Gait Recovery in spinal cord injury subjects

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GAIT RECOVERY IN SPINAL CORD INJURY SUBJECTS:

FROM CLINICAL EXPERIENCE TO RESEARCH DEVELOPMENTS

BY
TAMBURELLA FEDERICA

DISSERTATION SUBMITTED 2014

AALBORG UNIVERSITY
DENMARK

AALBORG UNIVERSITY
Department of Health Science and Technology
Denmark

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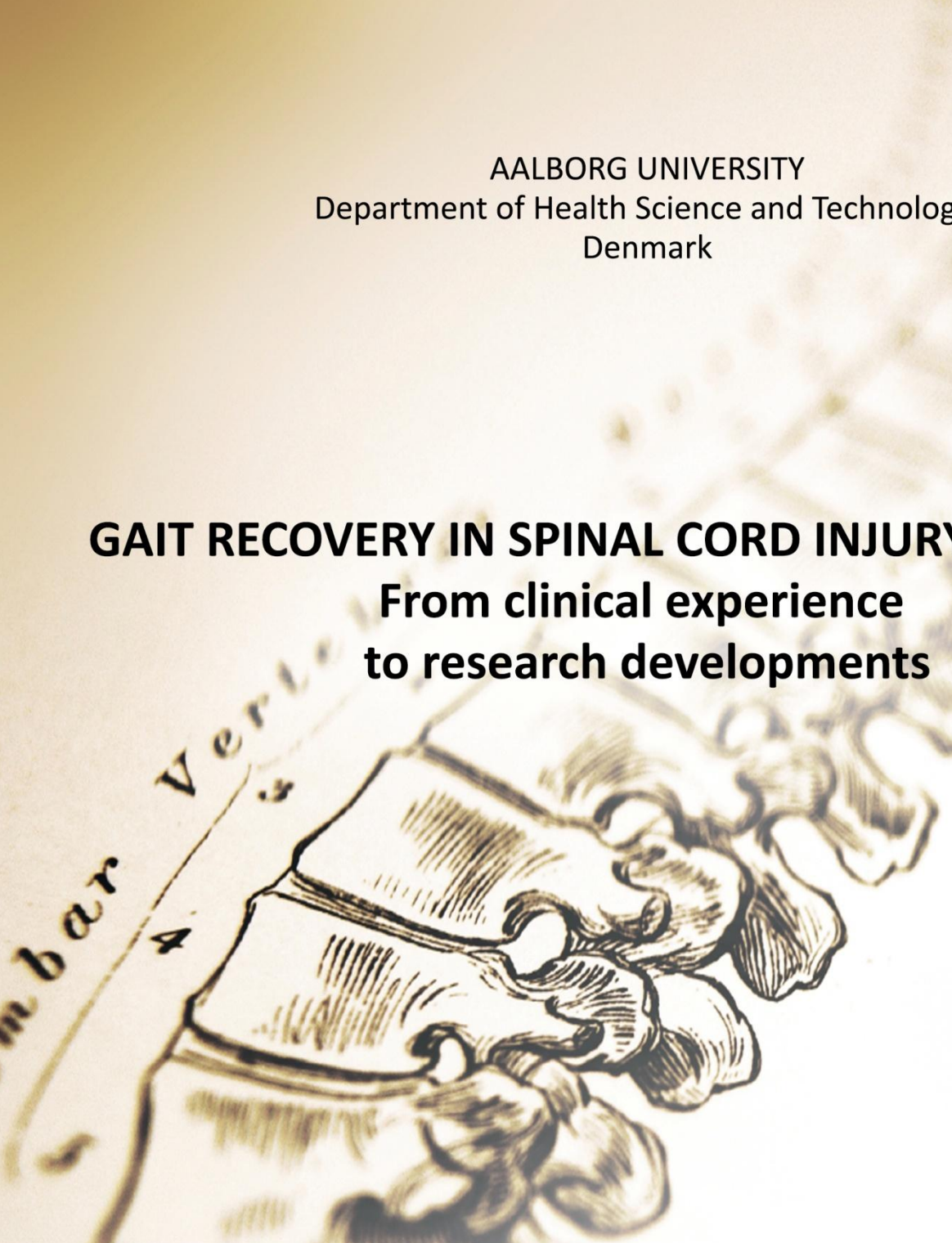

A PhD Thesis
By
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Submitted for the degree of
Doctor of Philosophy, Biomedical Science and Engineering

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Dedicated to my father:

"Don't walk in front of me, I may not follow;

Don't walk behind me, I may not lead;

Walk through me and just be with me"

… To my family, and especially my sister…

… To my mentor Dott. Marco Molinari…

… To my special friend Giorgio, who constantly believed in me…

… To Maria's smile…

… To all other people who believed in me …

… To the value of friendship…

1 English Summary

Walking recovery is one of the main goals after a spinal cord injury (SCI), although almost never attainable in subjects with complete lesion it's a realistic object for subjects with incomplete lesions, among which recovery of walking is rated at first place among rehabilitation objectives[1]. Epidemiological studies indicate in the last years a progressive increase of incomplete lesions among SCI in the last years (e.g., with chances of walking recovery)[2] and recovery of ambulation has become the target of several rehabilitative approaches[3].

In subjects with SCI, age and lower extremity muscle strength have been commonly considered the main factors affecting walking function[4]. Consequently, most rehabilitation approaches aimed at reinforcing the lower extremities. However, as recently reported by our group, many factors besides muscle strength influence the recovery of walking function[5]. In particular, we demonstrated that balance and spasticity, as well as weight and distance from the lesion, are key factors affecting walking performance in SCI subjects [5]. From this statistical evidence derived the hypothesis that weight unloading as well as balance and spasticity specific treatments might improve gait performance in SCI. In this line, the present study aimed at testing different approaches to improve gait and at investigating gait effects of body weight reduction due to a water environment in subjects with SCI:

i) Efficacy of task-specific biofeedback balance training in supporting walking functions:

Recently it has been demonstrated that balance is a key factor of walking recovery. The object of the study was to assess parameters and indexes for balance testing in subjects with SCI and to determine the efficacy of visual biofeedback task-specific balance training (vBFB) in improving balance performance and gait compared with conventional over-ground rehabilitation. Two different studies designs have been employed. A serial cross-sectional study paradigm was employed to assess reliability, validity, and responsiveness of balance platform parameters while an open-case study with retrospective control was used for the vBFB training study. Results allowed to focus reliable, valid, and effective parameters for balance assessment in SCI subjects and demonstrated that vBFB training is effective in improving balance and gait in chronic motor incomplete SCI subjects.

ii) *Efficacy of neuromuscular Kinesio Taping (KT) in decreasing spasticity and improving gait:*

In recent years, the application of Kinesio Taping has been proposed to enhance sensory inputs, decreasing spasticity by proprioception feedback and relieving abnormal muscle tension; therefore our goal was to analyze the effects of ankle joint KT on spasticity, balance, and gait in SCI subjects. A randomized crossover case control design was used to compare the effects of KT and conventional non elastic silk tape in 11 chronic SCI subjects, AIS level D. Data demonstrated that short-term application of KT reduces spasticity and pain and improves balance and gait in chronic SCI subjects.

iii) *Effect of water buoyant force on gait characteristics of SCI subjects:*

Aim of this study was to characterize gait features of subjects with incomplete SCI walking in water and on land in comparison with healthy controls to identify the specificity of water environment on influencing gait in SCI subjects. Kinematic gait parameters and range of motion of joint angles of 15 SCI subjects and 15 controls were analyzed. Data indicated that gait in water of the SCI subjects is associated with kinematic parameters more similar to those of the CTRLs, particularly regarding speed, stride length, and stance phase, supporting the idea that walking in a water environment may be of rehabilitative significance for SCI subjects.

Balance, somatosensory inputs and body weight are clearly closely related in influencing gait functions. Weight, spasticity and impaired balance are also the chief limitations to over-ground ambulation in subjects with SCI[5]. Balance impairment is obviously associated with an increase in the prevalence of falls and subsequent injuries[6]; ankle spasticity is rated as one of the major gait impairment in incomplete SCI[5;6] and there is general consensus on considering water environment useful for gait recovery in SCI[7]. Present study addresses these three factors by specific approaches demonstrating the transfer of balance improvement into gait improvement, by opening a new line of spasticity treatment by taking advantage of somatosensory inputs trough KT, and by characterizing the effects of water environment on gait from a kinematic point of view.

Gait control mechanism are multifarious including spinal, suprapsinal and peripheral inputs, it is conceivable that treatments aiming at restoring gait would take advantage of all the systems involved. Present study demonstrate the importance of defying the contribution of the different system in affecting gait after SCI and of developing specific patient centred protocols to improve gait by selectively targeting the impaired systems.

2 Danish summary / Dansk sammenfating

Titel: ***Genoprettelse af gang for forsøgspersoner med rygmarvsskader: Fra klinisk erfaring til forskningsudvikling***

Genoprettelse af gang er et af hovedmålene efter rygmarvsskader. Selv om det næsten aldrig opnås af forsøgspersoner med komplette læsioner, er det et realistisk mål for forsøgspersoner med ukomplette læsioner, for hvem genoprettelse af gang det første blandt træningsmålene[1].

Epidemiologiske studier indikerer en stigende andel af ukomplette læsioner blandt rygmarvsskader (dvs. med en chance for at genoprette gangevnen)[2], og genoprettelse af gang er blevet målet for flere rehabiliteringsteknikker[3].

Blandt forsøgspersoner med rygmarvsskader har alder og muskelstyrke i benene almindeligt set været hovedfaktorerne, der påvirker gangfunktionen[4]. Som følge heraf forsøger de fleste rehabiliteringstilgange at styrke musklerne i benene. Som tidligere påvist af vores gruppe har mange andre faktorer ud over muskelstyrke dog indflydelse på genoprettelse af gangevnen[5]. Især demonstrerede vi, at balance, spasticitet såvel som vægt og distance mellem læsionen og benene er hovedfaktorer, der påvirker gangevnen hos forsøgspersoner med rygmarvsskader. Baseret på disse statistiske resultater blev følgende hypotese opstillet: Aflastning af kropvægt såvel som balance- og spasticitetsspecifikke behandlinger kan forbedre gangevnen hos rygmarvsskadede forsøgspersoner. Som følge heraf forsøgte dette studie at teste forskellige tilgange til at forbedre gang og at undersøge effekterne af vægtreduktion som følge af et akvatisk miljø på rygmarvsskadede forsøgspersoners gang evne:

i) Effektivitet af opgave-specifik biofeedback balancetræningtil at understøtte gangevne:

For nyligt er det blevet påvist, at balance er en hovedfaktor for genoprettelse af gangevnen. Målet med studiet var derfor at vurdere passende parametre og indekser for balancetræning for rygmarvsskadede forsøgspersoner og bestemme effektiviteten af opgave-specifik visuel biofeedback balancetræning (oVBBT) til at forbedre balanceevne og gang i sammenligning med konventionel rehabilitering på fast underlag. To forskellige forsøgsdesigns blev anvendt; et serielt tværsnitsundersøgelsesparadigme blev brugt til at estimere rehabiliteringen, validiteten og følsomheden af balance-platformsparametre, mens et åbent casestudie med retrospektiv kontrol blev brugt til studiet af oVBBT-træning. Resultaterne gjorde det muligt at definere pålidelige, valide og effektive parametre til at evaluere balanceevnen hos rygmarvsskadede forsøgspersoner og demonstrere, at oVBBT-træning er effektiv til at forbedre balance og gang for forsøgspersoner med kronisk ukomplet rygmarvsskade.

ii) Effektivitet af neuromuskulær kinesiotaping (KT) til at reducere spasticitet og forbedre gang:

I de senere år er KT blevet foreslået anvendt til at forstærke sensorisk input, reducere spasticitet fra proprioceptiv sansefeedback og aflaste anormal muskelspænding. Vores mål var at analysere effekterne af KT anvendt på ankelled for spasticitet, balance og gang hos rygmarvsskadede forsøgspersoner. Et randomiseret crossover case-kontrolstudie blev anvendt til at sammenligne effekterne af KT og konventionel ikke-elastisk silketape på 11 kroniske rygmarvsskadede forsøgspersoner. Resultaterne viste, at kortsigtet brug af KT reducerer spasticitet og smerte samt forbedrer balance og gang hos kronisk rygmarvsskadede forsøgspersoner.

iii) Effekten af vands opdriftskraft på gangkarakteristik hos rygmarvsskadede forsøgspersoner:

Målet med dette studie var at karakterisere gangegenskaber hos forsøgspersoner med ukomplet rygmarvsskade, der går i vand og på land, i forhold til raske kontrolforsøgspersoner for at identificere, hvordan af det akvatiske miljø påvirker gangevnen hos rygmarvsskadede forsøgspersoner. Kinematiske gangparametre og bevægelseområderne for ledvinkler for 15 rygmarvsskadede forsøgspersoner og 15 kontrolforsøgspersoner blev analyseret. Resultaterne indikerer, at gang i vand for rygmarvsskadede forsøgspersoner var associeret med kinematiske parametre og mere lig de raske kontrolpersoners gang, især i forhold til hastighed, skridtlængde og standfase, hvilket understøtter hypotesen, at gang i vand kan være signifikant for rehabiliteringsprotokoller for rygmarvsskadede forsøgspersoner.

Balance, somatosensoriske input og kropsvægt er tydeligvis tæt relaterede i påvirkningen af gangfunktioner. Vægt, spasticitet og nedsat balance er også begrænsende faktorer for normal gang hos forsøgspersoner med rygmarvsskade[5]. Balancenedsættelse er tydeligvis associeret med en stigning i prævalensen for fald og efterfølgende skader[6]; ankelspasticitet anses for at være en af de hyppigste forstyrrelser af normal gang hos ukomplet rygmarvsskade[5;6] og der er en generel konsensus om, at træning i akvartisk miljø er brugbart til genoptræning af gang efter rygmarvsskade[7]. Dette studie undersøgte disse tre faktorer ved hjælp af specifikke tilgange og demonstrerede videreførelsen af forbedring i balancen til forbedring af gang; ved at følge nye veje til spasticitetsbehandling, ved at udnytte somatosensoriske input via KT og ved at karakterisere effekten af et akvartisk miljø på gang fra et kinematisk synspunkt.

Gangkontrolmekanismer er mangfoldige og inkluderer spinale, supraspinale og perifere inputs, og det er tænkeligt, at behandlinger, der sigter mod at genoprette gangevnen, burde udnytte alle involverede systemer. Dette studie demonstrerede vigtigheden af at definere forskellige systemers bidrag til gangnedsættelsen efter rygmarvsskade samt vigtigheden af, at udvikle patientcentrerede protokoller, som selektivt målretter en passende behandling til det skadede system.

3 List of abbreviations

- 6MWT: Six Minute Walking Test
- A: area of the ellipse encompassing 90% of COP samples
- AIS: ASIA Impairment Scale
- AIS A: complete spinal cord lesion
- AIS B: sensory incomplete spinal cord lesion
- AIS C: motor incomplete spinal cord lesion
- AIS D: motor incomplete spinal cord lesion
- AIS E: normal
- ASIA: American Spinal Injury Association
- BBS: Berg balance scale
- BBS: Berg Balance scale
- BWS: body-weight support
- BWSTT: supported treadmill training
- CE: eyes closed
- CI: coactivation index
- COM: body's center of mass
- COM: centre of mass
- COP: he center of pressure
- COP: the center of pressure
- CPG: central pattern generators
- CV: coefficient of variation
- DTS: double-time support phase
- EHL: extensor hallucis longus
- EMG: electromyographic
- ES: effect size
- FA: feet apart at a comfortable distance
- FES: functional electric stimulation
- FT: feet together
- G: gastrocnemius
- GPS: Global Pain Scale
- HD: heel distance
- ICC: intraclass correlation
- KT: KinesioTaping
- L: COP path length
- LEMS: lower extremities motor score
- MAS: Modified Ashworth Scale
- MDC_{95}: minimal detectable change
- MVC: maximal voluntary contraction

- NTSCI: non-traumatic spinal cord injury
- OE: eyes open
- PSFS : Penn modified Spasm Frequency Scale
- RGO: reciprocating gait orthosis
- ROM: range of motion
- RMS: Root mean square
- S: soleus
- SA1 and SA2: length of A semiaxes
- SCATS : Spinal Cord Assessment Tool for Spastic Reflexes subscale for clonus assessment
- SCI: spinal cord injury
- SEM: the standard error of measurement
- SOA: state of the art
- SP: stabilometric platform
- Spearman correlation coefficient (
- ST: non elastic silk tape
- TA: tibialis anterior
- TMWT: Ten Meters Walk test
- TS: Tinetti scale
- TSCI: traumatic spinal cord injury
- TUG: Timed Up and Go test
- V: COP mean velocity
- V_{AP}: COP anteroposterior velocity
- VAS: visual analog scale
- vBFB: visual biofeedback
- V_{LL}: COP laterolateral velocity
- WHO: World Health Organization
- WISCI: walking index for SCI
- WISCI: Walking Index for Spinal Cord Injury
- WL: walking on land
- WW: walking in water
- X: mean position of COP along the planar laterolateral coordinates on the platform
- Y: mean position of COP along the planar anteroposterior coordinates on the platform

4 INTRODUCTION

The Edwin Smith papyrus, an ancient Egyptian physician textbook, described, in 1700BC, Spinal Cord Injury (SCI) as an ‘‘ailment not to be treated’’[8]. Actually SCI can be defined as lesion that occurs in any portion of the spinal cord and results in complete or incomplete impairment in motor, sensory and autonomic functions below the injury level[8]. SCI aetiology may be traumatic or non-traumatic. As recently reported by Lee et al. [9] “traumatic spinal cord injury (TSCI) is a catastrophic event that is sudden and unexpected and can be devastating and costly in human and social terms. TSCI in developed (high income) and developing countries primarily affects males aged 18–32 years, and in developed countries, due to an ageing population, males and females over the age of 65 years. Globally, knowledge on the number of people living with TSCI (prevalence) as well as the number of new cases annually (incidence) is minimal, particularly in developing countries, hindering injury prevention, health care and other social planning”. Also New at al.[10] reported that “damage to the spinal cord can arise from many causes other than trauma, often referred to as non-traumatic spinal cord injury (NTSCI). Compared with TSCI, there are relatively few publications on NTSCI. It is anticipated that with the aging of the global population in coming decades the incidence of NTSCI will increase substantially”.

Depending on the lesion level and severity, SCI may impact sensorimotor and/or autonomous functions. In affected subjects the overall goal of rehabilitative interventions is the regaining of independence associated with a good quality of life. Quality of life can be scored quite differently. From patient’s perspective targeting restoration of bladder and bowel function is the principal gals in subjects with paraplegia, while subjects with tetraplegia consider recovery of upper limb function as prominent [11]. However, recovery of locomotor ability is also of high priority by SCI subjects independently from severity, time after injury and age at the time of injury[11]. Walking recovery is a realistic goal for subjects with incomplete lesions, among which recovery of walking is rated at first place of rehabilitation objectives[1].

Consequently, walking recovery has become the target of several rehabilitation approaches. SCI gait rehabilitation is based on the re-organization of pre-existing and new neural circuits[12] by optimising those parts of sensorimotor system still intact[13, 14]. Recent studies underlined the crucial role of task-specific sensory cues to favour the recruitment of both spinal circuitries and spared supraspinal connections during rehabilitation. Even if standardized rehabilitation procedures became established in the past 20 years, there is still no full consensus on the most effective approaches.

Worthy to note that in subjects with SCI, age and lower extremity muscle strength have been commonly considered the main factors affecting walking function[4]. Consequently, most rehabilitation approaches aimed at reinforcing the lower extremities. However, as recently reported by our group, many factors besides muscle strength influence the recovery of walking function[5]. In particular, we demonstrated that balance and spasticity, as well as weight and distance from the lesion, are key factors affecting walking performance in SCI subjects[5]. From this evidence derived the

hypothesis that weight unloading as well as balance and spasticity specific treatments, might improve gait performance in SCI. In this line, the present thesis aimed at testing different approaches to improve gait and at investigating effects on gait of body weight reduction in water environment in subjects with motor incomplete SCI.

5 SPINAL CORD INJURY LESION

The spinal cord is situated within the spinal column (*Figure 1*), it extends down from the brain to the L1−L2 vertebral level, ending in the conus medullaris.

