekly). This was also verified by the assessors via control questions about their exercise regimes.	●	●		
Physical activity in daily life	Questionnaire. Frändin & Grimby [128].			●	

* Height in standing position or length (for those not able to stand) in the prone position (from joint to joint in the event of contractures. ** In Sweden, usually obtained at age 16 years after 9 years of school.

4.3.1 Clinical assessments

Functional ambulation was registred according to the criteria by Hoffer et al. [1, 33, 38, 42, 129].

- *Community ambulators:* Walking both in- and outdoors, may use crutches and/or orthoses. Wheelchair only for long trips (or not at all).
- *Household ambulators:* Walking indoors with assistive devices. Wheelchair for some indoors activities and for all activities in the community.
- *Non-functional ambulators:* Walking only in therapy. Wheelchair for all activities of daily living (ADL) activities.
- *Non-ambulators:* Wheelchair use for mobility.

In Paper 2 (for the secondary aim) participants were dichotomised to either ambulators (community or household ambulators) or wheelchair users (including non-functional ambulators).

This thesis uses the classification according to levels of muscle function (MF), MF1 to MF5 by Bartonek et al. [38], Table 3. Based on bilateral manual muscle examination according to the criteria by Hislop [108] participants' different levels of muscular function [38] were determined. An additional level of MF was used for those with no muscular impairments in the lower limbs, MF 0 [1]. For participants with an asymmetric motor function the most severely impaired side was used for classification [130, 131].

Table 3. Levels of muscle function (MF) 1 – 5, according to Bartonek et al. [38].

MF 1	Weakness of foot intrinsic muscles. Good-to-normal plantar flexors, grade 4–5.
MF 2	Fair or less plantar flexion, grade ≤3. Fair or better knee flexion grade ≥3. Poor to fair or better hip extension and/or hip abduction, grade ≤2–3.
MF 3	Good to normal hip flexion and knee extension, grade 4–5. Fair or less knee flexion, grade ≤3. Traces of hip extension, hip abduction and below knee muscles.
MF 4	No knee extension activity. Poor or less hip flexion, grade ≤2. Fair or good pelvic elevation, grade 2-4.
MF 5	No muscle activity in the lower limbs. No pelvic elevation.

According to the level of MF community ambulators were expected to be graded as MF levels 1 and 2, household ambulators levels 3 and 4 and non-functional ambulators as level 5 [38, 42].

The neurological level of the spinal cord impairment is in this thesis based on clinical examination of both motor and sensory function according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) [109, 110]. This is the most common classification of neurological level and completeness of the spinal cord impairment for persons with SCI. The motor level of impairment is established based on ten key muscle groups and the sensory level from a dermatome map with 23 levels on each side (Figure 4). The most caudal level with intact motor and sensory function is "the neurological level of injury". The extent of the spinal cord impairment is graded according to the classifications by the American Spinal Cord Injury Association (ASIA) Impairment scale (AIS) from A – E, Table 4.

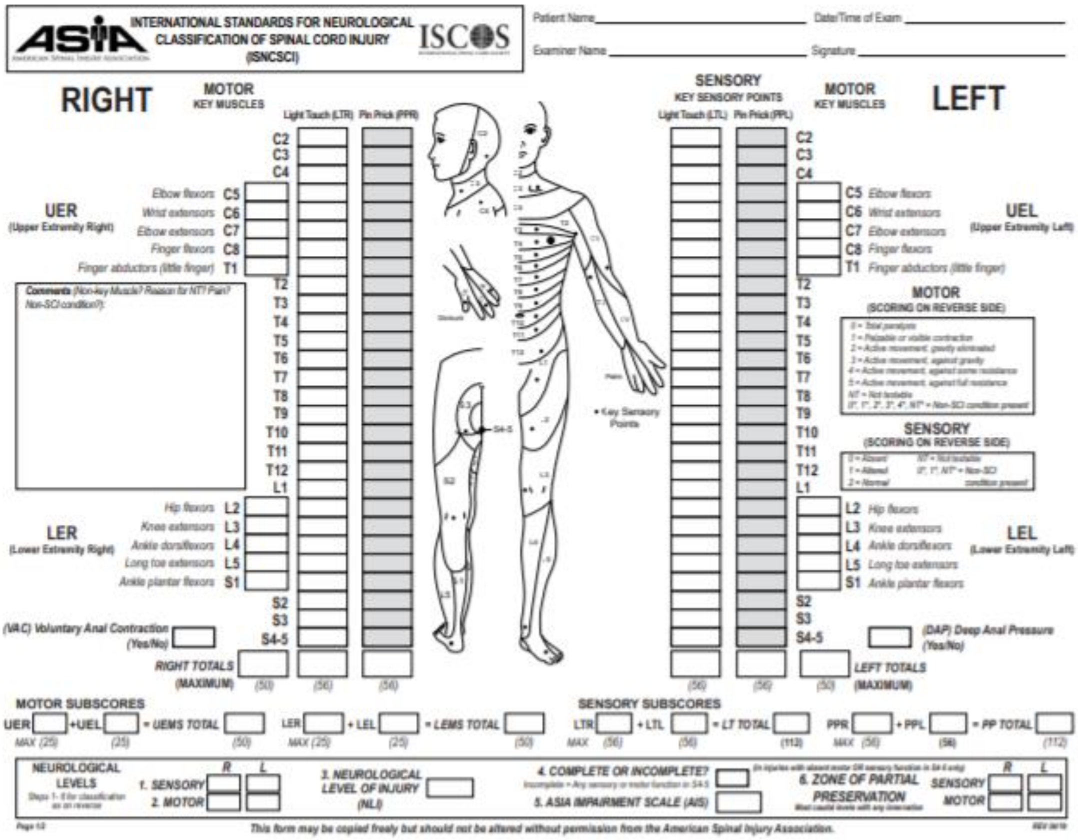


Figure 4. Worksheet according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) [132].

Table 4. Classification of the extent of SCI according to ASIA Impairment scale [109, 110].

A	Complete	No sensory or motor function is preserved in the sacral segments S4-5.
B	Sensory Incomplete	Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-5 (light touch or pin prick at S4-5 or deep anal pressure) AND no motor function is preserved more than three levels below the motor level on either side of the body.
C	Motor Incomplete	Motor function is preserved at the most caudal sacral segments for voluntary anal contraction (VAC) OR the patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segments S4-5 by LT, PP or DAP), and has some sparing of motor function more than three levels below the ipsilateral motor level on either side of the body. (This includes key or non-key muscle functions to determine motor incomplete status.) For AIS C – less than half of key muscle functions below the single NLI have a muscle grade ≥ 3.
D	Motor Incomplete	Motor incomplete status as defined above, with at least half (half or more) of key muscle functions below the single NLI having a muscle grade ≥ 3.
E	Normal	Sensory and motor functions are normal.

Dynamic balance was assessed with the Mini-BESTest [116], based on the framework by Horak et al. [56]. The instrument has been tested for validity and reliability for persons with SCI (similar neurological prerequisites) [133] and persons with multiple sclerosis [134] (similar neurologic dysfunction and balance related problems).

The last item on the Mini-BESTest, the Timed Up and Go (TUG) with dual task (TUGcog), i.e., TUG while counting backwards by threes was used as a separate outcome. As a DT outcome with a more clinical approach.

4.3.1.1 Cognitive assessment

A neuropsychological test battery was constructed to assess different cognitive domains. The included tests are frequently used in clinical practice to assess cognitive function in patients with different neurological disorders such as multiple sclerosis, Parkinson's disease, stroke as well as traumatic brain injury and Alzheimer's disease [135].

The test battery consisted of episodic memory tests, verbal ability tests, test for cognitive processing speed and executive function. Also tests for attention and visuomotor processing, speed verbal reasoning, non-verbal problem solving, and visuospatial construction abilities were included. See Table 2 for the specific tests.

4.3.1.2 Gait analysis

Spatial and temporal gait parameters were collected with a sensor-based motion analysis system (Opal, APDM Inc.) [115] and Mobility Lab™ software was used for analysis [136]. The normative material provided by the Mobility Lab, based on a total of 70 subjects (20-90 years old 10 subjects/decade, 5 men, 5 women) was used in the analysis [137]. Six sensors were used and placed via elastic straps as in Figure 5.

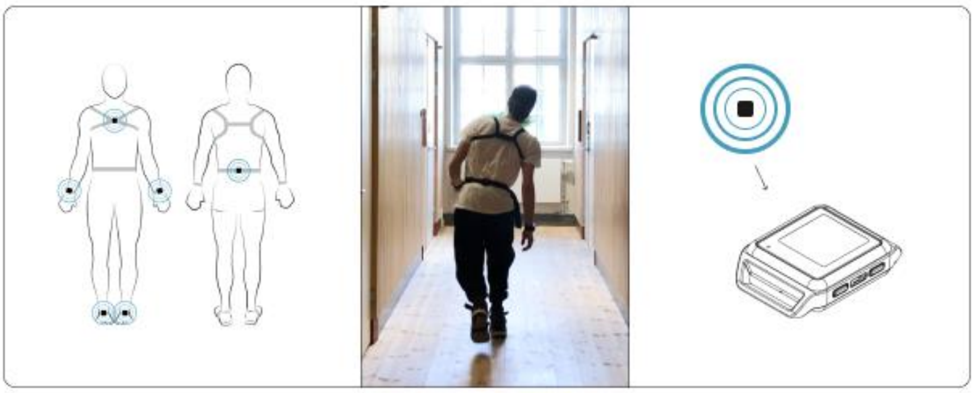


Figure 5. From left to right the Opal sensor placements, a walking participant and an Opal sensor.

The sensors collect gyroscope and accelerometer data that are wirelessly transferred to a computer where temporal and spatial gait parameters are calculated (from the total number of registered gait cycles) and pre-analysed in Mobility Lab.

Participants walked in a comfortable self-selected gait speed in a straight corridor of 12 metres. At the end of each side of the corridor there was a cone that the participants walked around. An average of the trials was used in the statistical analysis (for those with muscular asymmetry, the most affected side was used). Participants were asked to stand as still as possible, and when they heard a tone, they should start to walk until they heard a second tone.

4.3.1.3 The auditory-Stroop task

The auditory Stroop task (a cognitive task addressing shifting and inhibition i.e., executive functions) was used [126], a useful test for measuring executive functioning with auditory stimuli [138-140].

Wireless headphones, Corsair Void, were used in which four different stimuli were delivered randomly for 30 seconds every 1.5 or 2 seconds; the times were randomised to come irregularly. The stimuli were the Swedish words for “high” or “low” in congruent or incongruent high or low pitch. Four different stimuli were used as illustrated in Figure 6.

	Word "High"	Word "Low"
Pitch "High"	Congruent	Incongruent
Pitch "Low"	Incongruent	Congruent

Figure 6. Illustrates the four different stimuli presented in the auditory Stroop test.

Stimuli were pseudo-randomised, so equal numbers of the different stimuli were presented. Participants were asked to ‘‘answer quickly and accurate’’ to the corresponding pitch and not the word. Audacity version 2.1.3 [141] was used to record and convert the auditory Stroop responses to WAV files (waveform audio files). MATLAB (version R2021b) [142] and a computer algorithm determined the reaction time for all stimuli. The reaction time was calculated from the beginning of the stimuli to the beginning of the participant answer.

Three trials of 30 secs. were performed for both the gait analysis and the AS task. First in ST condition and secondly in DT condition. Rest was offered between the trials (to ensure that all participants could manage the task). Before the data collection started the participant was allowed to practice both ST and DT. They were asked to not prioritise one task over the other in the DT situation.

4.3.1.4 Dual task effect

The dual task effect (DTE) was calculated consistent with prior work by Kelly et al. [143] (DT– ST) / ST *100. To consider both RT and accuracy an overall DTE was calculated on cognition (DTEcog) consistent with prior work by Strouwen et al. [139] (DTE RT+DTE accuracy) / 2.

4.3.1.5 Prioritisation

Prioritisation was analysed according to DTE on gait speed and cognition as well as DTE on double support phase and cognition. Analysis was made for total cohort and divided according to gait speed (median gait speed in ST) and according to cognitive function (median results of TMTb). A negative value indicated a prioritization of the motor task (posture first strategy) and a positive value indicated a prioritization of the cognitive task (posture second strategy). For details see Paper IV.

4.4 STATISTICS

All statistical analyses were conducted with SPSS version 24 (Part 1) and version 28 (Part 2) (IBM Corp., Armonk, NY, USA). Throughout all papers mean and standard deviation (SD) were used for normally distributed variables and for variables with non-normal distribution (including small samples) median and interquartile ranges (or range) were used. The Shapiro-Wilks test, and visual inspection of QQ-plots and histograms were used to analyse normality.

An overview of the descriptive and statistical methods applied across Papers I - IV is presented in Table 5.

Table 5. Overview of the descriptive and statistical methods applied across Papers I - IV

Statistics	I	II	III	IV
Descriptive				
Counts	●	●	●	●
Percentage (%)	●	●	●	●
Mean (SD)	●	●	●	●
Median (IQR, min-max)	●	●	●	●
Inferential				
Qhi-square test*	●	●		
T-test				
- Single sample t-test*				●
- Dependent t-test				●
- Independent t-test	●	●	●	●
Mann-Whitney U test**	●	●	●	●
One-way Anova		●		
Armitage test of trend		●		
Bivariate logistic regression		●		
Multivariate regression		●		
Spearman´s rank correlation		●		●
Odds ratio		●		
Confidence intervals		●		
Hosmed-Lemeshow goodness-of-fit		●		
Effect size: Cohen's			●	●
Effect size: Z'value			●	●
Welch t-test				●
Wilcoxon signed rank test				●

Abbreviations: interquartile range (IQR), standard deviation (SD). *Normally distributed variables, **Non-normally distributed variables.

Between-group differences for presence or absence of HC were analysed among the variables for cognition. The chi-square test was used for dichotomous data, the t´test for normally distributed data, and the Mann-Whitney U test was used for non-normally distributed independent data, and effect sizes were calculated using the z'value ($r = z/\sqrt{n}$). The one-way ANOVA was used for normally distributed data of more than two groups and the Armitage test of trend was used to analyse the linear association between MF and dichotomic data.