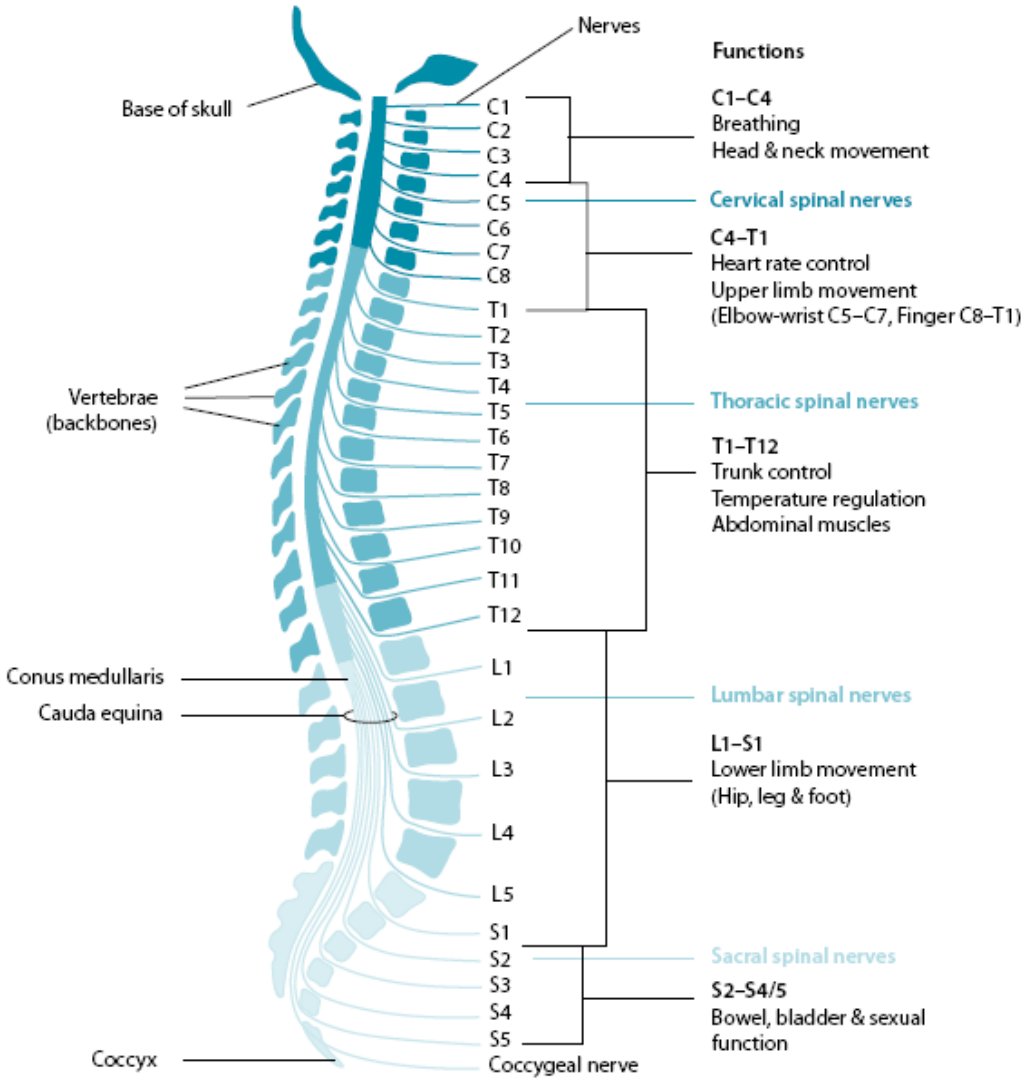


Figure 1: Longitudinal organization of the spinal cord (with cervical, thoracic, lumbar and sacral segments shaded), spinal vertebrae, and spinal nerves and a rough representation of major functions of the spinal cord.

Continuing from the end of the spinal cord, in the spinal canal, is the cauda equina (or "horse's tail"). The spinal cord itself has neurological segmental levels that correspond to the nerve roots that exit the spinal column between each of the vertebrae. There are 31 pairs of spinal nerve roots: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal. Owing to the difference in length

between the spinal column and the spinal cord, the neurological levels do not necessarily correspond to the vertebral segments[8].

Spinal cord injury lesion (SCI) may be traumatic (TSCI) or non-traumatic (NTSCI). Traumatic SCI can result from many different causes – including falls, road traffic injuries, occupational and sports injuries, and violence. Non-traumatic SCI, on the other hand, usually involves an underlying pathology – such as infectious disease, tumour, musculoskeletal disease such as osteoarthritis, and congenital problems such as spina bifida, which is a neural tube defect that arises during development of the embryo.

The symptoms of spinal cord lesion depend on the extent of the injury or non-traumatic cause, but they can include loss of sensory or motor control of the lower limbs, trunk and the upper limbs, as well as loss of autonomic (involuntary) regulation of the body. This can affect breathing, heart rate, blood pressure, temperature control, bowel and bladder control, and sexual function.

In general, the higher up the spinal cord the lesion occurs the more extensive the range of impairments will be. Cervical SCI commonly causes sensory and motor loss (paralysis) in the arms, body and legs, a condition called tetraplegia (the alternative term quadriplegia is now less used). Someone with C4 or higher lesions may require a ventilator to breathe because the lesion directly interferes with autonomic control. Thoracic SCI commonly causes sensory and/or motor loss in the trunk and legs, a condition called paraplegia. Lumbar SCI typically causes sensory and motor loss in the hips and legs. All forms of SCI may also result in chronic pain[15].

The extent and severity of sensory, motor and autonomic loss from SCI depends not only on the level of injury to the spinal cord, but also on whether the lesion is “complete” or “incomplete.” According to the International Standards for Neurological Classification of SCI, with the American Spinal Injury Association (ASIA) Impairment Scale (AIS), an SCI is considered complete if there is no sensory and motor function at S4–S5. While some sensory and or motor function is preserved below the level of injury in incomplete SCI, including the lowest sacral segments S4-S5, it is no less serious and can still result in severe impairments [15].

5.1 Understanding spinal cord injury

SCI is medically complex and life-disrupting condition. Historically, it has been associated with very high mortality rates. Yet today, in high-income countries, SCI can be viewed less as the end of a worthwhile or productive life and more as a personal and social challenge that can be successfully overcome. This change reflects better medical provision, which means that people are able to survive, live and flourish after injury. For instance, people who develop SCI can now usually benefit from improved emergency response, effective health and rehabilitation interventions, and technologies such as respirators and appropriate wheelchairs, together with more extensive social services and more accessible environments. As a result, lives can be saved and functioning can be maximized. Many people with SCI can now anticipate not just a longer life, but also a fuller and more productive life, than they would have had in previous generations[15].

In low-income countries the situation is very different. Traumatic SCI often remains a terminal condition. Most people with SCI in a country such as Sierra Leone die within a few years of injury.

In low-income countries, and in many middle-income ones, the availability of quality assistive devices such as wheelchairs is very limited, medical and rehabilitation services are minimal, and opportunities to participate in all areas of personal and social life are constrained. The situation in many developing countries today is comparable to what it was in Europe and North America in the 1940s. Poverty makes life even harder for people with SCI. Yet the fact that such dramatic progress in survival and participation has been seen in high-income countries over a relatively short period of time should be a reason to be optimistic for other parts of the world. With the right policy responses, it should be possible to live, thrive and contribute with SCI anywhere in the world [15].

5.2 Spinal cord injury classifications

The neurological damage caused by both traumatic and non-traumatic SCI prevents sensory and motor information from travelling to and from the brain below the level of the injury. The impact of SCI on function will depend on the level and severity of injury and the available health care. The International Standards for Neurological Classification of Spinal Cord Injury are often used in health-care settings to describe the extent of injury (including type and level of injury) on the basis of a systematic sensory and motor examination of neurological function [15].
SCI can be divided into two types of injury on the basis of severity , namely:

- *Complete injury* − people who experience a complete injury have no sensory or motor function below the level of the SCI and specifically at S4–S5.
- *Incomplete injury* – people who experience an incomplete injury retain some function

  (i.e. sensory and muscular) below the neurological level of injury, including at the lowest sacral segments S4–S5. There are different types of incomplete SCI, such as anterior, central and posterior cord syndrome, and Brown-Sequard syndrome, which can influence residual function.

The level at which the spinal cord is damaged determines which parts of the body may be affected by paralysis, i.e. loss of muscle function and sensation[15]:

- *Paraplegia* – refers to an injury to the thoracic (T2−T12), lumbar (L1−L5) or sacral (S1−S5) segments of the spinal cord, which includes the conus medullaris (distal bulbous part of the spinal cord) or to the cauda out from the spinal cord at L1−L2). It results in a loss of varying degrees of control of the lower limbs and trunk without involvement of the upper limbs. For example, people with complete injuries between T2 and T8 will have poor trunk control, due to a lack of abdominal muscle control, and total loss of function in the lower limbs; people with complete lower level injuries between T9 and T12 will have good trunk and abdominal control and total loss of function in the lower limbs; while people with lumbar and sacral injuries will have some control over their lower limbs. Figure 1.1 in Chapter 1 shows the location of the different segments of the spinal cord.

- *Tetraplegia* – is used to describe an injury to the cervical segments of the spinal cord, i.e. between C1 and T1. Depending on the severity and level of injury, tetraplegia results in varying degrees of functional loss in the neck, trunk, and upper and lower limbs. For example, people with complete C1−C3 injuries will require the assistance of a ventilator to breathe; people with complete C5 injuries will have shoulder/upper arm control but no wrist/hand control; people with complete C6 injuries will have wrist extension but no hand/finger function; and people with complete C7−C8 injuries will be able to control their upper limbs but will experience problems with hand/finger dexterity.

In addition to the motor-sensory loss, SCI affects the autonomic neurologic function of the body, resulting in multiple impairments such as loss of bowel, bladder and sexual functions. People with SCI also experience a range of activity limitations and participation restrictions in areas such as mobility (e.g. changing body position, transferring, walking), self-care activities (e.g. bathing, dressing, toileting, eating), domestic activities (e.g. cleaning, cooking, caring for others), education, employment, maintenance of social relationships, and participation in leisure activities[15].

5.3 Traumatic spinal cord injury

5.3.1 Incidence

In a very recent literatur review Lee et al. [9] updated the global maps for TSCI. A global-incident rate (2007) is estimated at 23 TSCI cases per million (179 312 cases per annum). Regional data are available from North America (40 per million), Western Europe (16 per million) and Australia (15 per million). Extrapolated regional data are available for Asia-Central (25 per million), Asia-South (21 per million), Caribbean (19 per million), Latin America, Andean (19 per million), Latin America, Central (24 per million), Latin America-Southern (25 per million), Sub-Saharan Africa- Central (29 per million), Sub-Saharan Africa-East (21 per million) [9] (*Figure 2*).

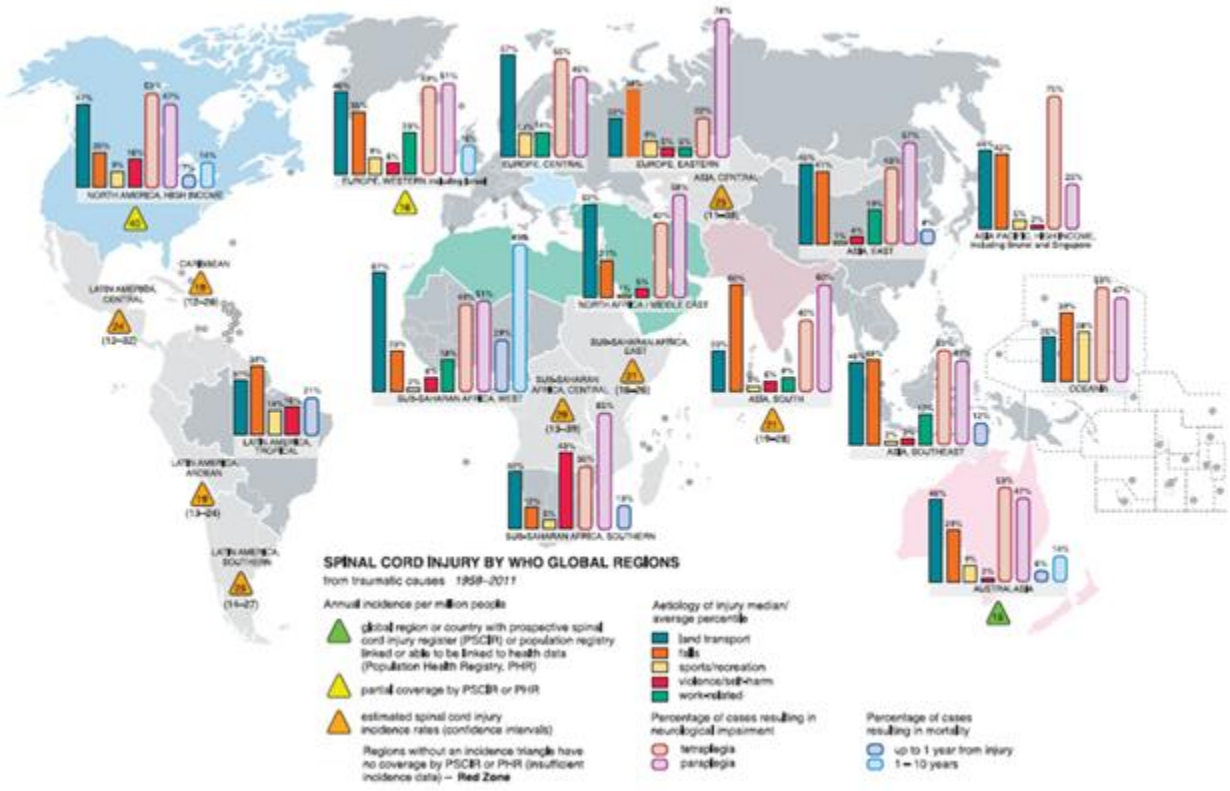


Figure 2: Spinal cord injury by World Health Organization (WHO) Global Regions from traumatic causes 1959–2011 [Lee et al. 2014].

5.3.2 Causes

It is estimated that globally in 2007, there would have been between 133 and 226 thousand incident cases of TSCI from accidents and violence. The proportion of TSCI from land transport is decreasing/stable in developed but increasing in developing countries due to trends in transport mode (transition to motorised transport), poor infrastructure and regulatory challenges. TSCIs from low falls in the elderly are increasing in developed countries with ageing populations. In some developing countries low falls, resulting in TSCI occur while carrying heavy loads on the head in young people. In developing countries high-falls feature, commonly from trees, balconies, flat roofs and construction sites. TSCI is also due to crush-injuries, diving and violence [9] (*Figure 3*).

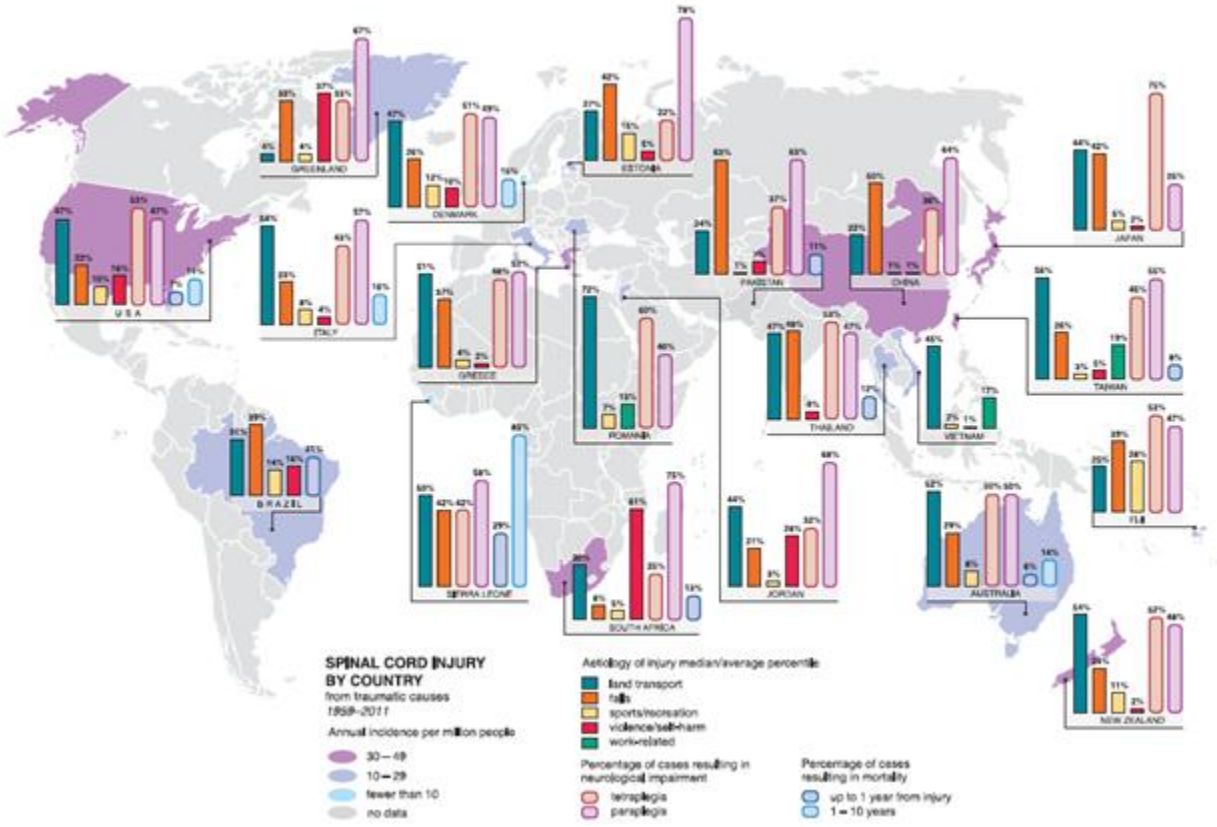
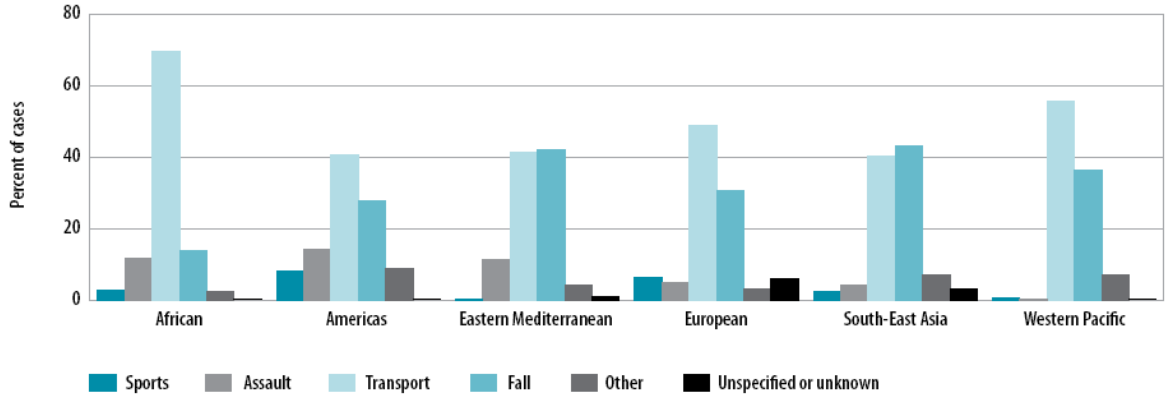


Figure 3: SCI by country from traumatic causes [Lee et al. 2014].

Based on available evidence on the etiology of TSCI across World Health Organization (WHO) [15] regions, the three most common causes are transport (road traffic crashes in particular), falls and violence (*Figure* 4) and is evident the higher incidence of falls among the elderly (*Figure 5*)



Note: The numbers of countries providing data for regional summary are as follows: African 3 countries; Americas 4; Eastern Mediterranean 5; European 13; South-East Asia 3; and Western Pacific 3 countries.
Sources: African – (*38–45*); Americas – (*12, 30, 32, 35, 46–52*); Eastern Mediterranean – (*4, 53–56*); European – (*2, 3, 9, 13, 17, 18, 20, 26, 57–67*); South-East Asia – (*68–72*); Western Pacific – (*16, 21, 22, 34, 73–80*).