In Paper II a bivariate logistic regression analysis was used for factors potentially associated with ambulation [15, 23] for participants at MF3 level and dichotomised as either ambulatory (community and household ambulators) or wheelchair users (including the non-functional ambulators), according to the criteria by Hoffer et al. [42]. Age [15], sex, height, weight, BMI [9], scoliosis [9, 23], daily incontinence (bladder and/or bowel), sensory function in the feet and cognitive capacity [15] (the coding test [21], FAS test [22] and Block Design test [21]) were used in the analysis. In line with the "rule of thumb" of ten persons per variable [24], five variables with the lowest p-values were included (together with age considered a possible confounder), and a multivariate model was used with backwards enter mode. Spearman's rank correlation was used to analyse the collinearity between the variables (pre-set at less than 0.6). The regression analysis results were presented with odds ratios (OR), 95% confidence intervals (CI) and Hosmer–Lemeshow goodness-of-fit statistics were used for model fit of the final multivariate model.

The Welch t-test was used to analyse differences between individuals included in the DTE analysis and those not included. Spearman rank correlation analysis was used to analyse associations [144]. A dependent t-test was used to assess the intraindividual difference between performance in ST and DT and Wilcoxon's signed rank test was used for variables with a non-normal distribution. Effect size was calculated using Cohen's d or by using the z value ($r = z/\sqrt{2n}$). A single samples t-test was used to assess if the mean was significantly different from zero on the prioritisation. Between-group differences regarding task prioritisation were assessed using an independent t-test.

Scaled scores on the WAIS-IV [145] and D-KEFS tests [123] were calculated using the standard age-corrected norms. The Van der Elst et al. norms [146] were used for the RAVLT and the ROCF results were transformed to scale scores (z[age and gender]x3)+10, with a mean of 10 and a standard deviation of 3 (covering the 25^{th} to 75^{th} percentile).

Statistical significance was determined at p≤.001 (Paper 1) and at p≤.05 (Papers II, III and IV).

4.5 ETHICAL CONSIDERATIONS

The research projects within the thesis were performed in line with the ethical principles of the Declaration of Helsinki [147]. In general, ethical issues of the thesis were considered as modest compared to the benefit for the SB group. The testing procedure was not considered to include any additional risks compared to regular clinical gait and balance assessments and living their everyday lives. Assessments (of gait, physical function, and cognitive function) were carried out in a familiar environment for the participants and performed with extra caution as they may be perceived as stigmatising. Risk of falling and fatigue were concerns discussed and therefore the gait assessments were carried out in a calm corridor with no other disturbances. Only the PT and the participant were present. An extra safety concern was whether there was a high risk of falls. In such cases, an extra person could assist and walk very near to the participant. The cognitive assessments were performed in a calm room with the door closed to avoid disturbance from others. Participants had the opportunity to discuss results/performance with researchers in the research group.

4.5.1 Informed consent

Informed written consent was provided from the participants. As a large number of the participants had cognitive impairments, the aim of the research and the possibility of withdrawing the informed consent were thoroughly explained. The participants were provided information both verbally and in writing regarding the data collection, and on how data would be handled. An assistance provider (due to cognitive impairment) supported five participants to answer some of the questions, mainly for confirmation.

As the PT had a dual role of both researcher and the participants' clinical PT effort was made to clarify to the participants the voluntariness of participation and that participation in the studies would not influence their regular care [148].

Data were handled to protect confidentiality. Personal data were pseudonymised and coded, and the key was separated from the data and only available to the responsible researchers. For Papers I and II digital files were stored at Aleris Rehab Station on a secure server and documents in a locked document cabinet. For Papers III and IV digital data were stored at the Karolinska Institutet (KI) IT department server and only researchers involved in the project had access to the data. In accordance with the General Data Protection Regulation (GDPR, or Dataskyddsförordningen) for the processing of personal data, processing activities were registered at KI. The material will be destroyed 10 years after the publication of the results.

4.5.2 Ethical approval

Papers I and II were approved by the Regional Ethical Review Board in Stockholm in May 2014 (Dnr: 2014/1111-31). Papers III and IV were approved by the Regional Ethical Review Board in Stockholm in February 2019 (Dnr: 2019-00244 and with a supplement in March 2019 Dnr: 2020-01142).

Data collection for Papers III and IV had just started when the pandemic was underway. The data collection was paused, and a risk analysis was undertaken and sent to the Research and Development unit of Aleris Rehab Station and to the chief physician. After adaptations of the data collection (e.g., to always call the participant the day before data collection to ensure that they were healthy, to offer hand sanitiser to the participants and to keep a distance when possible and always used face masks) the decision was made to continue.

5 RESULTS

Detailed results of each paper are provided in the four papers. An overview of participant characteristics, included in Part 1 (Papers I and II) and Part 2 (Papers III and IV), is shown in Table 6.

Table 6. Overview of participant characteristics, included in Part 1 (Papers I and II) and Part 2 (Papers III and IV).

	Paper I and II	**Paper III and IV**
Type of Spina bifida, n (%)		
MMC	179 (91)	36 (88)
Lipomeningocele	14 (7)	5 (12)
SB occulta	3 (1)	-
Hydrocephalus, n (%)	123 (63)	23 (56)
Age group, n (%)		
18-30 years	90 (46)	18 (44)
31-45 years	60 (31)	13 (32)
46-60 years	38 (19)	10 (24)
≥61 years	8 (4)	-
Level of muscle function, n (%)		
MF 0	17 (9)	-
MF 1	18 (9)	3 (7)
MF 2	36 (18)	12 (29)
MF 3	58 (30)	26 (64)
MF 4	33 (17)	-
MF 5	34 (17)	-
Neurological category, n (%)		
T3 – T12 AIS A	49 (25)	-
T3 – T12 AIS B, C, D	2 (1)	1 (2)
L1-L2 AIS A	34 (17)	1(2)
L1-L2 AIS B, C, D	6 (3)	-
L3 AIS A	62 (32)	26 (63)
L3 AIS B, C, D	18 (9)	6 (16)
L4-S1 AIS A	8 (4)	7 (17)
L4-S1 AIS B, C, D	9 (5)	-
AIS E	8 (4)	-
Ambulatory level, n (%)		
Community ambulation	84 (43)	27 (66)
Household ambulation	22 (11)	14 (34)
Non-functional ambulation	17 (9)	-
Non-ambulators	73 (37)	-
Cognition, mean (SD)		
Block Design	6.9 (2.7)	8.0 (2.9)
Coding	6.8 (3.1)	7.8 (3.2)
Verbal Fluency (FAS)	7.3 (3.7)	9.9 (4.7)
RAVLT Total*	8.7 (3.4) **	9.5 (3.4)
RAVLT Delayed*	7.3 (3.6) **	9.4 (3.3)

*Non-normal distribution presented with Median (IQR). ** Previously presented by Ehren et al. [80] based on the data collection from Part 1.

5.1 PART 1 (PAPERS I AND II)

The most frequent diagnosis was myelomeningocele in 179/196 participants (91%), lipomeningocele was the second most frequent diagnosis with 14 participants (7%) and three participants (2%) had spina bifida occulta (with neurological impact). The most frequent level of neurological impairment was L3 (mid-lumbar), 80 participants (41%). MF level 3 was the largest group with 58 participants (30%).

Of the total cohort 84 (42%) were community ambulators, 22 (12%) were household ambulators and 90 (46%) used a wheelchair for mobility. Orthoses were used by 55 (28%) and walking aids by 25 (13%).

The participants' BMI were in Md 27 (IQR 8) and 123 (63%) had a BMI over 25 and 96 (49%) reported no regular exercise. Pain on the examination day was reported by 78 participants (40%), and load-related pain in the legs was most common (37%) followed by backpain (35%). Tethered cord symptoms were reported by 58 (30%).

Differences in the cognitive level were seen between participants with and without HC. A cognitive level within the reference values as expected for the participants' age for the general population were seen for those without HC and one SD below for those with HC performed ($p \leq .001$).

To manage daily life 86 (44%) participants had state or municipal assistance, extra help from relatives were needed for 48% as the assistance they received was not enough.

5.1.1.1 Relation to age

Among the youngest (18 to 30 years) participants a higher prevalence of HC was seen compared to the other age groups ($p \leq .001$) and core subjects in compulsory school was approved to a lower degree ($p \leq .001$) than the older participants. Also, they had previously had, or still had, symptoms associated with tethered cord, to a larger degree than the older participants ($p \leq .001$).

5.1.1.2 Relation to level of MF

The presence of HC, contractures >20 degrees in the lower extremities and presence of scoliosis showed a linear (increasing) association ($p \leq .001$) with a lower degree of muscle function. Lower scores were seen on the subtests for cognitive function for participants with MF level 4 and 5($\leq .001$) and they were also shorter than other participants ($p \leq .001$). In the youngest age group, there were participants in all MF levels whereas among the oldest participants there was no participant in MF level 4 and 5.

5.1.1.3 Participants with MF level 3

Of participants with a MF level 3 (n=58), one third (16, 28%) were community ambulators, one third (19, 32%) were household ambulators and a little more than one third (23, 40%) were wheelchair users. The community ambulators and the wheelchair users were older than the household ambulators (p=.012 and p=.017). The community ambulators had lower prevalence of HC as compared to the household ambulators and the wheelchair users (p=.003).

Ambulation was independently associated with BMI, scoliosis and the coding test, Table 7. The OR of being ambulatory decreased by 24% for one unit more of BMI, a 97% lower OR of being ambulatory were seen with the presence of scoliosis and the OR for being ambulatory increased by 7% f or every unit the coding test increased (better results).

Table 7. (Modified from Paper II). A multivariate logistic regression analysis of factors associated with ambulation for participants with MF level 3.

Variable	**β**	**p-value**	**OR**	**95% CI**
Age	-0.03	0.37	0.97	0.90 - 1.04
Sex (ref woman)	2.06	0.05	7.87	0.98 - 63.23
BMI[1]	-0.27	**0.02**	0.76	0.61 - 0.95
Scoliosis (ref yes)[2]	-3.50	**0.01**	0.03	0.00 - 0.42
Coding test	0.07	**0.03**	1.07	1.01 - 1.14

[1]Body Mass Index (BMI) (kg/m2), [2]Presence of scoliosis and/or spine surgery. P-values ≤.05 in bold. Overall model fit (Hosmer and Lemeshow Test): $\chi 2$ = 1.495, df = 8, p = .993. Cox & Snell R^2 = .468, Nagelkerke R^2 =.637.

5.2 PART 2 (PAPERS III AND IV)

Among the included participants 36 (88%) had MMC and 5 (12%) had lipomeningocele, and the most frequent neurological impairment level was L3 (mid-lumbar) [23] with 32 participants (79%). The most common MF level was MF3 with 26 participants (64%). Two thirds of the group were community ambulators 27 (66%), and one third were household ambulators 14 (34%). Orthoses were used by 19 (46%) and walking aids by 3 (7%).

The group median BMI was 27 (IQR 8) and 26 participants 63%) had a BMI over 25 and 26 (63%) reported no regular exercise (Level 1-3 according to the Fränding and Grimby scale [128]. Pain on the examination day was reported by 17 participants (41%) and tethered cord symptoms by 6 (15%).

5.2.1.1 Gait characteristics

Adults with SB walked slower, had a longer double support phase (a shorter swing phase and a longer stance phase), had shorter strides and a larger step width variability than the corresponding normative data. Also, they showed a larger lumbar rotation in the trunk, and a larger lateral thoracic sway and forward/lateral sway than the corresponding normative data of the Mobility Lab software [115, 137].

For participants in MF level 3 gait speed was slower than for participants in MF1 and 2 ($p=.04$). Stride length was shorter and elevation at mid-swing higher ($p=.03$ and $p=.01$ respectively). Lumbar lateral sway and rotation were larger ($p=.05$ and $p\leq.001$ respectively) as well as thoracic lateral sway ($p\leq.01$). Table 8 presents spatial and temporal gait characteristics for the cohort and for participants divided into levels of MF.

Table 8. (Modified from Paper III). Spatial and temporal gait characteristics for the group and divided into levels of muscular function (MF). Levels of significance are shown for participants in MF level 3 compared to participants in MF levels 1 and 2 together. Also, data for the 5th to 95th percentile for the normative data from Mobility Lab are presented. Data deviating from the normative material in bold and p-values in italics show statistical significance.