Figure 4: Distribution of TSCI by WHO region [International Perspectives on Spinal Cord Injury, ISCOS, 2013]

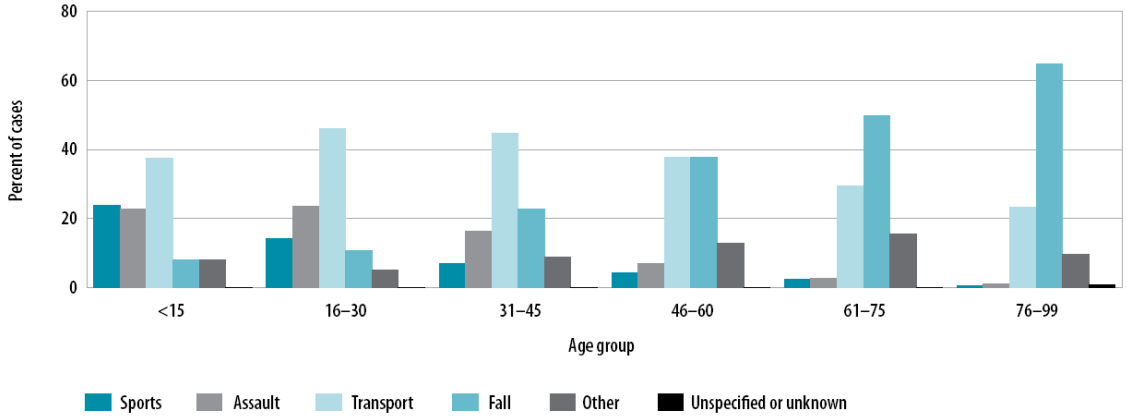


Figure 5: Aetiology of SCI by age group [International Perspectives on Spinal Cord Injury, ISCOS, 2013]

5.4 Non-traumatic spinal cord injury

5.4.1 Incidence

There are far fewer studies on NTSCI incidence than TSCI incidence[10]. Global and regional incidence rates cannot be estimated because existing studies are not representative or comparable, owing to methodological issues such as different inclusion/exclusion criteria, incomplete case ascertainment, or inadequacies in reporting population at risk. The NTSCI incidence rate in Canada is estimated to be 68 per million. Australian estimates, using data from the State of Victoria, report an incidence of 26 per million . Data from a hospital with a specialized SCI unit in Spain report 11.4 per million. The incidence of NTSCI varies by both age and sex. As with TSCI, incidence rates of NTSCI are higher among males than females. In contrast to TSCI, NTSCI incidence increases steadily with age, with risk probably influenced by the increase of ill health with increasing age. Since NTSCI is more common in older age groups, and given global ageing, NTSCI incidence will increase and may overtake that of traumatic TSCI in the next decades. Recently New et al. [10] reviewed 377 publications and 45 reports from 24 countries in 12 of the 21 lobal regions including informations on the incidence, prevalence, survival, level of injury and aetiology of NTSCI. There was a paucity of quality population-based incidence data on NTSCI. Global maps of NTSCI epidemiological outcomes (1959–2011) are presented by WHO global regions (*Figure 6*) and countries (*Figure 7*).

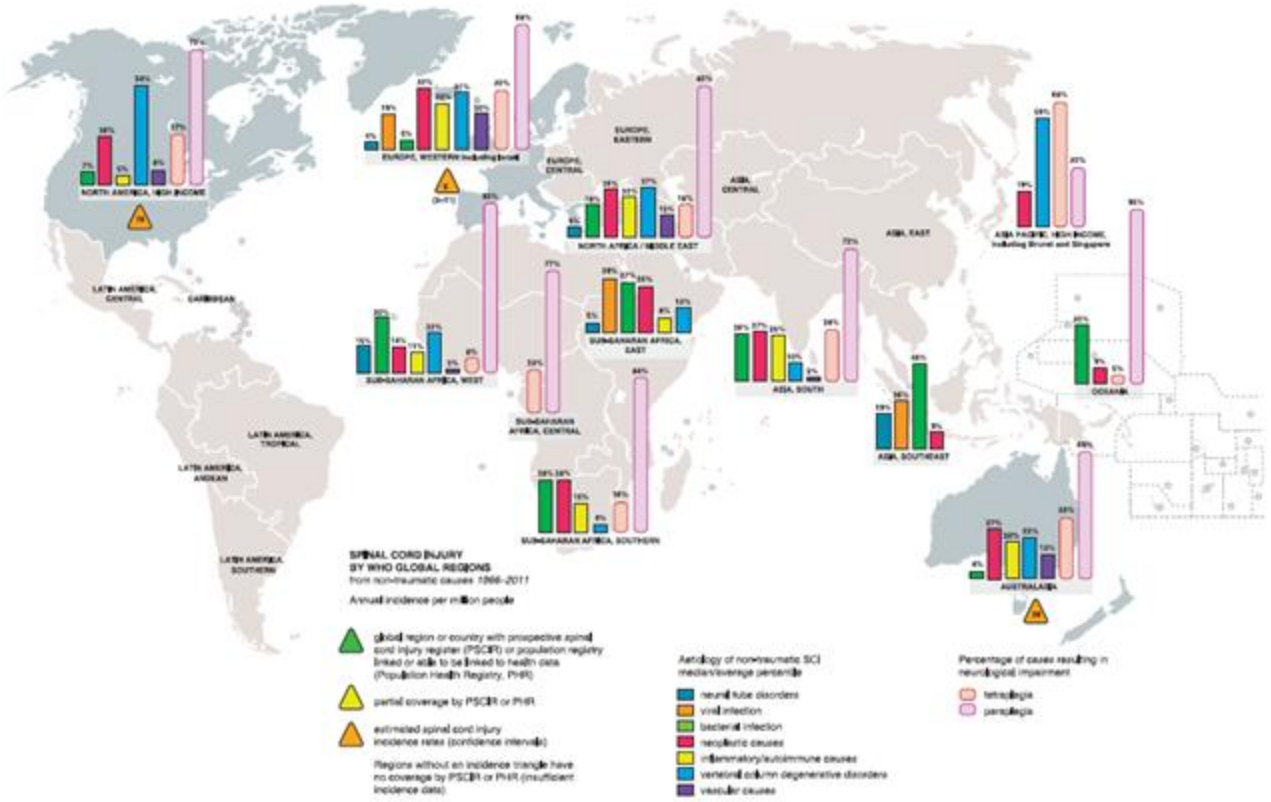


Figure 6: Global maps of NTSCI epidemiological outcomes (1959–2011) by WHO global regions [New et al. 2014].

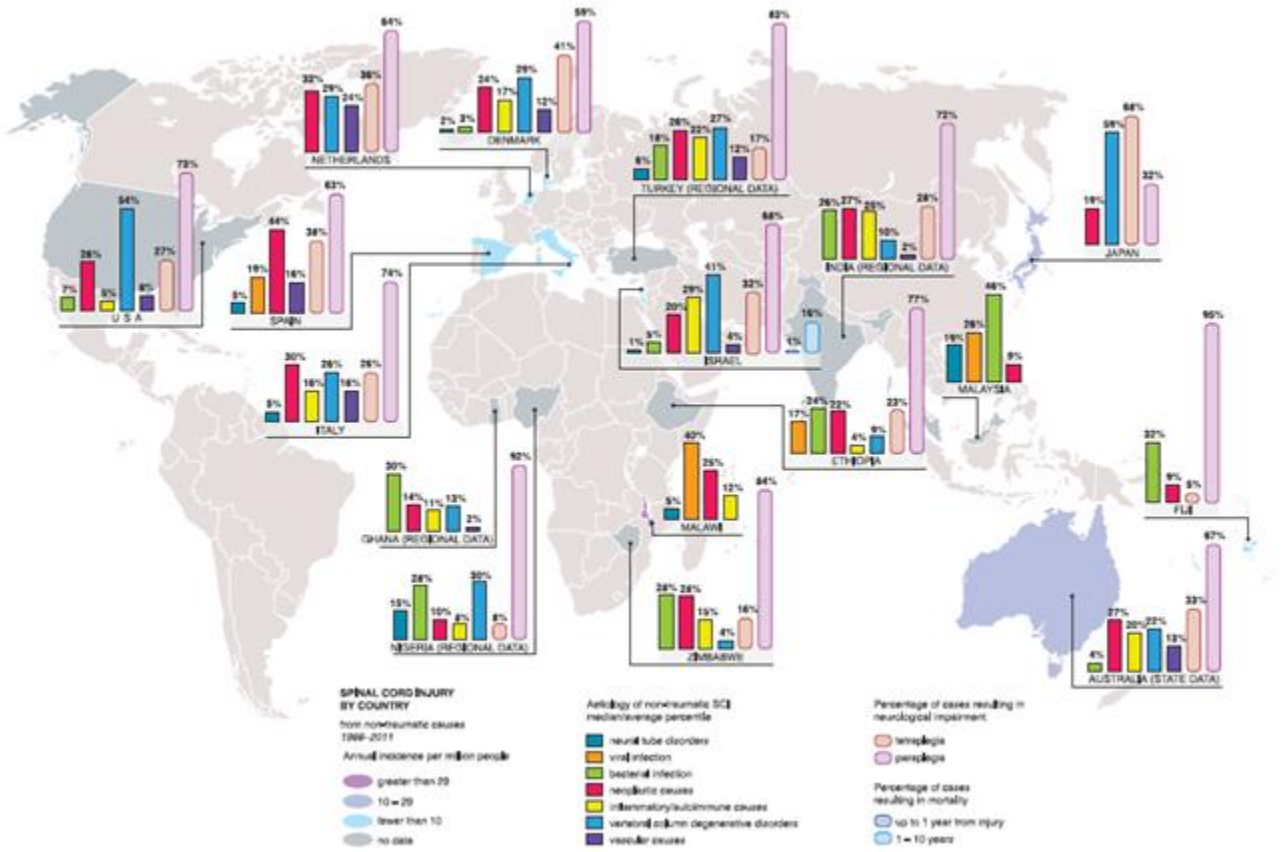


Figure 7: Global maps of NTSCI epidemiological outcomes (1959–2011) by country [New et al. 2014].

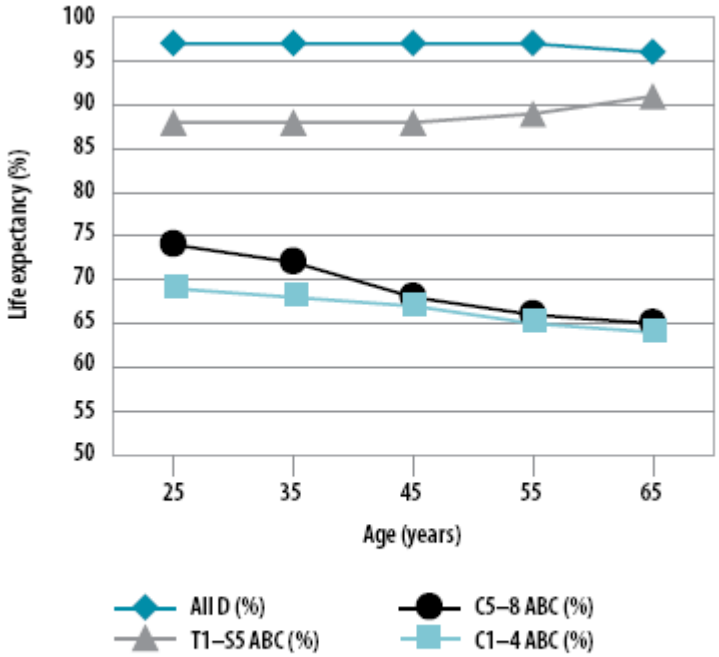
5.4.2 Aetiology

There are few reliable national data concerning the etiology of NTSCI, but studies suggest that the leading causes are neoplastic tumours and degenerative conditions of the spinal column, followed by vascular and autoimmune disorders . In countries such as India, Peru and Sweden, where there are high levels of tuberculosis and other infectious diseases, these dominate all causes of NTSCI except tumours . Congenitally and genetically caused cases such as spina bifida are not recorded in these studies, as these are typically collected in different settings.

5.5 Mortality and life expectancy

Improvements in SCI recognition, evaluation, pre-hospital management, trauma care services, general clinical care and rehabilitation service have resulted in longer life expectancy for people with SCI in high-income countries, alongside a decreased risk of mortality from secondary conditions. People with SCI remain more likely to die – and to die earlier – than people without SCI. They are also more likely to die from certain health conditions than people in the general population. In most cases, the first year after injury holds the highest risk of death for people with SCI, and many people with SCI in low-income countries are dying from preventable secondary conditions[15]..

- *People with SCI die earlier than people without SCI.* Overall, studies have indicated that people with SCI are 2 to 5 times more likely to die prematurely than people without SCI. Another way to assess the effect of SCI is to consider its impact on life expectancy, how long a life someone can expect to live. Few studies compare people with SCI to the general population. However, one Australian study showed that individuals with a spinal cord lesion level between C1 and C4 have only 70% of the life expectancy of the general population at the age of 25 (*Figure 8*). The first year after injury has the highest risk of mortality for people with SCI.



Note: A: complete paralysis; B: sensory function only below the injury level; C: incomplete motor function below injury level; D: fair to good motor function below injury level.

Figure 8: Life expectancy in Australia by attained age for people with SCI in comparison to general population [International Perspectives on Spinal Cord Injury, ISCOS, 2013].

- *Among people with SCI, mortality risk depends on the level and severity of the injury.* Tetraplegics die earlier than A Finnish study found that the SMR for paraplegia was 2.3 as compared to 3.0 for tetraplegia, while in Australia the SMR for paraplegia is 1.7 as compared to 2.2 for tetraplegia. The Finnish study also showed that mortality is higher in people with complete lesions as compared to incomplete, with a complete injury nearly doubling the mortality rate of people with paraplegia, and nearly tripling it for those with tetraplegia.
- *Secondary conditions of SCI are no longer the main cause of death of people with SCI in high-income countries.* In high-resource co untries, there has been a shift in principal causes of death from urologic complications, such as urosepsis or renal failure, to causes of death similar to the general population, such as respiratory problems, especially pneumonia and influenza. Some studies have found high rates of mortality caused by heart disease, suicide, and neurological problems. People with SCI however die of these conditions more frequently than people in the general population. In low-income countries, people with SCI continue to die from preventable secondary conditions, e.g. urologic complications and pressure sores. In low-resource countries, although there are few data because of the extremely high rate of "lost to follow-up", evidence indicates that urologic complications remain a common cause of death. Fatal infections from untreated pressure ulcers, because of the absence of adequate medical care, are a common cause of death in low-income countries.

5.6 Spinal cord injury as a challenge to health systems and to society

The complexity of the lived experience of SCI and the variations in that experience around the world mean that, despite being a comparatively low-prevalence condition, SCI has wider implications for monitoring health care. In principle, an individual with SCI will experience nearly every clinical setting that his or her country provides: emergency services, intensive care, surgery, stabilizing medical care, and particularly rehabilitation, including return to the community, vocational rehabilitation and ongoing primary care. SCI care thus provides evidence about the adequacy of a country's services, systems and policies. It can also help clinicians, health professionals, researchers and policymakers to understand the strengths and weaknesses of their health-care system. SCI care is a good indicator of how the overall health system works – or fails to work[15]..

Beyond the health sector, the individual with SCI will require services, resources and access to the social, educational and economic sectors to lead a full and rich life. Turning to civil society, self-help groups, patient groups and other advocacy and disabled people's organizations play a crucial role in offering knowledge, advice and support, and in lobbying for policy change.

If governments and societies fail people with SCI, it is likely that they will fail people with other health conditions as well. Research and data on the experience of SCI is generally relevant to sound public health policy and to wider efforts to remove barriers to care. researchers can benefit from research into other more prevalent conditions that share some or many of the impairments

and daily challenges that confront people with SCI. Given that research into, for instance, accessible public transportation or return-to-work services will tend to concentrate on higher-prevalence health conditions and disabilities, the best evidence available may not involve SCI directly but may focus on people with “mobility problems” or “wheelchair users.” This report takes advantage of all relevant highquality research, whether directed specifically at SCI or taking a broader disability focus.

Estimated global SCI incidence is 40 to 80 new cases per million population per year, based on quality country-level incidence studies of spinal cord injury from all causes. This means that every year, between 250 000 and 500 000 people become spinal cord injured[15]..

Studies that report incidence data for both traumatic and non-traumatic causes of SCI pro-vide information about the overall constitution of SCI populations. This information is important to collect since the resource needs and characteristics of traumatic and non-traumatic populations are different. The proportion of TSCI varies within a wide range and appears to differ across regions. Historically, up to 90% of SCI has been traumatic in origin, but data from the most recent studies indicate a slight trend in recent years towards an increase in the share of NTSCI. The NTSCI population is generally older, with progressive diseases requiring more expensive care, although for a shorter period.

Most studies of SCI incidence cover either TSCI or NTSCI, perhaps because of differences with data sources and data collection methods. The incidence and etiology of TSCI and NTSCI are therefore examined separately below. Data for NTSCI are limited compared to those for TSCI[15]..

6 PREDICTING OUTCOMES IN SPINAL CORD INJURY

6.1 Assessment of spinal cord injury lesion

SCI can disrupt upper and/or lower motor and sensitive pathways and it results in either a complete or an incomplete lesion. Although recent advances in primary damage healing, rehabilitation and prevention of complications have improved the prognosis of SCI[16], the consequences are still traumatic and disabling. The need to predict outcome based on expected neurological recovery and associated functional recovery has been emphasized as essential for health care planning[17] and this need is partially unmet.

A better knowledge of the course and prognosis of recovery after SCI and an understanding of the underlying mechanisms would help in the development of strategies and treatments to enhance neurological recovery.

Prognostic data are essential to evaluate the efficacy of new drugs and therapies (for example to distinguish between the natural recovery and the effect of treatments) and to project the clinical trials (for example to calculate the number of patients needed to obtain statistical power)[18].

The initial neurological examination is the most important instrument for the assessment of the severity and level of the injury. For optimal reliability of the initial examination, the patient must be able to cooperate and follow the instructions of the examiner and should not have major distracting injuries such as a complicated tibia midshaft fracture[19]. Since its introduction in 1969, the Frankel scale, a 5-point severity scale, has commonly been used to determine the severity of the SCI [20](*Table 1*).

Table 1: The Frankel Scale for Spinal Cord Injury That Classifies the Extent of the Neurological/Functional

Frankel Scale		
A	Complete	No motor or sensory function below level of lesion
B	Sensory only	No motor function, but some sensation preserved below level of lesion
C	Motor useless	Some motor function without practical application
D	Motor useful	Useful motor function below level of lesion
E	Recovery	Normal motor and sensory function, may have reflex abnormalities

Deficit into Five Grades

Patients are classified as complete (grade A), sensory only (grade B), motor useless (grade C), motor useful (grade D), or no neurological deficit/complete recovery (grade E). This scale provided a simple, though nonspecific, scheme for the categorization of SCI. Two major limitations of this scale have been identified: (1) the level of the injury is not incorporated into the classification and (2) the scale's inherent subjectivity in judging what constitutes "useful" motor strength. Moreover, the Frankel scale has limited responsiveness to subtle neurological improvements during recovery. These methodological shortcomings of the Frankel scale were recognized by the classification committee of the American Spinal Injury Association and a

major revision of the International Standards for Neurological and Functional Classification of Spinal Cord Injury Patients (International Standards) was published in 2014. Today, the most recent revision of the International Standards[21] are used worldwide for the assessment of the severity and level of the injury (*Figure 9*,*Figure 10*).