	Total cohort n=40	*MF 1 n=3*	*MF 2 n=12*	*MF 3 n=25*	*P value*	*Normative data****
Lower Limb						
Gait speed (m/s)	**0.96 (0.20)**	**1.13 (0.21)**	**1.02 (0.18)**	**0.92 (0.19)**	*0.04*	*1.04 - 1.64*
Cadence (steps/min)	107.15(10.96)	113.92 (10.68)	107.40 (9.83)	106.20 (11.60)	0.50	*103 - 133*
Gait cycle duration (s)	1.13 (0.12)	1.06 (0.10)	1.13 (0.10)	1.15 (0.13)	0.42	*0.90 - 1.16*
Stride time (s)	0.57 (0.06)	0.53 (0.05)	0.57 (0.52)	**0.58 (0.07)**	0.39	*0.45 - 0.58*
Swing phase (%GCT)	**36.87 (2.87)**	**37.52 (0.96)**	**36.87 (2.20)**	**36.79 (3.33)**	0.83	*37.7 - 43.9*
Stance phase (%GCT)	**63.13 (2.87)**	62.48 (0.96)	63.13 (2.20)	**63.21 (3.33)**	0.83	*56.1 - 62.3*
Double support (%GCT)	**26.82 (5.37)**	**25.17 (1.89)**	**26.59 (4.04)**	**27.13 (6.21)**	0.64	*12.4 - 24.6*
Stride length (m)	**1.08 (0.17)**	1.18 (0.21)	1.14 (0.15)	**1.03 (0.16)**	*0.03*	*1.11 - 1.66*
Lateral Step variability (cm)	**4.80 (1.63)**	**5.01 (1.05)**	4.15 (1.17)	**5.09 (1.81)**	0.11**	*2.22 - 4.53*
Circumduction (cm)	3.19 (1.86)	3.37 (1.53)	2.72 (1.86)	3.40 (1.91)	0.37	*1.97 - 6.13*
Elevation at midswing (cm)	2.17 (1.02)	1.94 (0.51)	1.59 (0.84)	**2.47 (1.03)**	*0.01*	*0.37 - 2.40*
Lumbar RoM (◦)						
Frontal (lateral sway)	11.60 (5.17)	11.19 (2.40)	8.55 (3.20)	13.14 (5.59)	*0.05***	*4.90 - 13.7*
Sagittal (forward/backward tilt)	9.25 (5.88) *	**10.83 (4.82)**	6.70 (3.79) *	**10.41 (3.33) ***	0.14	*2.88 - 9.71*
Transverse (rotation)	**21.33 (11.43)**	7.94 (1.71)	13.14 (3.98)	**23.63 (11.47)**	*<0.001***	*5.20 - 18.8*
Thoracic RoM (◦)						
Frontal (lateral sway)	**15.31(14.86) ***	**12.30 (5.08)**	**12.94 (5.00)**	**21.00 (12.84)**	*0.01***	*2.70 - 9.15*
Sagittal (forward/backward tilt)	**7.34 (3.72) ***	5.44 (0.66)	6.67 (2.30)	**8.39 (1.76) ***	0.03	*3.43 - 6.72*
Transverse (rotation)	12.24 (6.29)	10.55 (1.64)	11.22 (3.72)	**13.60 (4.29)**	0.07	*4.85 - 13.0*
Upper Limb						
Arm swing velocity (◦/s)	235.71 (123.52) *	319.48 (239.05)	211.64 (81.22)	266.36 (125.30) *	0.14	*115 - 364*
Arm swing RoM (◦)	44.25 (25.75) *	44.98 (26.33)	44.36 (22.75)	45.70 (21.96) *	0.19	*21.4 - 90.8*

Abbreviations: Number (N), Range of Motion (RoM). *Non-normal distribution presented with median (IQR). **Equal variances not assumed, presented with MD (IQR). The normative data of the APDM system is based on an average of a pool of 70 subjects, age 20 – 90 years, with 5 men and 5 women per decade and presented with 5th-95th percentile.

5.2.1.2 Dynamic balance

Mean score on the Mini-BESTest was 11.3 (SD 6.9) (min-max 0-28) with balance performance reduced in all four subdomains. For participants with MF level 3 lower scores were seen (MF3 vs. MF1 and MF2 $p \leq .001$, MF3 vs. MF2 $p = .004$).

5.2.1.3 Falls and concerns about falls

Almost two thirds of the participants had fallen the last year (26, 63%) and nearly half of them were afraid of falling 18 (44%). Their scoring according to FES-I "concerns about falling" was 27 (SD 9), indicating a moderate to high concern of falling [119]. A correlation was seen between those not being able to perform TUGcog (n=15, 37%) and those who had fallen the last year and those afraid of falling ($p \leq= .01$ and $p \leq= .01$ respectively).

5.2.1.4 Cognition

The level of cognitive functioning for the ambulatory adults included in the DTE analysis was within the average range expected for the subject's age.

For those not included in the DTE analysis the cognitive level was considerably lower than expected for the subject's age. A significantly lower score was seen in two of the cognitive tests; the verbal fluency test ($p = .003$) and the RAVLT Total test ($p = < .001$) between the participants included in the DTE analysis and those not included (n=7). No other differences were seen in the cognitive test results with regards to gender, age, or prevalence of HC.

5.2.1.5 Dual task effect

Nine out of 11 gait parameters (82%) in the lower limb showed a DTE. Movements in the trunk did not show the same change in DT. Only the thoracic rotation changed (p≤=.05). For variability the largest DT cost was seen with a DTE of 12% for cadence (p≤ =.05). The DTE for TUG showed a DT cost of 25%.

No statistical difference was seen between ST and DT for reaction time (p=.152). However, for accuracy there was a difference (p=.021). The total DT effect for cognition (reaction time and accuracy together) was a 3% cost. Figure 7 shows DTE for gait characteristics and auditory Stroop. Absolute values are presented in Paper IV, Table 2.

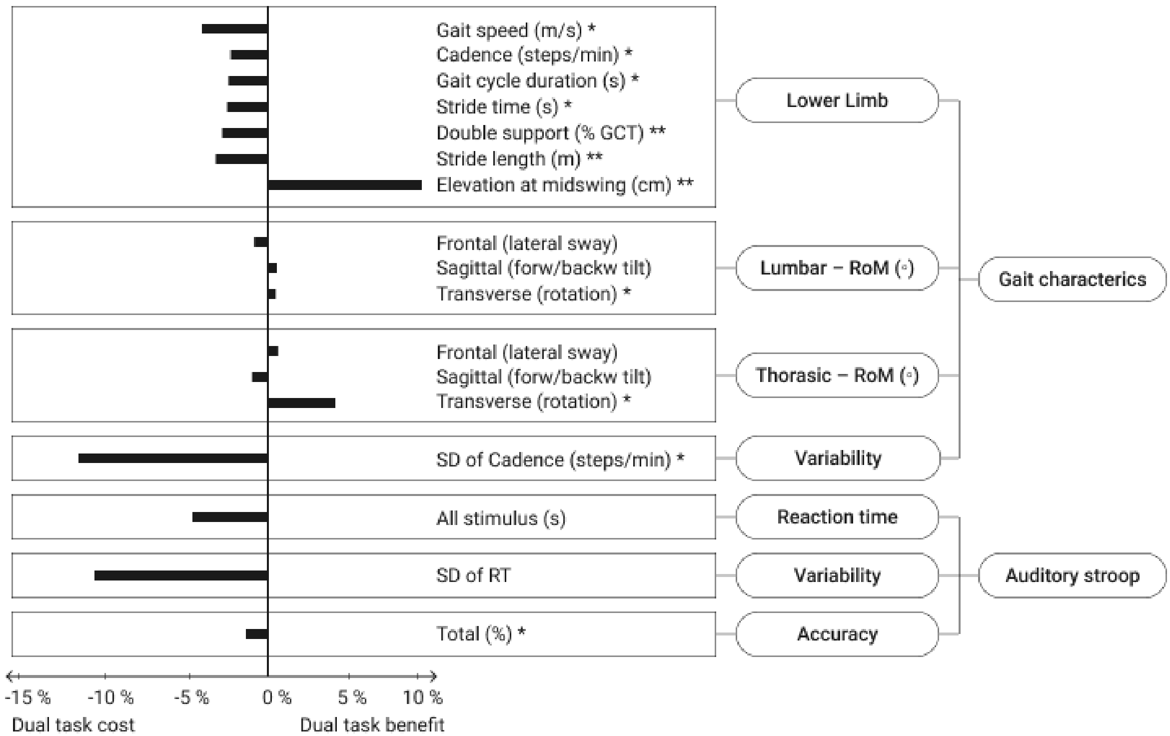


Figure 7. Overview on DTE's for gait characteristics (those with a significant change are presented) and the DTE's för auditory Stroop. Significant differences between single and dual task performance are marked with asterisks (* p≤.05, ** p≤.001).

5.2.1.6 Patterns of prioritisation

No differences were seen in the group's prioritisation, neither in the total group nor in the explorative sub analyses with the group divided according to gait speed and cognitive function.

Interestingly, participants with a higher gait speed seemed to prioritise the cognitive task (4.6% Cognition-gait speed). Likewise, those with a lower cognitive level seemed to prioritise the cognitive task (5.8% Cognition-gait speed). Figure 8 illustrates a non-conclusive pattern of prioritisation.

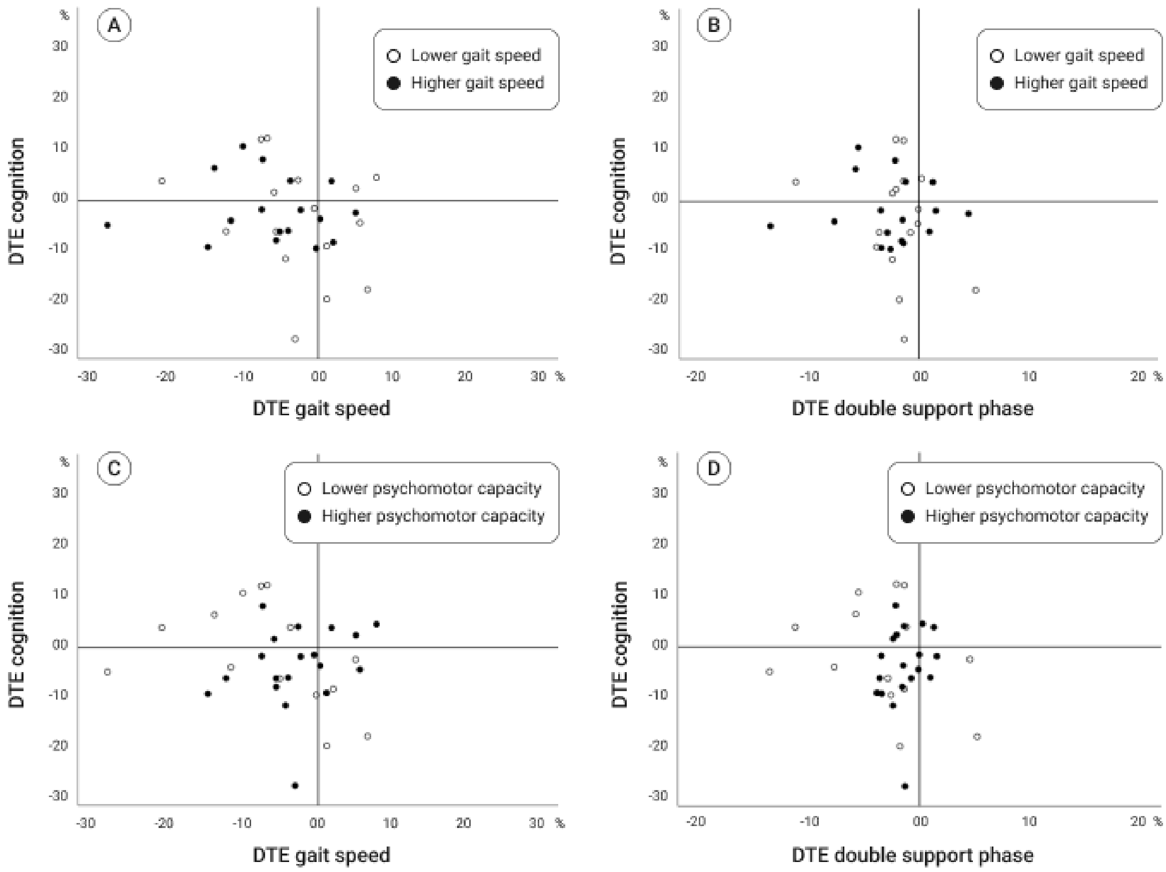


Figure 8. Illustrates patterns of prioritisation of dual task effect (DTE) on cognition and gait. Panels A and B represent patterns of prioritisation of the cohort divided by gait speed (median gait speed in single task). Panels C and D represent patterns of prioritization by psychomotor capacity (median results on the TMTb test).

6 DISCUSSION

This thesis is the first comprehensive description with a focus on factors affecting health and living conditions in relation to mobility, gait, dynamic balance, and cognition of adults with SB in Sweden. It describes an almost total regional population showing the complex interplay of physical, medical, and cognitive challenges many persons with SB experience in their everyday life. In addition, perspectives of age and muscular function are discussed. Other reports by the SB team at the Spinalis outpatient clinic [76, 80, 89, 149, 150] contribute to a more complete picture including additional perspectives.

The cohort this research is based on is unique and as SB is today considered a rare disorder the number of adults living with SB will most probably decrease in the future, due to fewer being born with SB. Therefore, these data will be important as reference material for the future. This thesis contributes to increased knowledge about adults with SB especially regarding gait, mobility, and DT. Also, it provides a deeper insight into this group's daily life, physical and cognitive function and thereby gives adults with SB, and clinicians in the field, insights for future life situations.

6.1 HEALTH AND LIVING CONDITIONS

Around half of the participants were ambulators and around half used a wheelchair for mobility. Mode of mobility, use of walking aids and walking distance varied greatly even among participants with similar muscular function, in particular this was seen in those with MF level 3. In this group around one third were community ambulators, one third household ambulators and one third used a wheelchair for mobility. The ambulatory persons in MF3 had a lower BMI, lower incidence of scoliosis and a higher psychomotor speed and executive function (tested with the coding test). An unanswered question is the causality dilemma; does a high BMI result in wheelchair use or is a high BMI the reason for wheelchair use "which came first?" Also, as the non-ambulators had a higher prevalence of scoliosis they might have a more severe spinal malformation or other related problems, potentially also affecting mode of mobility. Moreover, the community ambulators had a significantly lower prevalence of HC compared to the others, which also potentially influences the fact that they were ambulators as adults.

The youngest participants (born 1985-1997, 18-30 years old) were distributed among all MF levels. They had a higher prevalence of HC and tethered cord symptoms and fewer had passed compulsory school compared to the older participants. These younger participants have grown up in a different medical era than the older participants with improved medical treatments (for example shunting, urinary and bowel-related treatments) and systematic medical follow-up programmes as well as screening for other potential conditions. Potentially this group will need more care in the future as they have more SB-related problems at a younger age, that will likely have an impact on their forthcoming life [151].

Those with least muscle function had more severe complications, a higher proportion of HC, scored the lowest in the subtests for cognitive capacity, and had a higher prevalence of contractures in the lower limbs and scoliosis. Among the oldest participants no one had MF level 4 or 5, probably because no one with those MF levels had survived to this age. The older participants in our cohort may have been born with a more modest malformation.