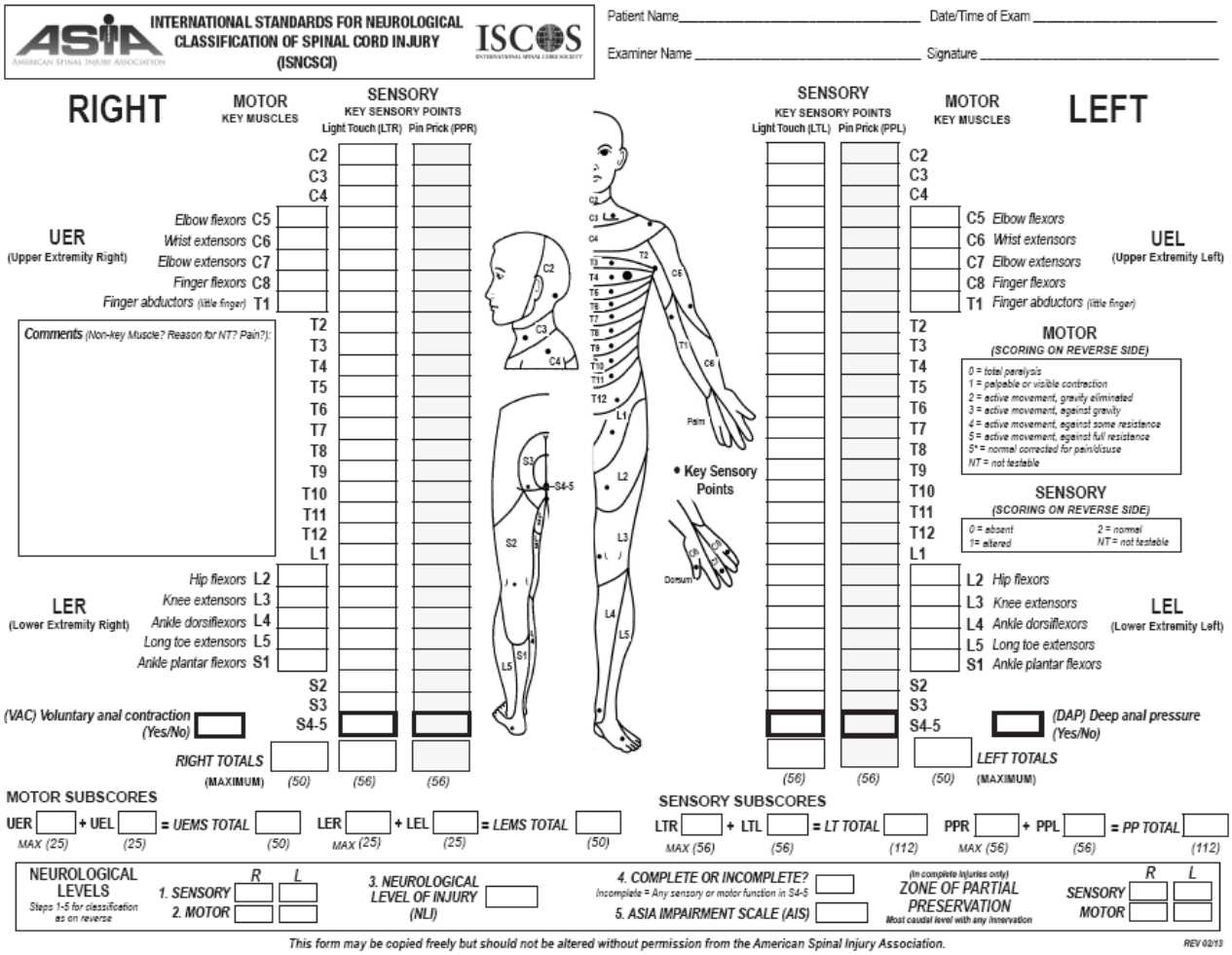
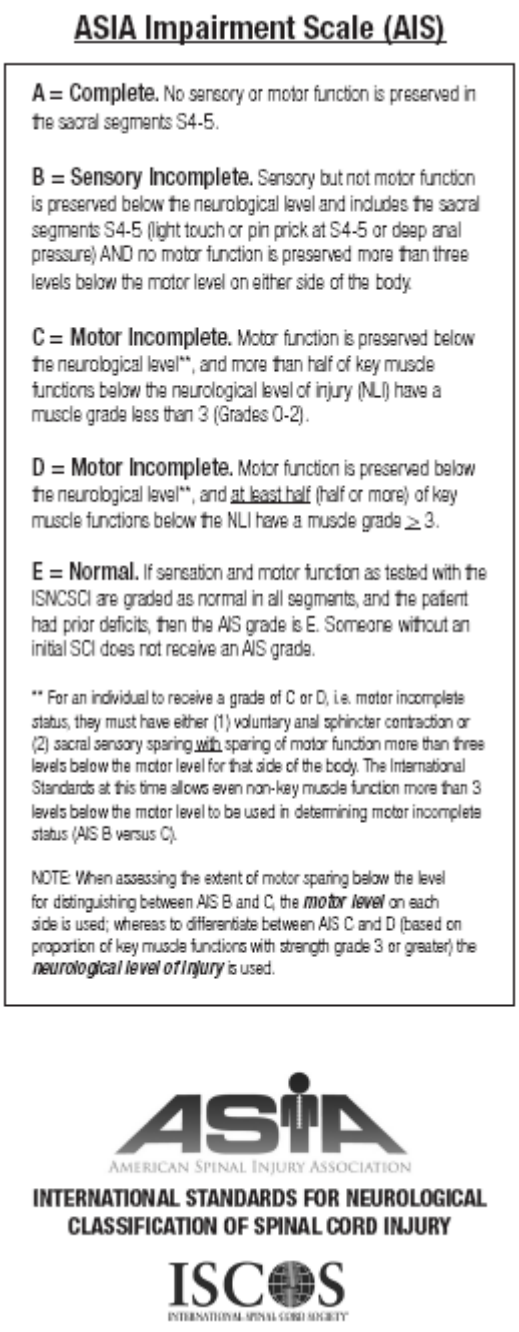


Figure 9: The scoring form of the International Standards for Neurological and Functional Classification of Spinal Cord Injury Patients.

Based on this examination it is possible to establish the neurological level of injury, as well as the severity of the lesion (impairment). Components also include a rectal examination for voluntary anal contraction and anal sensation. According to the ASIA Impairment Scale (AIS), patients are considered to have a complete lesion (AIS A), in the absence of sensory or motor function at the lowest sacral segments. Incomplete lesions are defined when sensation and/or motor function are preserved below the neurologic level of injury, and in particular in the lowest sacral segments (anal sensation, including deep anal pressure and voluntary external anal sphincter contraction).

AIS scores are considered essential when classifying persons with SCI as to their neurological status as follows:



ASIA Impairment Scale (AIS)

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 below the neurological level**, and more than half of key muscle functions below the neurological level of injury (NLI) have a muscle grade less than 3 (Grades 0-2).

D = Motor Incomplete. Motor function is preserved below the neurological level**, and at least half (half or more) of key muscle functions below the NLI have a muscle grade ≥ 3.

E = Normal. If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

** For an individual to receive a grade of C or D, i.e. motor incomplete status, they must have either (1) voluntary anal sphincter contraction or (2) sacral sensory sparing with sparing of motor function more than three levels below the motor level for that side of the body. The International Standards at this time allows even non-key muscle function more than 3 levels below the motor level to be used in determining motor incomplete status (AIS B versus C).

NOTE: When assessing the extent of motor sparing below the level for distinguishing between AIS B and C, the ***motor level*** on each side is used; whereas to differentiate between AIS C and D (based on proportion of key muscle functions with strength grade 3 or greater) the ***neurological level of injury*** is used.

ASIA
AMERICAN SPINAL INJURY ASSOCIATION
INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY
ISCOS
INTERNATIONAL SPINAL CORD SOCIETY

- A: complete. No sensory or motor function is preserved in the sacral segments S4-S5.
- B: sensory incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 (light touch, pin prick at S4-S5 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 below the neurological level and more than half of key muscle functions below the single neurological level of injury) have a muscle grade less than 3.
- D: motor incomplete. Motor function is preserved below the neurological level and at least half of key muscle functions below the NLI have a muscle grade of 3 or greater.
- E: normal. If sensation and motor function as tested with are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

Figure 10: AIS scores for neurological status classification.

Generally as concerns neurological improvement:

- Overall patients who present with AIS A at initial evaluation have a chance of AIS grade improvement of 11% at discharge and of 15% at one year

- For AIS B the respective chances of improvement are 58% and 80%, with 33% of the patients improving to AIS D at one year

- For AIS C subjects the percentages are 57% at discharge and 75% at one year and 67% reach an AIS D grade.

- Finally, only 4.2 % of AIS D subjects improve due to a ceiling effect

- The percentage of patients with complete lesion who become incomplete is reduced if, in addition to the presence of sensory or motor activity in the anal level, motor activity is required in at least one of lower extremities key muscles.

- Most of the neurological recovery occurs in the first 2-3 months after injury.

Neurologic recovery is of fundamental importance for the patients, as the completeness or incompleteness of the lesion are one of the most relevant determinant of the functional outcomes. The general picture of recovery after spinal injury is well known. A proportion of patients with severe sensorimotor loss will achieve a partial or almost complete neurological recovery, particularly if they have some retained neurological function below the level of injury. Overall about 30% of the patients achieve an improvement of their AIS grade; 19% improve by one AIS grade, 8% by two grades and 3% of 3 grades[22].

When talking about neurologic improvement, several issues must be taken into account: the conversion of AIS grade and its nature, the improvement of motor scores, the improvement of lesion level in tetraplegic patients, the timing of recovery and the relationship with the zone of partial preservation below the level of injury.

6.2 State of the Art (SOA) on gait recovery prediction

Walking recovery is one of the main goal of patients after SCI: walking is rated at first place by patients with incomplete lesions[1]. Furthermore, epidemiological studies show an increase of the number of patients with incomplete lesions (e.g. with chances of walking recovery)[23]. Therefore, the recovery of ambulation has become the target of several pharmacological and rehabilitative approaches. Consequently a precise evaluation of the natural recovery of walking and of the prognostic factors influencing this function has become mandatory[5;24].

Furthermore, for the selection of people with SCI who might profit most from a locomotor training programme, an early prediction of ambulatory function is helpful. For example, rehabilitation of people with an (almost) complete SCI and an unfavourable prediction, rehabilitation should be focused on wheelchair driving and on other neurological deficits rather than on the lost stepping ability. Using clinical and electrophysiological assessments, a reliable prediction of stepping ability can be made that consequently allows the planning of rehabilitation procedures, e.g. locomotor training, within 4 weeks after a SCI. The essential criteria for a such a stratification are the initial lower limb motor scores combined with preservation of spinal impulse

conductivity (i.e. presence of tibial somatosensory potentials) or, combined with lower limb light touch sensation[25].

Walking recovery is defined as the regained ability to walk independently in the community, with or without the use of devices and braces. This is also defined "functional walking" and has been described as the capacity to walk reasonable distances both in and out of the home unassisted by another person [26]. Crucial factors for walking recovery are described below.

6.2.1 AIS grade

For a long time AIS grade conversion has been considered the basis to predict the possibility of achieving functional walking[27]. Patients with AIS A (motor and sensory complete lesion) at their first examination have very few chances of neurological recovery below the lesion (2.5-20% depending on the time of first examination) [28]. Accordingly, the possibility of patients with AIS A of achieving functional walking is very limited too. Furthermore, also between the patients who converted to an incomplete lesion only 14% recovered some walking function [29]. AIS A patients who achieve some walking function usually are low thoracic or lumbar levels (T12-L3) and usually need braces and devices to walk [30]. Finally these patients are usually limited ambulators, with slow average velocities and great energy expenditure [31].

AIS B patients usually show some motor recovery and they can convert to AIS C or even AIS D grade. However, the overall recovery of ambulation is considered to be about 33% [29;32]. The percentage of walking recovery may vary depending on the modality of the sensation spared at the lowest sacral segments. Several studies reported a relationship between light touch and pinprick preservation and walking recovery in AIS B patients compared to light touch preservation only. AIS grade B patients with light touch and pinprick preservation have a better walking recovery than those with light touch only [32;33]. This finding has an anatomical basis at the spinal cord level. The preservation of pin-prick and light touch sensation, indicates the integrity of spino-thalamic as well as posterior columns tracts. These structures are relatively close to the corticospinal tracts; therefore, the preservation of the sensitivity structures could indicate some possible sparing of the motor pathways [34].

Motor incomplete (AIS C) patients have a better prognosis for walking recovery than sensory incomplete ones. The overall rate of recovery is about 75% [4;35]. This percentage includes both the patients who converted to AIS D and those who remained AIS C but achieve at least some walking function[29]; these patients probably have low thoracic or lumbar lesions and walk with braces and devices. In these patients several characteristics are of prognostic value for walking recovery: lower extremity strength and upper extremity strength for tetraplegics patients, motor recovery timing and age are the most important ones[4;35]. With regard to the relationship between lower extremity strength at first examination and walking recovery in incomplete paraplegics all patients with an initial (1-month) lower extremity motor score of ≥ 10 points ambulate in 1 year compared to 70% of those with an initial motor score between 1

and 9 [33]. Furthermore, all patients with an initial hip flexor or knee extensor Grade ≥ 2–5 ambulated in the community at 1 year [29]. In incomplete tetraplegics, although the relationship between initial lower extremity motor score and walking hold true, the odds of walking recovery are lower than for paraplegics[36]. In addition, Waters stressed the relationship between upper extremities strength and ambulation recovery in tetraplegics: patients who are community or household ambulators have significant higher motor scores. The author linked this datum to the importance of upper extremities strength for devices use during walking [36]. With regard to the timing of recovery, early recovery of quadriceps strength is an excellent prognostic factor for ambulation [35]. All patients with an initial quadriceps strength of at least grade 2/5 who attain a grade of ≥ 3/5 in at least one quadriceps by 2 months post-injury, achieve functional ambulation at follow-up. However, only 25% of those who do not recover quadriceps strength of 3/5 within 2 months are able to walk at follow-up. With regard to the relationship between age and walking recovery, it will be examined in the paragraph on age effects.

Finally, AIS D patients at admission have very good ambulation prognosis at one year post-injury [37]. All patients, regardless of age, who initially are classified as AIS D (within 72 hours) are able to walk at the time of discharge from inpatient rehabilitation [38].

6.2.2 Strength

Lower extremity muscle strength is the factor most studied in SCL in relation to both functional independence and walking[39]. Early recovery of muscle strength has been identified as a predictor of ambulatory capacity. Waters et al [33] reported that lower extremity motor recovery 1 month postinjury was a good predictor of whether an individual would become a community ambulator at the 1-year follow-up. Moreover, Crozier et al[35] found that individuals who recovered good strength in the less affected quadriceps (greater than grade 3) in the 2 months after SCI had an excellent prognosis for ambulation.

Lower extremity muscle strength has been found to correlate with gait speed and ambulatory capacity in people with both acute and chronic SCI[40]. Kim et al [41] found a correlation between lower extremity muscle strength and gait speed and endurance and with functional classification of community walking. In agreement with these data, in the present study the total motor score and the lower extremity motor score were significantly related to both walking level (Walking Index for Spinal Cord Injury: WISCI) and walking performances assessed at the time tests. Greater muscle strength (particularly of the proximal muscles in the lower extremities) produces lower Timed Up and Go test (TUG) performances, better endurance (distance walked in 6 minutes at Six Minute Walking Test: 6MWT), and a higher walking speed (Ten Meters Walk test: TMWT). Worthy of note is the relationship between upper extremity level and WISCI and 6MWT, which has been demonstrated for the first time in this study. It appears that the use of the upper extremities is particularly relevant for walking, particularly in tests requiring the use of walking aids.

The only study in the literature dealing (indirectly) with the importance of upper extremity strength was carried out by Wirz et al, who found that patients with tetraplegia require substantially more lower limb strength to obtain the same walking function as paraplegic patients [42]. The author attributed this phenomenon to the need to compensate for postural instability because of the upper extremity and trunk weakness [42]. This is in agreement with Waters et al [43], who indicated that subjects with cervical lesions must be more neurologically intact to ambulate because they may have upper extremity weakness that limits their ability to use crutches or walkers.

6.2.3 Age

The negative effect of age on the walking abilities of SCI patients has already been reported in the literature: Burns et al[4] found that walking recovery in patients with incomplete SCI depends on age and is more frequent in young patients in 2003, Scivoletto et al [37] studied 2 cohorts of patients over or under 50 years of age, assessing walking with the WISCI, and showed that the younger patients reached the walking function more frequently. According to previous data, age is correlated with TUG (positively) and with 6MWT (negatively); in the regression analysis, the relationship emerged only with 6MWT. It appears, therefore, that age particularly affects tests requiring long distance walking. This finding is probably associated with the different resistance of elderly patients to physical effort: the 6MWT, in fact, is the test that requires resistance and it might be affected by energy consumption and muscle fatigue, twofactors that can condition performance in the elderly.

6.2.4 Balance

No studies in the literature have dealt with the issue of balance alone in SCI patients. In 2003, Adegoke [44]et al. studied balance in a group of patients with SCI, but took into account only non-standing patients performing a functional reaching test. In 1993, Kralj [45]et al highlighted the issues of balance control during functional electric stimulation (FES) assisted gait in SCI patients and proposed a rehab approach based on statically unstable dynamic weight-transfer phases. In 2006, Leroux [46]et al studied the postural adaptation of SCI patients during walking and concluded that this posture could lead to a loss of balance or a fall.

Our group demonstrated that good balance allows walking with fewer aids and enables patients to have lower times (to walk faster) in the timed test and to walk for longer distances[5]. In a very recent report[47] the authors claimed similar finding in a randomized clinical trial where balance was used together with walking speed, 6MWT, WISCI, and TUG as outcome measures.

6.2.5 Spasticity

The relationship between spasticity and walking has been debated for a long time. In 1975, Norton[48] et al found no significant correlation between spasticity and gait speed in subjects

with hemiplegia. Furthermore, on an empirical base it has been conjectured that spasticity could be an advantage in patients with a lower limb strength deficit because it might increase the support function. However, more recent studies have demonstrated the negative relationship between spasticity and walking ability in patients with neurologic lesions of various aetiology (e.g., cerebral palsy)[49]. Furthermore, in patients with stroke and other neurologic pathologies it has been shown that treating spasticity is associated with an amelioration of walking performances [50;51].

Studies on the relationship between spasticity and walking in SCI patients are scarce and mainly focused the issues of the mechanisms of spasticity during ambulation[52-54] and of the effects of several therapeutic approaches for spasticity on walking[55;56]. These latter studies concluded that spasticity treatment is correlated with amelioration in walking and indirectly demonstrated that spasticity affects negatively walking performances in SCI patients. Elevated muscle tone impairs the fluidity of movements and, therefore, constitutes an obstacle in timed tests in which patients are asked to get up, walk, and sit down in the shorter time possible (TUG) or to walk at maximum speed (TMWT). Furthermore, the inability to perform fluid movements and the need to overcome spasticity (which also tends to increase with an increase in physical work) causes an increase in effort and energy consumption during walking; this becomes more evident as distances increase and, therefore, may lead to a reduction of the distance walked[5].

7 SPINAL CORD INJURY GAIT REHABILITATION

7.1 THE PHYSIOLOGICAL BASIS OF GAIT REHABILITATION

SCI is an event that, depending on the level and severity, impacts sensorimotor and autonomous function. In affected subjects the goal of rehabilitative interventions is the regaining of independence and thus a good quality of life. From the patients perspective this is probably best achieved by targeting restoration of bladder and bowel function, and in tetraplegic subjects upper limb function[11]. However, recovery of locomotor ability is also of high priority by SCI subjects independently from the severity, time after injury and age at the time of injury [11].

Walking recovery is one of the main goals after SCI, although almost never attainable in subjects with complete lesion it's a realistic object for subjects with incomplete lesions, among which recovery of walking is rated at first place among rehabilitation objectives[1].

Gait rehabilitative interventions to harvest such potential must take into consideration fundamental aspects of motor skill learning, as these motor tasks become computationally demanding on spinal cord circuits once severed from supraspinal input[57]. Designing effective neurorehabilitation after SCI depends on having knowledge about the neuronal mechanisms involved in normal and pathological movement conditions, such as the interactions between central programs and afferent feedback as well as the coordination of human locomotion.

7.1.1 Neuronal basis of human locomotion

The question, how does the central nervous system coordinate limb movements during locomotion in a seemingly "simple" and automatic manner challenged neuroscientists for more than a century. At the beginning of the last century Graham-Brown postulated his "half-center" hypothesis based on the demonstration of the intrinsic capacity of the mammalian spinal cord to generate rhythmic motor patterns without descending or sensory inputs. Subsequently Grillner defined these spinal neuronal circuitries central pattern generators (CPGs). CPGs are embedded within the lumbosacral spinal segments and are capable of generating stepping-like activation patterns [58].

However, CPGs alone are not sufficient for overground walking. Gait is achieved through interactions among innate patterns and environmental requirement which require continuous modulation of central circuits. Feedback from a variety of sources, e.g., visual, vestibular and proprioceptive systems, is interpreted by and then integrated into the activity of the CPG [59]. The CPG can open and close reflex pathways in a context- and task-dependent manner. The sensory feedback and the context-specific requirements of the motor task determine the mode of organization of muscle synergies. Additionally, supraspinal control is needed to provide both the drive for locomotion as well as the coordination to interact with a complex environment. Corticospinal access to locomotion control in humans is phase-dependent. Brain centres can initiate CPG activity but the fundamental rhythmicity is hard-wired[11]. It is important that the neuronal mechanisms underlying human locomotor control in the normal and pathophysiological

condition are understood, as it is only then that it is possible to maximize the recovery of locomotion in patients following central nervous system damage.

7.1.2 Clinical aspect of rehabilitation: the role of neuroplasticity

Neuroplasticity comprises the adaptive (including maladaptive) changes within spared neuronal circuitries and thus reflects the reorganization of the nervous system after it has been injured. Neuroplasticity after SCI occurs at several anatomical and physiological levels of the central nervous system, i.e. spinal cord, brainstem and cortex [25]. It includes changes in synaptic formations and synaptic strength, axonal sprouting and changes of intracellular properties[60; 61]. There is also a spontaneous recovery of sensorimotor functions within the first few months after a SCI because of factors such as the resolution of neuropraxia [62] and remyelination of spared axons. It is hard to distinguish the relative contributions of these factors to recovery and there might be an overlap of mechanisms involved in the recovery of neuronal excitability[61].
Changes in sensorimotor system function can be reliably determined by assessing the neurological status (clinical and functional examinations) and electrophysiological recordings (impulse conductivity of the spinal cord and of peripheral nerves by recordings of somatosensory-evoked potentials and neurographic examinations, respectively[63]). According to these assessments, performed over 1 year in individuals with SCI, most of the recovery of sensorimotor deficits and of somatosensory evoked potentials takes place over 12 to 15 weeks[62] . At later stages after the acute injury, a stable phase dominates during which training-induced changes can still be initiated ([64; 65; 66]).
Recovery of motor functions does not solely rely on neuroplasticity, but also on compensation and adaptation. For example, through the assistance of the non-affected or less affected limbs [62]. In the case of locomotor function, the affected leg shows little change in the leg muscle EMG pattern despite a gait recovery [67]. In particular at an early stage restoration of function is achieved by adaptive changes that are based on neural plasticity and, therefore, can hardly be separated. Nevertheless, compensation and adaptation can be viewed as a form of motor learning and thus, by definition, as neuroplasticity.

7.1.3 Functional training approach to enhance plasticity in incomplete SCI

For individuals with SCI, functional training is the most effective approach to direct and enhance plasticity as a mean to recover motor function. Functional training can be defined as the direct/task specific training of a motor function. The mechanisms underlying the effects of facilitating neuroplasticity by functional training have been explored in rodent and cat models of SCI [25]. Using these animal models, rehabilitation of sensorimotor function after SCI is directed toward training lost/impaired movements[68]. Among others, these studies demonstrate that training rats or cats with a transected spinal cord on a moving treadmill leads to a partial recovery of locomotor ability. Thus, neuronal circuits for locomotion in the spinal cord can ‘learn’ by

training independently of the connection to the brain. The mechanisms underlying this training-induced plasticity that lead to an improved recovery of locomotion include, among others, the adaptation of neurotransmitter systems within the spinal cord (glycinergic and GABAergic systems) and enhanced collateral sprouting[69]. Based on these animal studies, training of functional movements (e.g. stepping) was successfully translated to individuals with incomplete SCI[70;71] .

Worthy to note that plasticity promoting approaches, such as functional training to improve outcomes, are restricted to people with incomplete SCI (*Figure 11*).

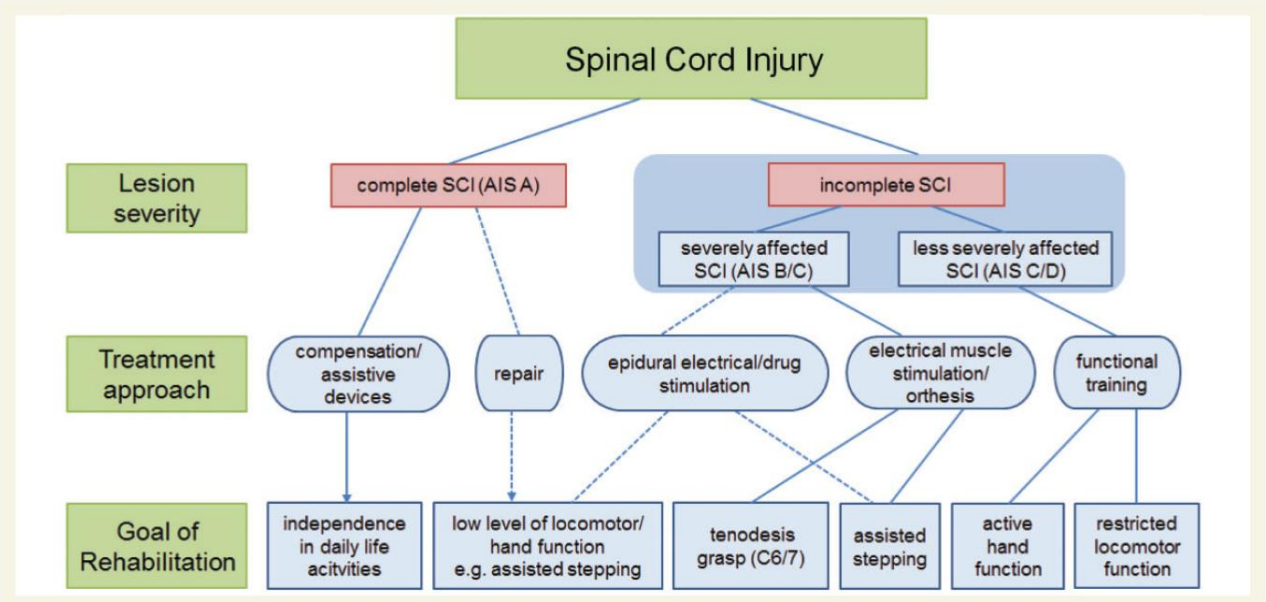


Figure 11: Rehabilitation of a SCI. Schematic overview of actual perspectives of rehabilitation approaches (circular borders) to influence the outcome of a spinal cord injury (angular borders). The individual impairment depends not only on the 'lesion severity' but also on the level of lesion. The selection of an appropriate approach has to be based on an early prediction of outcome and the completeness of injury, respectively. Solid lines indicate currently applied approaches, interrupted lines indicate interventions being on translation to human application *[Dietz V. and Fouad K. 2014]*.

7.2 FACILITATION OF PLASTICITY BY LOCOMOTOR TRAINING

Spinal neuronal circuits below the level of lesion can be activated by an appropriate afferent input leading to the generation of a locomotor EMG pattern and, consequently, to training effects (Dietz 2014) (*Figure 12*). This evidence is crucial to sustain functional recovery after an SCI[59]. In contrast, typical movement disorders after SCI, e.g., spastic movement disorder, are due to the defective utilization of afferent input in combination with secondary compensatory mechanisms[72]. It has been shown that neuronal networks underlying the generation of locomotor

patterns of cats and humans have an impressively high level of flexibility after SCI [11] and that the plasticity of spinal neuronal circuits is task specific and use-dependent.

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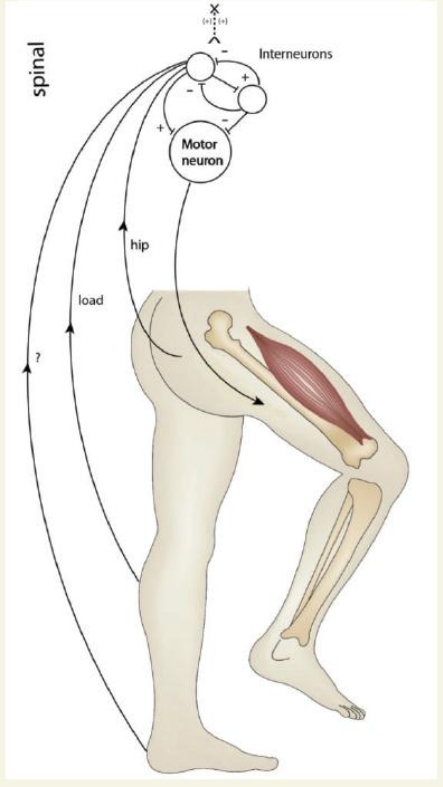


Figure 12: Neuroplasticity after spinal cord injury. Schematic drawings showing the mechanisms underlying neuroplasticity after spinal cord injury *[Dietz V. and Fouad K. 2014]*

Rehabilitative interventions after SCI should therefore focus on exploiting the plasticity of neuronal circuits, i.e., at supraspinal and/or spinal level, rather than focusing on improving isolated clinical signs, such as muscle tone or reflex excitability.

Comparable with what has been shown in animal studies, locomotor training following SCI can improve locomotor ability even in individuals with a low motor score[73]. Also in chronic incomplete SCI, when no more spontaneous recovery can be expected, an improvement in mobility can be achieved by functional training [64,11]. The gain in function achieved during such a specific training in the stable phase of a SCI might mainly be attributed to plasticity.

7.2.1 Timing of locomotion training

The question regarding the early timing of a training therapy after SCI is still unresolved. Animal models indicate that there might be a 'therapeutic window' for rehabilitation after an injury [74;75]. In subjects with a SCI such a therapeutic window has not yet been defined although there is evidence that an early onset of training might be favourable [76;77;65]. Of course, spinal shock associated with flaccid paresis and problems in circulation prevents a locomotor training

programme in the acute/early stage after trauma. However, this might not necessarily be a disadvantage as rodent experiments indicate that training onset that is too early might be deleterious to motor recovery[78].

For the selection of people with SCI who might profit most from a locomotor training programme, an early prediction of ambulatory function is helpful, in order to focus rehabilitation of people with an (almost) complete SCI on wheelchair driving (see *6.2: State of the Art (SOA) on gait recovery prediction*)

7.2.2 The role of appropriate sensory cues to facilitate plasticity

Training effects depend on a number of physiological prerequisites (*Figure 12* and *Table 2*) necessary to evoke a pattern of muscle activation similar to that found in individuals without injury of the nervous system as this is required to facilitate meaningful plasticity.

Table 2: Factors influencing training effects. In this table the factors that might influence training effects are listed. They concern locomotor and/or hand/arm training after a SCI. The evidence differs considerably between the factors. The validity of the effects are indicated: (?) some evidence from animal experiments, no evidence in humans; (+) moderate evidence from human experiments/studies (evidence grade I); (+ +) stronger evidence from human experiments/studies for positive effects of the approach (evidence grade II) *[Dietz V. and Fouad K. 2014]*.

Factor		Function	Validity	References
1.	Training duration	Locomotion Hand function	+ + (stroke) ?	Kwakkel *et al*., 1999
2.	High intensity training	Locomotor function	+ +	Barbeau and Rossignol, 1994; Dietz and Harkema, 2004; Curt *et al*., 2008
3.	Movement velocity	Locomotion Hand/arm function	+ + (stroke) ?	Pohl *et al*., 2002
4.	(Spastic) Muscle tone	Locomotion Hand function	+ + ?	Dietz *et al*., 1995
5.	Augmented feedback	Locomotion Hand function	+ + +	Riener *et al*., 2006; Kamper 2012
6.	Virtual reality	Locomotion Hand function	+ +	Mirelman *et al*., 2009; Riener *et al*., 2010
7.	Load receptor input	Locomotion	+ +	Harkema *et al*., 1997; Dietz *et al*., 2002
8.	Hip related afferent input	Locomotion	+ +	Dietz *et al*., 2002
9.	Drug (noradrenergic; serotonergic) application	Locomotion	?	Remy-Neris *et al*., 1999; Courtine *et al*., 2009 (rodent)
10.	Epidural stimulation	Locomotion	+	Harkema *et al*., 2011

After an incomplete SCI, spared corticospinal and/or propriospinal pathways can play an active role in the recovery of locomotion. However, under these circumstances the intrinsic capacity of spinal locomotor circuitries and the sensory feedback information still remains as the basis for generating a locomotor pattern. The spinal locomotor circuitries interact dynamically with specific afferent inputs from receptors located in muscles, joints, and skin, and this interaction shapes the locomotor output [59].

The sensory input most relevant for locomotion comes primarily from stretch- and load-sensitive mechanoreceptors located in the muscles and skin. Furthermore, skin receptors on the dorsal foot play a role during the swing phase of walking over obstacles in humans [79].

Load information is provided for proprioceptive input from leg extensor muscles, namely Ib afferent signals from Golgi tendon organs, and probably also from mechanoreceptors in the foot sole [80]. This information is thought to be integrated into polysynaptic spinal reflex pathways that adapt the autonomous locomotor pattern to the actual ground condition and it is assumed that the Ib afferent input from leg extensors during the stance phase inhibits the flexor activity.

A crucial factor that is needed to trigger a locomotor EMG pattern in individuals with SCI is afferent input from load receptors [81;82]. This statement is based on the observation that without loading the sole of the foot during the stance phase no meaningful leg muscle activation occurs in individuals with complete SCI during supported stepping. Proprioceptive inputs from leg extensor muscles, and probably from mechanoreceptors in the sole of the foot, provide load-related afferent informations[82]. The role of this specific afferent input is to generate and shape the locomotor pattern, to control phase-transitions and to reinforce ongoing activity.

In addition, corresponding to studies in cats [83], hip extension movements, i.e. hip-joint related afferent input (but less knee or ankle joint excursions) are essential for the initiation of the swing phase and the generation of a locomotor EMG pattern in people with incomplete SCI[84]. Besides load receptor informations, a hip joint-related afferent input was shown to be required for the generation of a locomotor pattern, as it was shown to be also the case for stepping in human infants[84].

The observations that in motor complete paraplegic subjects assisted stepping movements within a driven gait orthosis and restricted movements of the hips (blocked knees) induces a patterned leg muscle electromyographic (EMG) activity, highlights the significance of hip joint receptors in the generation of locomotor activity[85]. Such that assisted stepping movements restricted to imposed ankle joints were followed by no, or only focal reflex responses in the stretched muscles[85].

Body un-loading and re-loading are considered to be of crucial importance to induce training effects upon the neurological locomotor centres, because the afferent input from receptors signalling contact forces during the stance phase (corresponding to the initiation of new-born stepping by foot sole contact) is essential for the activation of spinal neuronal circuits underlying locomotion.

7.2.3 Limitations of training-induced plasticity

In humans, the amount of sensorimotor deficits and the consequent chances for a recovery of function after SCI are determined by the level and severity of spinal cord damage[25]. In individuals with chronic incomplete SCI that are severely affected [ASIA Impairment Scale (AIS) C] some locomotor function can be re-established by intensive training [64;11]. Nevertheless, even after such training, patients still need support (e.g. braces and/or manual assistance) to compensate for their

limited stepping abilities. In contrast, individuals with less severe SCI (AIS D) usually learn to walk without support. In other words, the amount (and location) of spared spinal neural tissue determines the effectiveness of training. In the future, individuals with (almost) complete lesions might profit from a combination of training and epidural stimulation to facilitate the initiation and performance of stepping movements [65].

There is also a limitation of changes in cortical structures after SCI. This is reflected in the observation that there is little remapping in the representation of limb function after SCI. In people with chronic para/low tetraplegia, somatotopical representation during movements of non/moderately affected body parts is preserved or only slightly expanded[86]. In line with this, little cortical expansion towards more denervated lower body parts occurs when cortical areas of preserved limb function are stimulated [87]. From a clinical point of view, these results are not surprising as upper limb function hardly profits from cortical areas denervated from lower limbs during rehabilitation.

Age also limits plasticity and the subsequent restoration of function after SCI. Although similar results were obtained regarding the recovery of neurological deficits in young and older individuals, older patients have greater problems in translating this recovery into improvements of daily life activities [88]. Therefore, older individuals would probably profit from age-adapted rehabilitation programmes, e.g. to focus the training on a limited number of everyday functions at home.

Also, biological rehabilitation confounders have to be considered. Co-morbidity, in particular infections, can have a limiting effect on the neurorehabilitative potential not only for neuroimmunological processes and stroke but also, as shown recently, for SCI [25].

Another limitation of training found in animal models is the observation that specific training can interfere with untrained tasks [89;90]. Training effects are known to be fairly task-specific[91]. The finding that the training of one task limits another has, however, not yet been described in the clinical setting. Further investigations of the interaction of training paradigms appear warranted. Lastly, following complete thoracic SCI, training focuses on motor skills relevant to the individual, including wheelchair propulsion, transfer and muscle strength. In such a condition, adaptations of the nervous system can hardly overcome the lack of descending control.

7.3 REHABILITATION APPROACHES FOR GAIT RECOVERY

The main aims for rehabilitation of an individual with SCI are compensating for functional loss and use those parts of sensorimotor system that are still intact[13]. In general cortical re-organization occurs after SCI with evidence that sensory-motor cortex may play a role in the recovery function in SCI subjects[92]. This re-organization may be attributed to pre-existing and new neural circuits[12]. Additionally recovery function can be also related to the re-activation of parts of sensory motor system that are still intact[14] and it can be optimized by using task-specific sensory cues and favouring the recruitment of both spinal circuitries and spared supraspinal connections during rehabilitation.

Therefore, the aim of rehabilitation procedures should concentrate on the improvement of outcome by exploiting the plasticity of neuronal centres using a functional training. It should less be directed to the correction of isolated clinical signs, such as the reflex excitability or muscle tone.

Some standardized rehabilitation procedures became established only in the past 20 years. Nevertheless, there is still no full consensus on the most effective approaches. In fact neurorehabilitative approaches are multifactorial, vary to some degree between rehabilitative centres and are frequently lacking evidence for their effectiveness [25].

Today, clinical neurorehabilitative approaches in individuals with incomplete SCI are largely based on observations originally made in animal studies [93;90;94;89;95]. These animal-based developments of neurorehabilitative approaches are an ongoing process aimed at improving rehabilitation procedures. They can generally be viewed as training of lost/impaired sensorimotor functions. It is, however, important to acknowledge that rehabilitation after SCI also involves the learning of new tasks.

7.3.1 Functional locomotion training interventions

With the amount of research growing, changes have also occurred in the management of SCI. Even though clear evidence is not available and mechanisms are not entirely understood, most rehabilitation strategies are based on the concept of central nervous system plasticity detailed above, facilitated by early, intensive, and task-specific therapies to enhance the natural recovery processes[96]. Actually locomotor training is defined as any “therapeutic program aimed at the recovery of walking through intense practice of the task of walking”[97].

Possible interventions included overground walking training with or without body-weight support (BWS), manual assistance and/or functional electrical stimulation (FES), treadmill training with or without manual assistance and/or FES, body-weighted supported treadmill training (BWSTT) and robotic gait training.

7.3.2 Non robotic locomotion training approaches

Rehabilitation approaches, such as FES or bracing, enable a person to stand up and practice overground walking. Mechanical leg braces are also useful for supporting standing and walking, particularly for people with complete SCI. These range from single-joint braces (e.g. anklefoot orthosis, usually for individuals with low, incomplete spinal lesions), to whole-leg/longleg braces that extend from the lower back to the ankle. These devices must be used with a walking aid (e.g. crutches or walker) for functional ambulation. Several studies have examined the efficacy of combining these different therapies to further maximize functional ambulation. Systems that combine FES and bracing have been available for several years[98]. One example is the "reciprocating gait orthosis" (RGO), which is a long-leg brace with a reciprocal hip joint combined with FES to the thigh muscles. The rationale underlying these 'hybrid' systems (FES + bracing) is that while the brace provides postural stability, FES can be used to assist the leg movements required for functional ambulation[98].

7.3.2.1 Technology support for functional locomotion training

As soon as the concept of plasticity-based functional training became established in the early 90s, the idea of the technical assistance of impaired limb movements was considered [99;100]. These considerations were fuelled by the notion that longer and more intensive training with a high number of movement repetitions can best beachieved using robotic training devices and that this technology also allows for a monitoring of changes in movement performance over the course of rehabilitation [62;100].

Robotic devices can promote recovery by facilitating plasticity[101] and, corresponding to conventional training, they enable the performance of motor functions, which promotes activation and strengthening of neuronal pathways to a point where assistance is no longer needed. However, increased use of technology runs the risk of becoming uncritically applied. Considering that neuronal activity is a key for meaningful plasticity to occur, a robotic device should not overtake function. This requires an active involvement of the patient in movement performance. Just moving limbs does not lead to a meaningful muscle activity and, consequently, no training effect can be expected. Therefore, the robotic support provided has to be kept to a minimum so as to challenge the patient's own effort for movement performance [102;103]. Consequently, robotic-assisted training should be tailored to the individual patient's needs in order to challenge his/her own contribution to movement performance and some patient groups

Strategies that employ repetitive and intensive practice of gait (e.g. treadmill training) are thought to enhance walking through the provision of task specific sensory input associated with appropriate stepping movements. It has been more than a decade now since it was first demonstrated that BWSTT in animals can enhance locomotor activity after a SCI. In this approach, partial body weight support is provided by an overhead harness while leg movements are assisted by therapists and a moving treadmill belt. Since then, BWSTT strategies have been introduced as a promising approach to improve gait in people with SCI[98].