This cohort presented cognitively in general one SD under the reference values of the general population, lower results were seen for participants with HC. Cognitive dysfunction is known to influence and complicate various aspects of daily life [10, 20, 64, 152]. Potentially, this could also have an impact on BMI (increased in almost two thirds). Cognitive challenges make it difficult to follow routines such as regular physical activity or eating healthily. Overweight is associated with cardiovascular disease [7], decreased participation in physical activity, may have psychosocial consequences and an increases risk of pressure ulcers [86]. Also, it may negatively affect mobility [153] and thereby it might affect independence in daily life. A regular exercise habit at an intensity necessary to achieve health-related benefits [2, 154] was seen in half of the participants. Exercise results in health-related benefits and can contribute to a feeling of "being part of a context" and "getting out of the house" [149] all important aspects of health. A review concluded that many adults with SB typically have an inactive lifestyle, low aerobic capacity, low level of physical activity and a higher frequency of obesity [14]. Unfortunately, all this seems to apply to this cohort as well. It is essential to support a healthy lifestyle as the lack of it can have serious consequences [155].

6.2 GAIT, DYNAMIC BALANCE AND DUAL TASK

In the second part of the thesis the aim was to explore the group's walking performance in everyday, their dynamic balance life and the potential impact from a simultaneous cognitive task during walking.

Both spatial and temporal gait parameters and dynamic balance were highly reduced, especially for those in MF3 who displayed a slower gait speed, shorter stride length as well as a longer double support phase and a larger lateral thoracic sway. The most distinctive alteration though was a rotation in the lumbar back and a large lateral sway of the trunk compared to the normative material (70 subjects, 20-90 years) [115, 137] as well as compared to young and healthy adults [156]. Participants with MF level 3 had an almost three times larger lateral trunk sway. The large thoracic sway is necessary to compensate for weak hip abductors, by moving centre of mass above the hip joint in stance phase [4, 46].

Slower gait speed and shorter strides has been seen in adults with SCI [157], a group with similar neurologic impairments, having largely similar prerequisites for walking. To my knowledge only one paper has analysed gait in adults with SB with a movement analysis system [50], focusing on adults over 50 years, and not analysing movements of the trunk or lumbar back. Our group reported a moderate to high concern about falling [118, 119]. Corresponding concerns have been reported by the adults over 50 years by Larsen et al. [50]. It is hard to compare these groups as age differs, but as our participants are younger, they will potentially report an even higher concern of falling as they grow older.

Our group showed a DT cost on gait (4.3%) comparable to the cost seen for people with Parkinson's disease (4.9%) [158] and persons with a moderate multiple sclerosis (5.3%) [159]. Persons with mild multiple sclerosis (2.3%) and healthy controls (2.6%) showed a smaller DT cost on gait indicating a more automatic gait [159, 160].

The DTE on reaction time for this cohort (4.9%) showed a considerably smaller cost than for persons with Parkinson's disease (11%) [158]. However, the people with Parkinson's disease were in general almost 40 years older, which may partly explain the difference in DTE on the cognitive task. The study including persons with mild to moderate multiple sclerosis (7.5% and 3.1% respectively) [159] (mean age 50 years) showed a DT cost on RT more similar to the SB group. The healthy control group in the study by Wallin et al. [159] showed almost no difference (.1%). However, they included only the incongruent stimuli indicating that adults with SB had a larger DTE on RT as this study included equally represented incongruent and (the less challenging) congruent stimuli. The DTE of accuracy showed a significant cost for the SB group (1.7%) but no change for the Parkinson's disease group (0%) [158], the multiple sclerosis group (0%) or the healthy control group (0%) [158, 159]. The SB sample responded quickly but more often inaccurately. This could possibly be associated with the level of executive function and mental speed. However, the cohort with Parkinson's disease [158] and multiple sclerosis [159] had other neurological dysfunctions affecting the central nervous system in other ways. This may explain the difference in the cognitive results in our study when performing a DT.

No differences in prioritisation were found in the total cohort, or in the subgroups. A small tendency for participants with a higher cognitive level to be more scattered around zero (showing a minor DTE) and for participants with a lower cognition to be more diverged (indicating a larger DTE), could be seen especially in Panel D, Figure 8. Participants with higher gait speed and participants with lower cognitive capacity seemed to show a non-conclusive prioritisation for the cognitive task, one might argue that they employed a posture second strategy (the gait task had less focus), implying a gait with increased instability. In people with Parkinson's disease a similar posture second strategy has been seen in contrast to young and elderly controls, who showed a posture first strategy (gave the cognitive task less focus) in a study by Bloem et al. [161]. As adults with SB have a highly affected gait and dynamic balance, a posture second strategy may have serious consequences such as falls and injuries and thereby reduce the quality of life. For persons with multiple sclerosis a posture first strategy was seen by Postigo-Alonso et al. [162] as they prioritised the motor task, however they found no difference in prioritisation in their healthy control group.

To find a cognitive task appropriate for the participants is crucial. The AS is considered a good test for the executive functioning [138] but it was too challenging for 6/41 (15%) of the ambulatory adults with SB. To use a cognitive task, customized with different levels would perhaps be a solution for adults with SB as used in a study by Gursoy et al. [163]. The TUGcog is a DT test easily used in daily clinical work and the results can indicate different challenges, related to gait impairment and difficulties performing the subtraction task (counting backwards by 3), or problems in remembering the motor task (e.g., forgetting to return and sit down). However, the TUGcog was too challenging for 15 of our participants (37%).

A large amount of the ambulatory persons had a sensory function that was absent or reduced below the knees (it means no or limited sensory feedback on the position of the feet). This in combination with their reduced muscular function to stabilise the ankles, knees and hips affects their dynamic balance. Our group of ambulators had a more affected dynamic balance than persons with SCI in a study by Jørgensen et al. [164]. According to ASIA, 66% of the people in the SB group had a neurologically complete injury as compared to the ambulatory group with SCI, where only 7% had a complete neurological injury. This could indicate that adults with SB walk to a greater extent than adults with SCI even though they have more severe neurological impairments. Possibly this could be influenced by the multidisciplinary team approach these children were offered [43], which could have resulted in an expectation to walk.

The combination of a considerably affected dynamic balance, slow gait speed (0.96 m/s), high number of reported falls during the last year, the high number of participants being afraid of falling and a DT cost on gait most likely has a combined impact on everyday life, with potentially increased risk of falling. In older adults and persons with SCI [164, 165], a gait speed below 1.0 m/s, a history of falls and fear of falling have been strongly associated with falls. In combination with a DT cost of gait characteristics, as for adults with SB, it implies an even more affected stability in gait [166-168]. To improve everyday life and reduce the risk of falls, persons with SB should be offered systematic upgrading of assistive devices, orthoses, and when needed the chance to try a wheelchair in the follow-up programmes.

To combine ambulation (with or without assistive devices) and the use of a wheelchair in daily life could be a wise decision and enable a larger flexibility. Wheelchair use is for some associated with barriers [169], whereas for others it is more convenient [89] and a way to “save their body”. The use of a wheelchair in situations where balance is challenged could be appropriate. However, a retained walking function (when possible) may improve accessibility.