By unloading the body and standing on a moving treadmill, individuals with SCI are enabled to perform rudimentary stepping movements. These movements evoke an appropriate afferent input to the spinal cord leading to leg muscle activation comparable with that during walking, which is the basis for the promotion of meaningful neuroplasticity [73]. The benefit of such functional locomotor training does not depend on the approach used. That is, body weight supported treadmill training is equally effective as assisted over-ground walking [104;103]. However, compared with earlier rehabilitation approaches that were designed to influence physical signs, such as muscle tone, reflex activity or strengthening of muscle groups, locomotor training has been shown to be more effective in improving locomotor ability[105]. Such functional training leads to a task-specific improvement of leg muscle activation and, consequently of locomotor ability with only little increase in voluntary leg muscle force[42]. Even in subjects with severe SCI, locomotor ability can be improved by training with assisted leg movements and body unloading. This is associated with an increase in patterned leg muscle activity that enables a reduction of body unloading during stepping [70;106] and a strengthening of spared descending pathways [74]. Besides facilitation of neural plasticity it is expected that also changes in muscle properties, associated with the training, contribute to the improvement of function.

7.3.3 Effectiveness of different functional locomotion training interventions

Several systematic reviews addressed the issue of the effectiveness of various forms of locomotor training after SCI also because different locomotor approaches might play a role at different stages in the rehabilitation process[96]. Recently Morawietz[96] underlined that the effect of overground locomotor training is consistent with other locomotor interventions such as BWS or FES trainings, although it did show a trend for greater benefits with a chronic population. Because overground training requires the least resources in terms of equipment, this has an important implication for clinical practice. However, little is known about the optimal timing, intensity, and frequency of it.

8 EXPERIMENTAL STUDIES

As previously described balance, spasticity and weight are the chief factors affecting gait in SCI subjects (*Figure 13*). Balance and muscle tone are routinely addressed in rehabilitation protocols for improving gait and body weight is often controlled by the implementation of BWS systems. In spite of the general accepted importance of these factors there is little scientific evidence on the efficacy of the different rehabilitation protocols or consensus in testing parameters. Within this framework we addressed gait in chronic motor incomplete SCI subjects focussing on new protocols to treat balance and spasticity and on the effects of BWS provided by the water environment on kinematic gait parameters (*Figure 14*).

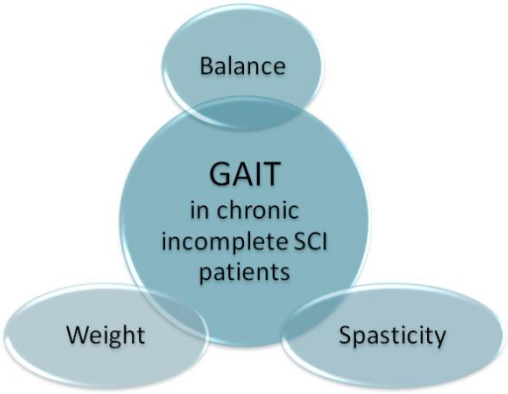


Figure 13: Factors influencing gait in chronic incomplete SCI subjects

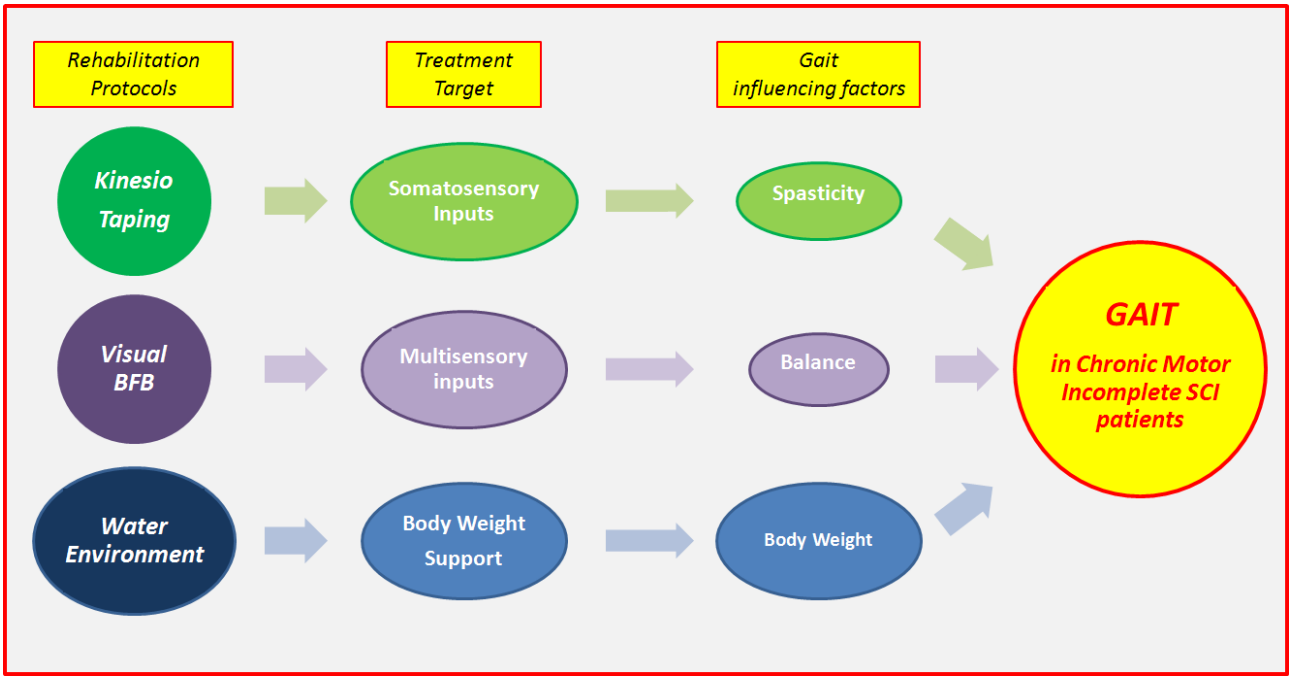


Figure 14: Experimental studies design

For each study different subjects affected by chronic motor incomplete SCI, with stable clinical and neurological features, have been enrolled. Controls groups have been used for Study 1 and 3. A specific statistical assessment of reliability, validity, and responsiveness of center of pressure (COP) parameters under different sensory conditions by means of stabilometric platforms (SPs), has been also conduced into Study 1. In Study 2 a cross over paradigm, non-requiring healthy controls, was employed.

In the table below (*Table 3*) are reported subjects/healthy controls enrolled for each study, the goal and the classification of the study. For Study 1 and 2 a battery of clinical scales and instrumental assessment have been used to analyse patients' improvements due to the task-specific biofeedback balance training or neuromuscular KinesioTaping. As regards Study 3, an instrumental gait assessment has been performed one time for each patient/healthy control for both environments.

Table 3: Study design and experimental groups

STUDY DESIGN AND EXPERIMENTAL GROUPS				
	Healthy Controls	**SCI Patients**	**GOAL**	**Type of the study**
Study 1	6	12	*Test the efficacy of task-specific biofeedback balance training in supporting walking functions*	*Open-case study with a prospective control*
Study 2	/	11	*Test neuromuscular Kinesio Taping efficacy in improving gait*	*Randomized crossover case control study*
Study 3	15	15	*Evaluate the effect of water buoyant force on gait charactirtistcs of SCI subjects*	*Observational case control study*

9 Study 1:

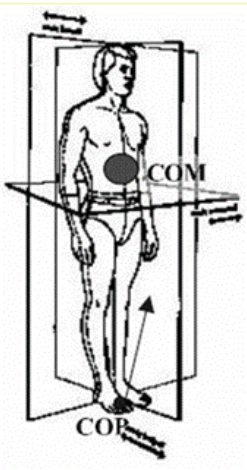
Efficacy of task-specific biofeedback balance training in supporting walking functions in chronic incomplete spinal cord injury patients

As detailed above, impairments in balance have recently been proposed to be highly predictive of functional recovery in patients with SCI. In addition to common observational clinical scales, more objective evaluation methods of balance have been implemented by using stabilometric platforms (SPs)and thus analyzing center of pressure (COP) parameters. COP analysis has been used in various pathologies, although psychometric measures of COP parameters have only been assessed in healthy subjects. On the other hand it is well known that psychometric properties of COP parameters vary according to the target population[39]. Specifically, concerning subjects with SCI, few studies have reported COP parameters, and none has addressed the reliability, validity, or responsiveness of this measures.

Therefore, to respond to the demand of defining psychometric properties and testing protocol for SCI subjects balance evaluation by SP we conducted a devoted serial cross-sectional study to define SCI testing protocol and to assess reliability, validity, and responsiveness of the different COP parameters in incomplete SCI subjects.

9.1 Reliability, validity, and effectiveness of center of pressure parameters in assessing stabilometric platform in subjects with incomplete spinal cord injury: A serial cross-sectional study

9.1.1 INTRODUCTION



Balance is usually defined as preservation of the vertical projection of the body's center of mass (COM) onto the support area that is formed by the feet [107]. Human balance is typically modeled as an inverted pendulum, in which the body is controlled as a single rigid segment that supports a single mass point—the COM—which rotates around the ankle joint [108]. The inverted pendulum is regulated through the development of ground-reaction forces, the vector sum of which is applied to a point that is defined as the vertical projection of the COM onto the ground[109]: the center of pressure (COP) (*Figure 15*).

Figure 15: COP (Centre of Pressure) and COM (Centre of Mass) body representation

The body's equilibrium is maintained by the central nervous system, which fixes the COM around a specific point—a goal that is under constant challenge by continuous perturbations to the COM by factors, such as breathing, heart rate, and muscle activity[110]. To maintain postural stability, several afferent inputs, such as visual, vestibular, and somatosensory, are integrated and converted into efferent motor outputs, which in turn are transmitted down to the spinal cord along various motor tracts [111]. Postural sway, such as spontaneous shifts in the COP during quiet standing, represents the integrated output of complex interactions between systems [112]. Damage to any of these systems can result in postural instability, affecting static and dynamic balance—ie, stance and gait. Spinal centers have a significant role in to the postural control systems, suggesting the clinical relevance of postural control deficits in SCI[113].

Despite the availability of many technical instruments to assess balance, the most common clinical tools remain observational scales, such as the Tinetti [114] and Berg balance scales [115]. Nevertheless, these scales are hampered by a lack of sensitivity and objectivity and are limited by floor-ceiling effects.[115;116]

To overcome these drawbacks, stabilometric platforms (SPs), consisting of a rigid plate that is supported by force transducers, and COP analyses have been introduced in clinical settings[112]. Many studies have reported the use of various SPs to evaluate balance deficits in healthy subjects [117]and in several pathologies, including orthopedic diseases [118], neuropathic lesions [119], Parkinson disease[119], multiple sclerosis[120], muscular dystrophy [121], cerebral palsy [122], cerebellar ataxia[123], and stroke[124]. Two recent studies assessed balance in SCI, examining recoveries after visual biofeedback rehabilitation by COP analysi[113]. Impaired balance is a significant limitation to overground ambulation in patients with SCI [115], and impairments in balance are predictive of gait recovery [5], thus meriting evaluation.

Despite the growing interest in balance, the standardization of COP parameters with regard to measurements and the related quality domains [125;126] (ie, reliability, validity, and responsiveness) [127]is poor [128] and is absent from the SCI population. COP measurements have been examined in healthy elderly individuals [112;129] and in patients with Parkinson[130] and orthopedic diseases [131]. Data from healthy subjects can inflate the reliability estimates, because measurements can be made in them more easily than in patients[112].

Measurement errors, and hence the reliability of a measure, are not fixed but depend on the study population [132] and can vary between test conditions[112]. Thus, measurement properties must be specified for a study population and test conditions.

No study has examined the properties of COP parameters by SP in subjects with SCI. Our serial cross-sectional study aimed to determine the reliability, validity, and responsiveness of COP parameters under various test conditions and define the protocol parameters that are suitable for specifically assessing balance in subjects with incomplete motor SCI.

9.1.2 METHODS

9.1.2.1 Population

This serial cross-sectional study included 23 subjects with incomplete motor SCI. The inclusion criteria comprised traumatic and nontraumatic etiology, subacute and chronic AIS D SCI, and the ability to maintain a standing position unsupported for at least 52 s. The exclusion criteria were the presence of cognitive impairments and any orthopedic or neurological pathology that could influence the assessment of balance. Neurological status was scored per American Spinal Injury Association (ASIA) standards, including the Impairment Scale (AIS)[21]. Patients' demographics, lesion levels, and etiologies are reported in *Table 4*.

Table 4: Patients' clinical and epidemiological features. TSCI: traumatic SCI; NTSCI: non traumatic SCI; Lesion level: C: cervical; T: thoracic; L: lumbar. Sensory test conditions: OF: open feet; CF: closed feet; OE: open eyes; CE: closed eyes; Y: assessment performed; N: assessment not performed. *: Patients with SCI who underwent at least 2 consecutive balance assessments, both clinical and instrumental

	Age	Gender	Weight	Height	Aethiology	Lesion Level	Time since lesion (months)	OF-OE	OF-CE	CF-OE	CF-CE
PT1*	19	M	62	173	TSCI	T7	6	**Y**	**Y**	**N**	**N**
PT2*	34	F	68	175	NTSCI (Inflammatory)	C5	24	**Y**	**Y**	**Y**	**Y**
PT3*	66	M	74	167	NTSCI (Degenerative)	T11	15	**Y**	**Y**	**Y**	**Y**
PT4	37	M	64	171	TSCI	C6	13	**Y**	**Y**	**Y**	**Y**
PT5*	52	M	68	169	NTSCI (Vascular)	T12	10	**Y**	**Y**	**Y**	**Y**
PT6*	33	F	55	167	TSCI	T11	8	**Y**	**Y**	**N**	**N**
PT7*	34	F	60	176	NTSCI (Vascular)	T8	6	**Y**	**Y**	**Y**	**Y**
PT8*	54	F	70	168	NTSCI (Degenerative)	L5	32	**Y**	**Y**	**Y**	**N**
PT9*	35	F	66	172	NTSCI (Degenerative)	L4	8	**Y**	**N**	**Y**	**N**
PT10	41	M	88	177	TSCI	L3	5	**Y**	**Y**	**N**	**N**
PT11*	64	M	78	160	NTSCI (Inflammatory)	T5	13	**Y**	**Y**	**N**	**N**
PT12	84	M	53	165	NTSCI (Inflammatory)	L1	8	**Y**	**Y**	**N**	**N**
PT13	52	M	80	173	NTSCI (Degenerative)	C7	8	**Y**	**Y**	**Y**	**Y**
PT14*	30	M	65	173	TSCI	L3	9	**Y**	**Y**	**Y**	**Y**
PT15	40	M	73	178	TSCI	L3	6	**Y**	**Y**	**Y**	**Y**
PT16*	29	M	65	181	TSCI	T10	8	**Y**	**N**	**N**	**N**
PT17*	61	F	80	159	NTSCI (Inflammatory)	T7	14	**Y**	**N**	**N**	**N**
PT18*	33	F	85	182	TSCI	C6	8	**Y**	**Y**	**Y**	**Y**
PT19*	59	F	60	158	NTSCI (Degenerative)	C5	72	**Y**	**Y**	**Y**	**Y**
PT20*	69	M	75	165	TSCI	C5	13	**Y**	**Y**	**Y**	**Y**
PT21*	44	F	57	178	NTSCI (Degenerative)	D1	75	**Y**	**Y**	**Y**	**Y**
PT22*	51	M	74	173	NTSCI	C7	9	**Y**	**Y**	**Y**	**Y**
PT23	60	M	65	170	NTSCI (Degenerative)	C7	8	**Y**	**Y**	**Y**	**Y**
Medium (s.d.)	*48,27 (15,94)*	*14M - 9F*	*69,22 (9,37)*	*163,45 (32,65)*	*60.9 % NT 39.1 % T*		*16.43 (19,03)*				

Enrolled patients were assessed repeatedly. Specifically, 6 patients were evaluated once, and the remaining 17 patients were assessed 2 to 12 times for 1 year, with 2 weeks between sessions. Overall, 111 evaluation sessions were analyzed, all of which administered clinical and instrument-based assessments of balance. The local ethics committee approved this study (Prot. CE/AG.4-PROG.231-65), and all patients gave informed consent for participation.

9.1.2.2 Clinical assessment of balance

For each evaluation, the Berg Balance scale (BBS) and Tinetti scale (TS) were used to assess balance clinically, and the Walking Index for Spinal Cord Injury (WISCI) [133] was used to determine the functional level of ambulation. The BBS is a 14-item task-oriented test that was validated recently in SCI patients [115] and can be considered a reflection of functional activity. Total scores range from 0 to 56, with higher scores indicating greater balance and functional independence.

The TS includes subscores for equilibrium (TS_E) and locomotion (TS_L)[114]. Fourteen items on this clinical test measure balance characteristics (scored out of 24), and 10 items examine gait features (scored out of 16), for a total score of 40, with higher scores indicating greater balance.

The WISCI has been validated specifically with regard to gait in subjects with SCI [47]. Total scores range from 0 to 20, with higher scores reflecting greater independent locomotion[133].

9.1.2.3 Instrument-based stabilometric assessment of balance

Stabilometric parameters were analyzed using a 320-cm by 75-cm (length x width) static force platform (Platform BPM 120, Physical Support Italia, Italy). The signals were amplified and acquired using dedicated software (Physical gait Software Vv. 2.66, Physical Support Italia, Italy). In assessing static stability, patients stood barefoot in a natural and relaxed position with their arms by their sides and with both heels lined up [112], under 2 sensory conditions: eyes open and facing a target 1.5 m away (OE) and eyes closed (CE).

The feet were placed with the forefoot open 30 degrees and the heels in 2 positions: together (FT) or apart at a comfortable distance (FA). For the FA condition, heel distance (HD) was measured manually by the operator and fixed for the FA-OE and FA-CE conditions and during the recordings. For each evaluation, 4 conditions (FT-OE, FT-CE, FA-OE, and FA-CE) were tested. Under each condition, measures were recorded 3 times, per Ruhe [112]. We selected 51.2 s as the testing time, per the platform manufacturer and other studies[134;135]. A slight pause was permitted between recordings to allow the arms to rest on bars, during which the patients were asked to maintain their foot position on the platform. During the data collection, subjects were asked to “stand as still as possible’’ while looking straight ahead, per Zok et al.[136].

We considered the following quantitative COP parameters:

- Length indicators: path length (L, mm), mean velocity (V, L divided by the trial duration), anteroposterior (V_{AP}) and laterolateral (V_{LL}) velocities (mm/s), and mean position of COP along the planar laterolateral (X) and anteroposterior (Y) coordinates on the platform (mm)
- Surface indicators: area of the ellipse encompassing 90% of COP samples (A, cm^2) and length of its semiaxes (SA_1, SA_2, cm).

9.1.3 Data analysis

9.1.3.1 Demographic features

The influence of demographic features on COP parameters was analyzed using the Spearman correlation coefficient (ρ), applied to data from the first session of each subject.

9.1.3.2 Measurement of COP parameters between test conditions

The *reliability* domain contains various measures for continuous data[125]: test-retest and intrarater reliability, measurement error, and minimal detectable change.

1. *Test-retest reliability,* or *repeatability,* reflects the reliability between tests by the same operator in the same session. Test-retest reliability was assessed using the coefficient of variation (CV). CV is a measure of data dispersion and was the standard deviation that was computed for the values in the 3 recordings, expressed as a percentage of the mean value. Because the ideal mean for planar coordinates is 0, CV was not computed for the Y or X COP.
2. *Intrarater reliability* determines the reliability across the time of evaluations by the same operator. For continuous data, intraclass correlation (ICC) is the preferred method[125], because it also takes systematic errors between repeated measurements into account. Of the various methods of calculating ICC, consistent with the Shrout and Fleiss reliability coefficients guidelines[137], we adopted the ICC(3,1) form. We analyzed the ICC, with a confidence interval (CI) of 95%, for patients who underwent at least 2 consecutive (within 15 days) assessments (17 subjects).
3. *Measurement error* indicates the absolute error in measurement and was calculated as the standard error of measurement (SEM)[125]. SEM represents the standard deviation of repeated measures of the same subject (ie, within-subject variability) by the same operator (ie, within-rater variability) and is expressed in units of the measurement tool—in this case, SEM = SD * $\sqrt{}$ (1-ICC).
4. *Minimal detectable change* (MDC_{95}) addresses the common problem of deciding whether results are significant or due to errors in measurement. MDC_{95} is defined as the minimal amount of change that is not due to the variation in measurement[138]. Calculated as SEM *1.65 * $\sqrt{}$2, MDC_{95} determines the magnitude of change that exceeds the threshold of measurement error at a 95% confidence level.

A 95% confidence interval, as with SEM, increases the precision of score estimates[138]. Further, the percentage of MDC_{95} that indicates the percentage of the minimal amount by which the results change versus baseline—not due to variations in measurement—is calculated per the following formula:

% MDC_{95} = (MDC_{95}*100)/ baseline assessment value.

Reliability assessments were also performed for the BBS, TIN, and WISCI using ICC, SEM, and MDC_{95}.

The *validity* domain refers to the degree to which an instrument measures the construct that it purports to measure[125] and is evaluated based on criterion and construct validity.

1. C*riterion validity* indicates the degree to which the scores of a measurement instrument are an adequate reflection of a standard. The preferred method for estimating criterion validity is correlation coefficient, which should preferably exceed 0.70[125]. For patients with SCI, the only validated tool for assessing balance is the BBS [115], rendering it the standard tool for determining criterion validity by Spearman correlation coefficient (ρ) .
2. C*onstruct validity* estimates the consistency of measurement instrument scores under the assumption that the instrument measures the construct validity [125], which is calculated as *convergent validity*. Construct validity refers to the degree to which COP parameters correlate with the related scales (BBS and TS_E)—not with other scales (WISCI and TS_L) (ie, *appropriateness*). Convergent validity was analyzed using correlation coefficients (R for Pearson coefficient and ρ for Spearman coefficient.)

The *responsiveness* domain reflects the sensitivity to changes and is frequently measured by effect size (ES)[139]. ES is based on the data distribution and is the mean difference between values in the first and second assessments, divided by the standard deviation of the baseline values (ie, the values in the first assessment). ES was calculated for patients who participated in at least 2 sessions (17 patients) with regard to clinical and instrumental data.

9.1.3.3 Effects of sensory conditions on assessment

The optimal sensory conditions for balance assessment were analyzed by analysis of variance (ANOVA), with vision and support base as the main factors. Further, Pearson correlation between HD and clinical scales was analyzed to determine the influences of HD on balance in SCI subjects.

Statistical analyses were performed using SPSS for Windows (version 9.0, Chicago, IL). Data were considered significant at $p<0.05$. Correlation analyses were performed per Munro's classification[132]: 0.00–0.25: little, if any correlation; 0.26–0.49: low correlation; 0.50–0.69: moderate correlation; 0.70–0.89: high correlation; and 0.90–1.00: very high correlation.

9.1.4 RESULTS

Not all subjects were tested under each sensory condition; subjects with more severe damage were unable to perform the most challenging tasks; CF or CE conditions. Overall, 111 OF-OE, 96 OF-CE, 83 CF-OE, and 73 CF-CE evaluations were performed.

By Spearman correlation analysis, no significant correlations between COP parameter and demographic features (age, height, weight, gender) were observed for any sensory condition (OE, CE, OF, CF) (p>0.05).

9.1.4.1 Measurement properties of COP parameters between test conditions

With regard to reliability*, test-retest reliability* was evaluated by CV for each COP parameter in 3 trials under each condition. The CV of all parameters was minimally affected by sensory condition, indicating their lack of effect on the reliability COP parameters. The most repeatable parameters—those with the lowest CV values—were L, V, and V_{LL}. The least repeatable parameter was A, with a mean CV of approximately 50% over all conditions (Table 5).

Table 5: Test-retest reliability of COP parameters by coefficient of variation. The assessment conditions and mean coefficient of variation (CV) for each COP parameter between the 3 trials are reported. The mean values between conditions for each COP parameter (last column) or COP parameters for each condition (last row) are in grey. For abbreviations of COP parameters and sensory conditions, see list of abbreviations.

Parameter	Coefficient of Variation [%]				
	OF-OE	OF-CE	CF-OE	CF-CE	Mean (SD)
A	46.4	46.7	47.2	42.4	45.7 (2.2)
L	**13.4**	**13.6**	**13.8**	**12.9**	**13.4 (0.3)**
SA1	27.7	24.9	22.6	26.0	25.3 (2.1)
SA2	27.5	26.3	27.8	25.1	26.7 (1.2)
V	**13.3**	**13.6**	**13.8**	**12.9**	**13.4 (0.4)**
V_{LL}	**13.2**	**13.3**	**12.7**	**14.2**	**13.4 (0.6)**
V_{AP}	16.2	15.6	18.0	13.3	15.8 (1.9)
Mean (SD)	**22.5 (12.3)**	**22.0 (12.2)**	**22.3 (12.3)**	**21.0 (11.1)**	

The *intrarater reliability* was assessed by ICC for the clinical scales and COP parameters. Of the clinical scales, the BBS had the highest ICC value, whereas the TIN had the lowest. For COP parameters, averaged between sensory conditions, L, V, and V_{LL} had the highest ICC values. In contrast, with regard to sensory conditions, averaged between COP parameters, the OF-OE and OF-CE conditions had the highest ICC values, whereas the CF-CE condition had the lowest ICC (*Table 6*). The ICC value of the BBS was the highest of all clinical scales and COP parameters.

Table 6: Intrarater reliability of COP parameters by ICC, SEM, MDC95, and %MDC. Significant ICC data are in bold (p<0.05:*, p<0.005:**, p<0.001:***). The mean ICC, SEM, MDC95, and %MDC values between conditions for each COP parameter (last column) or COP parameters for each condition (last row) are in grey The highest mean ICC and %MDC values are in bold. For abbreviations of COP parameters and sensory conditions, see list of abbreviations.

Scale	ICC	SEM	MDC_{95}	%MDC
BBS	0,97***	2,07	5,74	17,2
TIN	0,22	3,54	9,81	58,5
TIN_E	0,87***	0,86	2,37	26,3
TIN_L	0,78***	1,07	2,97	38,3
WISCI	0,95**	0,73	0,02	13,0

COP	OF-OE				OF-CE				CF-OE				CF-CE				*Mean (sd)*			
Parameter	ICC	SEM	MDC_{95}	%MDC	ICC	SEM	MDC_{95}	%MDC	ICC	SEM	MDC_{95}	%MDC	ICC	SEM	MDC_{95}	%MDC	ICC	SEM	MDC_{95}	%MDC
A	**0,64****	1,67	4,63	141,9	**0,94*****	2,33	6,46	74,6	**0,92*****	0,89	2,47	69,0	**0,65***	5,62	15,58	*116,9*	*0,79 (0,71)*	*2,63*	*7,29*	*100,6*
L	**0,89*****	37,23	103,2	46,5	**0,92*****	67, 27	186,46	49,6	**0,92*****	21,75	60,29	27,2	**0,74****	105,53	292,5	*55,5*	*0,87 (0,08)*	*57,95*	*160,62*	***44,8***
SA1	**0,85*****	0,34	0,94	64,7	**0,81*****	0,49	1,34	72,1	**0,88*****	0,22	0,62	43,3	**0,79***	0,69	1,93	*61,0*	*0,83 (0,04)*	*0,44*	*1,21*	*60.2*
SA2	**0,71*****	0,44	1,21	71,5	**0,89*****	0,54	1,5	58,0	**0,76****	0,39	1,08	58,9	0,38	6,17	17,09	*796,0*	*0,68 (0,22)*	*1,88*	*5,22*	*246,1*
Y	**0,7**	2,48	6,88	255,5	0,34	5,47	15,17	466,4	0,37	3,36	9,32	413,3	**0,54***	3,9	10,09	*189,0*	*0,49 (0,16)*	*3,8*	*10,55*	*331,0*
X	**0,54***	2,87	7,96	1297,2	0,34	2,35	6,52	1552,0	0,01	2,68	7,42	769,5	0,28	3,55	9,83	*18189,0*	*0,29 (0,22)*	*2,86*	*7,93*	*5451,9*
V	**0,89*****	0,72	2,01	46,3	**0,92*****	1,31	3,64	49,9	**0,92*****	0,43	1,18	27,4	0,74*	2,06	5,7	*55,4*	***0,87 (1,13)***	*1,13*	*3,13*	***44,8***
V_{LL}	**0,89*****	0,48	1,32	43,9	**0,9*****	0,73	2,03	47,9	**0,9*****	0,3	0,82	28,9	**0,83*****	1,14	3,15	***49,2***	***0,88 (0,03)***	*0,66*	*1,83*	***42,5***
V_{AP}	**0,82*****	0,59	1,64	65,0	0,89***	1,22	3,39	66, 7	**0,82*****	0,44	1,21	**45,1**	0,65*	1,65	4,57	*68,4*	*0,79 (0,1)*	*0,97*	*2,70*	*61,3*
Mean	*0,77*	*5,20*	*14,42*		*0,77*	*9,08*	*25,17*		*0,72*	*3,38*	*9,38*		*0,62*	*14,48*	*40,13*					
(SD)	*0,13*	*12,05*	*33,39*		*0,13*	*21,88*	*60,64*		*0,32*	*6,98*	*19.35*		*0,19*	*34,20*	*94,80*					

Due to differences between unit measures, percentage change in MDC_{95} between sessions was used instead of MDC_{95} for the statistical analysis. Of all clinical scales, the BBS and WISCI had the lowest percentage change due to measurement error, and L, V, and V_{LL} had the lowest percentage change due to measurement error of all COP parameters (*Table 6*).

Validity of the COP parameters was evaluated by correlation analysis with clinical scales, as reported in Table IV. Of the COP parameters, L, V, $V_{LL,}$ and V_{AP} correlated significantly and systematically with the BBS, TS, and TS_E. L, V, and V_{LL} also correlated with the TSL but only under the OF-OE/CE conditions, with low R values. Notably, the highest correlations between COP parameters and clinical scales were observed with each parameter in the OF-OE condition. X and Y data did not correlate with the clinical scales (*Table 7*).

Our evaluation of *criterion validity* by correlation of COP parameters with the BBS determined L, V, $V_{LL,}$ and V_{AP} in the OF-OE condition to be the only parameters with R values over the validity criterion of 0.70. *Convergent validity* was assessed by comparing COP parameters with balance- and nonbalance-related clinical scales. The correlation coefficients of the COP parameters were higher for balance scale scores (BBS, TS, TS_E) versus locomotion scale scores (TS_L, WISCI).

Table 7: Validity of COP parameters. Statistically significant values are in bold (p<0.05:*, p<0.005:**, p<0.001:***). The grey tabs highlight R values >0.7. The mean values of absolute values of these coefficients between conditions are in grey font. For abbreviations of COP parameters and sensory conditions, see list of abbreviations.

Coefficient of Correlation		Clinical Scales					
		BBS	TS	TS-E	TS-L	WISCI	mean(|R|)
A	OF-OE	**- 0.65*** **	**-0.49*** **	**-0.57*** **	**-0.23***	-0.09	0.41
	OF-CE	**-0.48*** **	**-0.27** **	**-0.42*** **	0.07	-0.14	0.28
	CF-OE	**-0.55*** **	**-0.44*** **	**-0.52*** **	**-0.25***	-0.08	0.37
	CF-CE	**-0.31*** **	-0.17	**-0.26*** **	-0.02	-0.16	0.18
L	OF-OE	**-0.73*** **	**-0.58*** **	**-0.64*** **	**-0.23***	**-0.21***	0.48
	OF-CE	**-0.54*** **	**-0.34*** **	**-0.43*** **	0.06	**-0.21***	0.32
	CF-OE	**-0.61*** **	**-0.54*** **	**-0.54*** **	**-0.23***	-0.16	0.42
	CF-CE	**-0.39*** **	**-0.24*** **	**-0.32*** **	0.01	**-0.39*** **	0.27
SA1	OF-OE	**-0.68*** **	**-0.53*** **	**-0.61*** **	**-0.30** **	-0.11	0.45
	OF-CE	**-0.52*** **	**-0.34*** **	**-0.47*** **	0.02	-0.19	0.31
	CF-OE	**-0.46*** **	**-0.40*** **	**-0.43*** **	-0.18	-0.09	0.31
	CF-CE	**-0.26***	-0.20	**-0.23***	-0.10	**-0.27***	0.21
SA2	OF-OE	**-0.66*** **	**-0.48*** **	**-0.57*** **	**-0.21***	-0.09	0.40
	OF-CE	**-0.50*** **	**-0.30** **	**-0.42*** **	0.02	-0.06	0.26
	CF-OE	**-0.58*** **	**-0.44*** **	**-0.53*** **	**-0.23***	-0.05	0.37
	CF-CE	-0.11	0.00	-0.11	0.07	-0.06	0.07
Y	OF-OE	-0.02	-0.08	-0.08	-0.05	**0.22***	0.09
	OF-CE	-0.13	-0.13	-0.14	-0.13	0.02	0.11
	CF-OE	0.02	-0.12	-0.08	-0.18	**0.29***	0.14
	CF-CE	-0.09	-0.03	-0.04	-0.05	**-0.31***	0.10
X	OF-OE	0.00	0.10	0.04	0.01	-0.13	0.06
	OF-CE	-0.01	0.04	0.01	0.17	-0.11	0.07
	CF-OE	-0.13	0.00	-0.10	-0.05	-0.18	0.09
	CF-CE	-0.17	-0.15	-0.12	-0.01	-0.14	0.12
V	OF-OE	**-0.73*** **	**-0.58*** **	**-0.64*** **	**-0.23***	**-0.22***	0.48
	OF-CE	**-0.52*** **	**-0.30** **	**-0.41*** **	0.10	**-0.24***	0.31
	CF-OE	**-0.61*** **	**-0.54*** **	**-0.54*** **	**-0.23***	-0.16	0.42
	CF-CE	**-0.39** **	**-0.24***	**-0.32** **	0.01	**-0.39***	0.27
V_{LL}	OF-OE	**-0.71*** **	**-0.60*** **	**-0.64*** **	**-0.30** **	**-0.22***	0.50
	OF-CE	**-0.54*** **	**-0.34*** **	**-0.44*** **	0.04	**-0.27***	0.32
	CF-OE	**-0.52*** **	**-0.49*** **	**-0.47*** **	**-0.26***	-0.18	0.38
	CF-CE	**-0.35** **	**-0.24***	**-0.29***	-0.07	**-0.39*** **	0.27
V_{AP}	OF-OE	**-0.74*** **	**-0.56*** **	**-0.64*** **	-0.18	**-0.20***	0.47
	OF-CE	**-0.53*** **	**-0.28***	**-0.40*** **	0.16	-0.19	0.31
	CF-OE	**-0.69*** **	**-0.56*** **	**-0.59*** **	-0.20	-0.13	0.44
	CF-CE	**-0.41*** **	**-0.24***	**-0.32** **	0.07	**-0.35** **	0.28

The evaluation of *responsiveness,* as measured by ES, is shown in Table V. The BBS was the most sensitive clinical scale, with an ES of 0.78. All COP parameters were more sensitive than the clinical scales, with nearly all ES values above 1. Averaging between sensory conditions, L, V, V_{LL}, and V_{AP} had the highest ES values. For the sensory conditions, averaged between COP parameters, the OF-OE and CF-CE conditions had the highest ES values (*Table 8*).

Table 8: Responsiveness of COP parameter assessment. Effect size (ES) between 2 sessions for 17 SCI patients. The mean values between conditions for each COP parameter (last column) or between COP parameters for each condition (last row) are in grey. The highest ES values among the clinical scales and COP parameters are in bold. For abbreviations of COP parameters and sensory conditions, see list of abbreviations.

	Effect size (ES)
Scale	
BBS	**0.78**
TIN	0.18
TIN_E	0.37
TIN_L	0.17
WISCI	O.07

Parameter	**OF-OE**	**OF-CE**	**CF-OE**	**CF-CE**	**Mean (SD)**
A	2.10	0.81	1.80	1.69	1.60 (0.55)
L	1.87	2.41	1.39	2.96	**2.16 (0.68)**
SA1	1.28	1.73	0.58	2.93	1.63 (0.98)
SA2	2.72	0.91	1.25	1.05	1.48 (0.84)
Y	1.36	2.29	1.53	1.43	1.65 (0.43)
X	1.52	1.08	1.11	0.49	1.05 (0.51)
V	1.87	2.41	1.39	2.96	**2.16 (0.68)**
V_{LL}	2.79	3.33	1.13	1.90	**2.29 (0,97)**
V_{AP}	2.60	1.39	2.56	2.88	**2.36 (0.66)**
Mean (SD)	2.01 (0.58)	1.82 (0.85)	1.42 (0.54)	2.03 (0.98)	

9.1.4.2 Effects of sensory conditions on assessment

Considering the data above, the effects of sensory conditions were examined, focusing on V—the most sensitive, reliable, and valid COP parameter (F*igure 16*). Overall, foot position had little effect on V, whereas vision affected V significantly. By ANOVA of V values, with vision and support base as the main effects, only vision had a significant effect [F(1.346)=76.10; vision: p<0.001, support base: p=0.535, interaction not significant: *p*=0.445.] The COP data were lower for the OE versus CE condition, indicating better balance with vision (*Figure 16*). The lack of a support base effect suggests that the foot conditions have little influence. These data are consistent with the lack of an effect of foot position on COP parameters or scale score correlation data (*Table 7*).

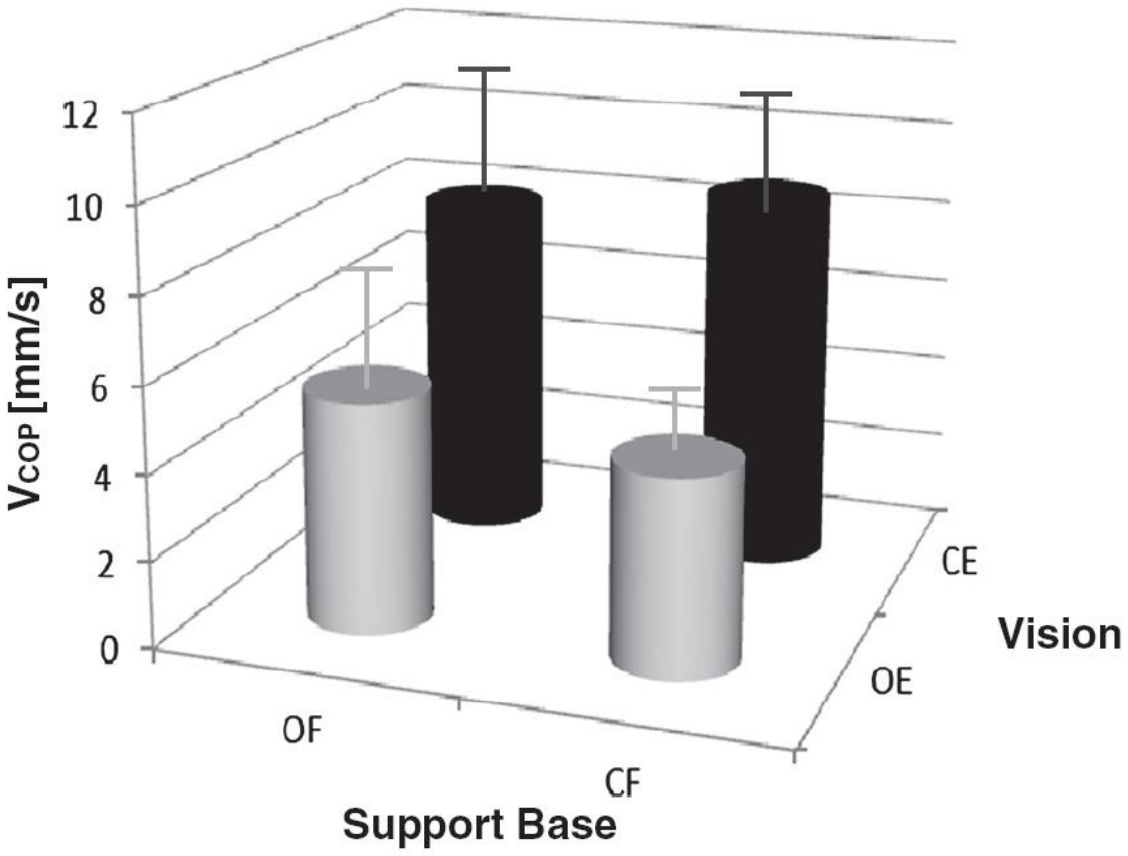


Figure 16: Effects of conditions on stabilometry. Histograms of mean COP velocity (V ± standard deviation) versus assessment conditions, depending on support base [open feet (OF) versus closed feet (CF)] and vision [open eyes (OE) versus closed eyes (CE)].

In contrast, in the OF condition, HD was self-selected, and patients used disparate HD conditions. By Pearson correlation analysis between HD and clinical scales, the BBS (ρ=-0.227, p=0.019), TIN_E (ρ=-0.275, p=0.003), and TIN (ρ=-0.289, p=0.03) were significant, but TIN_L was not (ρ=-0.112, p=0.24) (*Figure 17*)).