6.3 METHODOLOGICAL CONSIDERATIONS

The group described in Papers I and II consists of a near total regional cohort and includes more than 90% of the adults with SB in the Greater Stockholm area. For Papers III and IV the included group was much smaller. However, the distribution of persons in the different MF levels was comparable. As the level of healthcare and living conditions differs in the world it is not possible to generalise the findings to all adult persons with SB. However, it can be assumed that they are representative to adults with SB living in countries with similar living conditions and level of healthcare.

As the body of research focusing on adults with SB is sparse there are few instruments developed and validated for this group. This is a potential problem for the internal validity. However, the chosen instruments are used in the clinic and are mostly developed for persons with other neurological conditions with similar neurologic prerequisites or for older persons [110, 116, 118, 128, 133, 170].

Several scales have been used to classify the neurological level, the ambulatory function and muscular function in persons with SB [4, 33, 35, 110, 130, 171, 172] but unfortunately there is no international consensus on which method to use regarding muscle groups and impairment [8, 33]. Tita et al. [33] concluded that the classification system correlating best with ambulation status was the Broughton classification [171] and secondly the NSBPR (National Spina Bifida Patient Registry) scale [172]. However, the Tita et al. paper was published after the present study had started and unfortunately, none of these scales include sensory classification (they focus solely on the motor impairments). Including sensory classification was recommended by Verhoef et al. already in 2004 [8]. In this thesis the sensory level was assessed in accordance with the international standards for neurological and functional classification of SCI [109, 110]. We found ASIA to be relevant as sensory function influences dynamic balance to a large extent and as persons with SB and it is important to be informed of potential sensory impairments. The classification of MF levels by Bartonek et al. were used [38] in this thesis, this classification is also used by the Swedish national register for persons with SB [27]. The Hoffer classification, used in the Papers are developed for persons with SB [42] and is still used [33].

The Mobility lab software has been used for adults with Parkinson’s disease [136, 170] and multiple sclerosis [159, 173] and also for children with SB and cerebral palsy [174] as well as for healthy controls both young and old [170, 175]. It is a flexible and user-friendly sensor-based gait analysis system, easy to use in a normal clinical setting and is not dependent on advanced laboratory settings, the small sensors are attached over the clothes. Also, it assesses gait over numerous gait cycles giving a larger picture of regular daily walking, a gait pattern with high ecological validity. Participants can walk like they usually do and not focus on a given area, like on a pressure-sensitive gait analysis mat. Unfortunately, the system used in this thesis did not register the typical arm movements (in the frontal plane) for persons with SB, a limitation of the system.

To our knowledge the AS assessment has not been performed on persons with SB, but it has been used previously by the research group [158, 159] for persons with Parkinson's disease and multiple sclerosis presenting partly similar dysfunctions. Also, it is believed to be an appropriate test assessing executive functioning using auditory stimuli [138-140].

A problem for the internal validity is the lack of a healthy control group in Part 2. That implies an uncertainty regarding the results of adults with SB. However, comparisons were made with healthy controls provided by the gait analysis system [115, 137]. In Paper IV comparisons were made with other neurological disorders as well as healthy controls included in other papers [158, 159, 161, 162]. Also, in Part 2 persons over 65 years were not included as age-related changes in cognition might be present [107]. This can have affected the external validity for the oldest persons with SB.

As the DT assessments were performed indoors, we believe the results have a high ecological validity for indoor walking for adults with SB. However, for walking outdoors in the community the ecological validity is lower as walking outdoors often is associated with multiple other stimuli such as uneven and/or slippery surfaces, and different noises.

Considerations for the research group included the dual role of the first author, being both a researcher and the examining PT, in addition to that the research were carried out at the Spinalis outpatient clinic at Aleris Rehab Station. On one side, the participants felt safe with both the researcher and the environment on the other side this could potentially have affected the external validity. Even if a potential bias, the positive aspects of this were however dominated.

6.4 CLINICAL IMPLICATIONS

It is important to prioritise follow-up for this patient group [92]. However, the group is so heterogeneous that a thorough first assessment from a multidisciplinary team is needed in order to provide the best possible care and thereby improve health and living conditions. The team should preferably include a neuropsychologist as cognitive challenges are often present and to a high extent affect persons with SB and may influence the motor performance as well as many other aspects of life. The further follow-up should be individualised both in extent and frequency. For some, every year is preferred whereas for others every fifth year may be enough.

This thesis provides a deeper knowledge of gait and dynamic balance in adults with SB and the motor-cognitive performance. This is important in daily life and needs to be addressed in the clinical work. As deterioration in gait has been found in adults with SB within the fourth decade [50] it is important to introduce assistive devices and orthoses and an opportunity to try them as it might improve gait and dynamic balance. Perhaps the use of a wheelchair in some situations can improve independence. Also, in the daily clinical work include health aspects, to follow BMI and offer help to improve nutrition and level of exercise.

In our clinic we have a special team focusing on adults with SB which we think is a good solution as such a team has a deeper understanding of the special needs and impairments of the group. The team goes through the planned follow-up in advance in order to share their prior knowledge. Thereby the team can better understand the needs of the individual person and secure the best possible follow-up. This is important as a team can generate a larger perspective than the individual persons. Thereby the patients are provided the best possible tailored follow-up. Also, the social worker calls the patients before the visit to screen for current possible needs and also to remind the patient to think of the potential problems in daily life. All with the intention of providing the best possible help at the follow-up and leading to fewer missed appointments and better utilisation of the resources at our clinic and thereby for society.

6.5 FUTURE RESEARCH

To follow the total cohort over time and to analyse the needs and functions in different phases/ages in order to be able to give the best support.

Also, it is important to explore mortality, as according to a study by Oakeshott et al. [32] it was often sudden and unexpected and ten times the national average in the population. A better understanding and knowledge could help clinicians provide better care and help prevent conditions possibly affecting mortality.

In order to better understand dual task effects and possible patterns of prioritisation, it would be interesting to explore this in a larger cohort, also including those using a wheelchair for mobility.

As SB is a rare condition and larger samples are inevitably hard to obtain without multi-centre studies, collaborative efforts between research groups both nationally and internationally are necessary.

7 CONCLUSIONS

- This thesis has verified that adults with SB have a complex set of medical, physical and cognitive needs that must be addressed to improve their health and living conditions. They have an ongoing need for care and support throughout their life, but it is important to customise the follow-up both in frequency and content in order to meet the differing needs of the patients.

- The younger persons had a more complex set of problems and will most probably need more care in the future as ageing will also influence their life situation. With more complex medical conditions the interventions may need to be more comprehensive as more factors play important roles.

- Mode of mobility and cognitive capacity varied substantially across the cohort. In those with MF level 3 this was most evident, even though they had similar muscular prerequisites.

- As gait and dynamic balance are clearly affected in adults with SB, combining walking with the use of a wheelchair may be a wise decision to avoid challenging situations with regard to both stability and distances.

- Ambulatory adults with SB showed a significant DT cost on most of the analysed parameters of gait. The findings contribute to deeper knowledge and can help healthcare providers to develop and improve the care for adults with SB.

- This increased knowledge can improve interventions and the support for adults with SB. Thereby decrease the risk of secondary conditions, and probably reduced costs for society and improved health and living conditions for adults with SB.

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