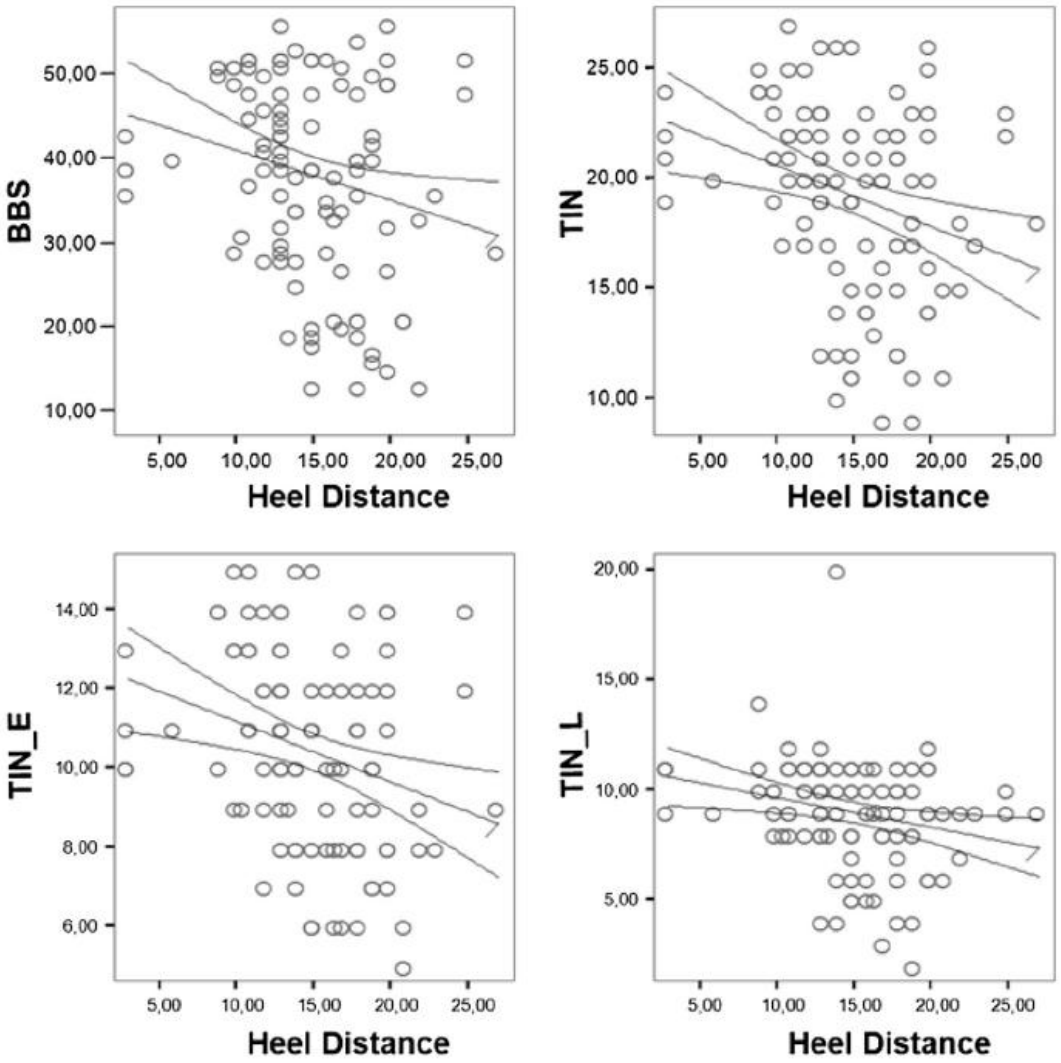


Figure 17: Correlation analysis between heel distance and clinical scales. Correlation between HD and BBS, TIN, TINE, and TINLOC.

The importance of the HD in assessing balance with regard to balance recovery was analyzed longitudinally for 17 patients who underwent rehabilitation by considering the HD during the evaluations over time. The mean R was high (R=-0.37, p<0.001), indicating a progressive reduction in HD of 3 cm for 150 days in patients who were assessed repeatedly.

9.1.5 DISCUSSION

Reliability, validity, and responsiveness are the key components of determining the suitability of a measurement; these parameters can vary by characteristic of the target population[132]. Our data allow us to define the COP parameters and assessment conditions that are suitable in evaluating postural balance in subjects with incomplete SCI.

9.1.5.1 Demographic features

Demographic features have been claimed to affect the reliability of COP measurements[112]. Although few studies have addressed the effect of gender, all of them agree in disputing sex-related influences on balance, consistent with our findings [140;141]. Height and weight affect COP parameters[142;143]. In our study, we adopted the approach of Salavati et al.[131] in mitigating the effects of height and weight by averaging COP measurements between 3 consecutive trials. Consequently, no correlations between height or weight data and COP parameters were observed.

The influence of age is debated[140;144]. In our cohort, there were no significant correlations between COP parameter and age, supporting the hypothesis that age does not affect SP evaluations in the SCI population. Nevertheless, our study did not specifically aim to determine the effects of age, and no specific measures were taken to correctly evaluate confounding factors.

9.1.5.2 Measurement properties of COP parameters between test conditions

Reliability can be measured in several ways, of which ICC is the most common in SP studies [112]. Independent of method (CV or ICC) and sensory condition (OF-OE, OF-CE, CF-OE, CF-CE), L, V, and V_{LL} were the most reliable parameters. L is directly (ie, arithmetically) related to V and recording time, and L and V provide the same information, if the recording time has been standardized [118]. Thus, all V and L measures should be considered related, because they are based on the same raw values. The reliability of V in SCI is consistent with findings on V in examining balance in young healthy[112] and old healthy[129] subjects and in patients with orthopedic diseases[131]. Current studies agree that V is the most reliable parameter in assessing balance.

When examining a patient population and possible treatment effects, the significance of a detected change—ie, whether a change is reliable or due to variations in measurement—must be determined[112]. This step is commonly addressed in clinical studies by SEM and MDC_{95} [129;131], the latter of which is most frequently used in SCI [145;146]. Notably, of the COP parameters, V and the related COP parameters L and V_{LL} had the lowest MDC_{95} scores.

As discussed and consistent with Scholtes [125]et al. , in addition to reliability, the quality of the instruments' measurements must be established by considering validity and responsiveness—2 parameters that are seldom reported in SP studies. *Validity* is established by reference to the gold

standard measurement in this field and by taking into account that the instrument measures the desired construct. BBS is the only balance scale that has been validated specifically for the SCI population[115]. Thus, we analyzed *criterion validity* by correlation analysis between BBS and COP parameters.

When dealing with validity measures, correlation coefficients that exceed 0.70 are considered significant[125]; in our data, V, L, V_{LL}, and V_{AP} were the only measures that had correlation coefficients above 0.70. High V validity was also evidenced by the results on convergent validity. Our comparison of correlation coefficients between V and the related COP data and clinical scale—with the same (BBS and TS_E) or different (TS_L and WISCI) constructs—demonstrated high correlation values for BBS and TS_E but not for TS_L or WISCI. Overall, these findings implicate V as a valid parameter in assessing balance in SCI subjects. Such evaluation methods are unavailable for healthy subjects and other clinically relevant populations. Thus, the validity of V in populations other than SCI patients must be determined.

Responsiveness is the ability of an instrument to detect changes in the construct that is measured over time[147]. Whereas validity refers to a single score, responsiveness reflects the validity of a score that has changed[147]. There is an ongoing debate about the ideal method for evaluating responsiveness[148;149]. It has been suggested that all responsiveness measures are measures of longitudinal validity or treatment effects and that, specifically for responsiveness, assessing longitudinal validity should be the preferred method[148;149]. However, no longitudinal validity assessment tool is available for SP. Based on the limitations that were discussed recently by Mokkink et al.[147], we used the most common method, ES, in evaluating responsiveness in SCI subjects. Consistent with previous domains, higher responsiveness was recorded for V and the related L, V_{LL}, and V_{AP} measures.

It could be argued that a high intersession ICC score is inconsistent with high intersession responsiveness, unless all subjects undergo similar changes between sessions, as was the case in our cohort—all patients had well-stabilized clinical profiles. Thus, very few changes were expected and recorded in the 2-week intersession period.

9.1.5.3 Effects of sensory condition on assessments

In a recent review, Ruhe et al. reported the absence of standardized methods for COP measurements and implicated trial duration, repetition, and visual and foot conditions as critical factors for obtaining reliable COP datasets[112]. Attempts to provide recommendations on the length and number of trials for assessing balance correctly have failed to reach a consensus.

Trial duration varies between studies. The recommended trial duration is 90 to 120 s to effect acceptable reliability with correlation coefficients > 0.75 for most parameters [112]. Nevertheless, early studies reported that a 10–60-sec duration was suitable for obtaining reliable COP data[150;151]. In our study, we did not examine the influence of differences in time on the reliability of COP parameters. The recording time was set to 51.2 per the platform handbook. Although it was short

compared with recent recommendations[112], this duration yielded high correlation coefficients (> 0.70) for most parameters.

With regard to *trial repetitions*, there is a tendency to increase trial number to generate more reliable data. Although this pattern might be reasonable when examining young healthy subjects, it becomes impractical when recruiting disabled persons in a clinical setting. Thus, we did not determine trial repetition effects and set a low number of repetitions to permit averaging (3, per Ruhe) [112].

Vision effects on the reliability of COP measures have been evaluated in several studies on population-related effects[112]. Recent studies have reported a trend toward higher reliability estimates under the eyes-closed conditions, prompting the recommendation to keep the eyes closed as the best practice. Our study subjects were tested with the eyes open (OE) and closed (CE), although not all subjects were able to perform under the CE condition, indicating the CE condition to be more challenging and discriminating. The significant effect of vision on V values also highlighted its significance.

There were no differences between the 2 visual conditions with regard to the reliability of V. Conversely, vision affected the validity and responsiveness of V indexes. The highest validity was obtained under the OE condition, and the best responsiveness was seen under the CE conditions. The discrepancy between the effects of vision on the validity and responsiveness of V and the lack of an effect of vision on the reliability of V is notable and contrasts the findings of Ruhe[112], suggesting that the eyes-closed condition should be applied, at least in healthy subjects. Validity and responsiveness refer to 2 different domains—ie, validity evaluates the construct that it purports to measure, whereas responsiveness reflects the sensitivity to patient changes. Thus, V can be evaluated with and without vision, at least in SCI subjects.

Foot position affects passive stability, decreasing the request of active neural control [142;152], but no consensus exists on the more reliable foot position [112]. Despite this lack of normative data, the best practice guidelines suggest standardization[112]. We tested subjects under 2 feet conditions: CF and OF. In the OF condition, subjects were asked to stand comfortably with their heels apart, and HD was recorded. This setting allowed us to test the closed versus open conditions and determine the effects of HD on COP reliability.

In general, a narrow stance is at least as reliable as a comfortable stance[112], but our findings indicate that foot position (CF or OF) does not affect the reliability of COP parameters. Conversely, the OF condition allowed us to record HD, for which the balance scales had high correlation values. The significance of changes in HD over time suggests that HD can be used to evaluate the effects of recovery and treatment on balance. Overall, OF in the comfortable position with HD recorded appears to be the ideal test condition for SCI subjects, consistent with the recommendations of Chiari [142] and Yoon [140] for healthy subjects.

Based on the limitations above, taking into account the V data, OF-OE is the most valid condition and OF-CE is the most responsive condition, suggesting that both should be implemented in testing SCI subjects.

The comparison of reliability and responsiveness between the V value of COPs in the OF-OE and OF-CE conditions and the balance scales merits further examination. To facilitate the comparison between the V and balance scale results, the ICC, %MDC, and ES data are presented in *Figure 18*. Because BBS is the reference standard, the V results only approximate the BBS ICC data. Yet, greater changes in V versus BBS in patient balance are required to obtain improvements that are not due to instrument error.

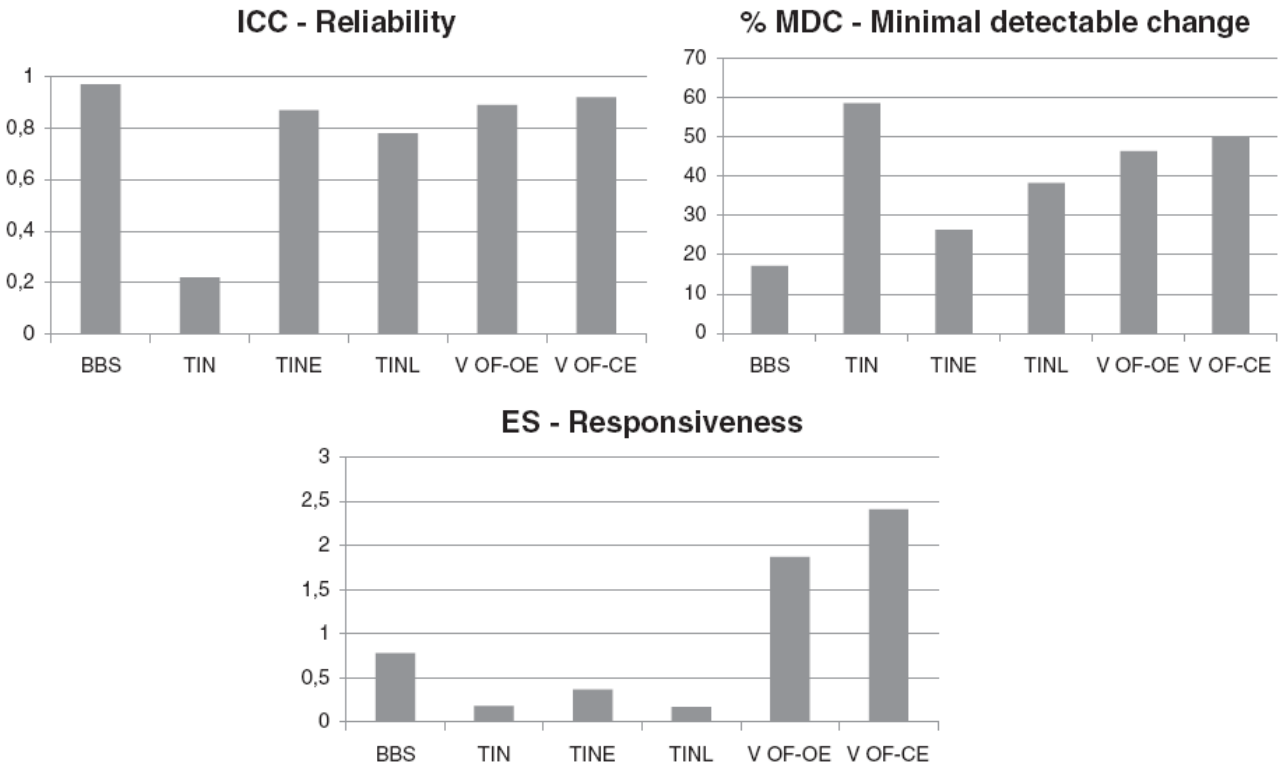


Figure 18: Comparison of ICC,%MDC, and ES results between balance scales and V data for OF-OE and OF-CE conditions.

The most notable comparison concerns responsiveness. V ES, particularly in the OF-CE condition, was superior to all clinical scales. The difference between ES values was 0.78 for BBS and 2.41 for V in the OF-CE condition. Thus, the proposed SP protocol significantly increases the ability to detect changes in the balance of SCI subjects compared with BBS.

Our study did not specifically evaluate the reliability, validity, and effectiveness of SP parameters for evaluating recovery after SCI. This aspect must be addressed in a devoted study, with repeated measures conducted during rehabilitation and balance recovery.

9.1.6 Study Limitation

Instructions to the patients, time of testing, and trial repetitions were present and were not tested experimentally. The reliability, validity, and effectiveness of COP parameters in assessing stabilometric platform were not been tested in healthy control subjects' group. The psychometric properties of COP measurements in healthy individuals have been examined in several studies[112], particularly in the elderly[129;144]. Nevertheless, the assessment of detailed data on healthy controls should be included in a devoted study.

9.1.7 CONCLUSION

For a reliable, validity and responsive balance assessment by SP in SCI subjects, COP V data must be acquired for OF-OE and OF-CE sensory conditions, reporting heel distance values for OF conditions.

9.2 Efficacy of task-specific biofeedback balance training in supporting walking functions in chronic incomplete spinal cord injury patients

9.2.1 INTRODUCTION

The body's equilibrium is maintained by the central nervous system, which fixes the COM around a specific point—a goal that is under constant challenge by continuous perturbations to the COM by factors, such as breathing, heart rate, and muscle activity [110]. To maintain postural stability, several afferent inputs, such as visual, vestibular, and somatosensory, are integrated and converted into efferent motor outputs, which in turn are transmitted down to the spinal cord along various motor tracts [111]. Damage to any of these systems can result in postural instability.

Lack of postural control is regarded as one of the main reasons for causing a fear of falling among the people with SCI during their rehabilitation programs that are designed to improve their ability to walk and stand [6;153]. Brotherton et al. [154] stated that falls by individuals with SCI often occurred in the home, especially during the day. The incidence of fractures has been reported as being 18%; (5–6% greater than that experienced by healthy older adults). In addition, the incidence rate for falls in people with SCI is 75%, which is higher than the incidence reported for healthy subjects aged 65 and older (35%),7,9 and is also higher than those reported for subjects with neurological disease resulting in peripheral neuropathy (50%) or Parkinson's disease (38–62%) [6].

Balance has seldom been analyzed in SCI patients; nevertheless, various groups have addressed this issue, suggesting its importance in determining gait performance [5;47;104]. Re-education of balance function in SCI patients by task-specific oriented training [155] has been examined, focusing on sitting balance recovery [155 156 110] and standing balance [113;157]. Even if it has been recently demonstrated that balance is a key factor of walking recovery [5], no data are available on the efficacy of task-specific biofeedback balance training in supporting walking functions in chronic motor incomplete SCI patients.

Thus, the object of this open-case study with a prospective control was to determine the efficacy of visual biofeedback (vBFB) task-specific standing balance training in improving balance performance and gait in subjects with chronic motor incomplete SCI compared with conventional over-ground rehabilitation.

9.2.2 MATERIAL AND METHODS

9.2.2.1 Study design

Six consecutive SCI subjects who were referred to the FSL spinal cord unit as outpatients between January 2009 and April 2010 and met inclusion criteria below were enrolled into the study as the experimental group (EXP). Subsequently, balance and gait data for 6 SCI patients with matching epidemiological, clinical, and neurological features, satisfying the same inclusion criteria, were extracted from our database [5], constituting the control group (CTRL). Balance and walking features were also collected from 6 healthy subjects who were comparable with regard to gender, height, weight, and age—constituting the healthy group (HEALTHY). The demographics and clinical features of the HEALTHY, CTRL, and EXP subjects are reported in *Table 9*.

Table 9: Clinical features of HEALTHY, CTRL, and EXP SCI subjects (all patients are ASIA level D, according to the inclusion criteria of the study). Abbreviations: SCI, incomplete spinal cord injury; HEALTHY, healthy subjects; EXP: experimental SCI patients; CTRL: control SCI patients; M, male; F, Female; NT, non-traumatic SCI lesion; T, traumatic SCI lesion.

	Age (years)	**Sex**	**Height (cm.)**	**Weight (Kg.)**	**Aetiology**	**Lesion Level**	**Duration of injury (months)**
HEALTHY1	50	M	175	87			
HEALTHY2	39	F	176	61			
HEALTHY3	56	F	175	64			
HEALTHY4	61	F	168	65			
HEALTHY5	37	M	166	59			
HEALTHY6	59	M	167	73			
HEALTHY (mean ± sd)	***50.33 ± 10.26***	***3 M – 3 F***	***170.67 ± 4.13***	***68.17 ± 10.40***			
CTRL1	54	M	169	68	NT	T 12	26
CTRL2	36	F	177	58	NT	T 9	24
CTRL3	61	F	158	60	NT	L 5	49
CTRL4	63	F	159	80	NT	T 7	23
CTRL5	39	M	175	86	T	L 3	29
CTRL6	68	M	167	74	NT	T 5	14
CTRL (mean ± sd)	***53.50 ± 13.21***	***3 M – 3 F***	***167.50 ± 7.89***	***71.00 ± 11.08***			
EXP1	52	M	169	68	NT	T 12	29
EXP2	37	F	176	60	NT	T 9	24
EXP3	54	F	168	70	NT	L 5	51
EXP4	66	F	172	66	NT	L 4	28
EXP5	40	M	177	88	NT	L 3	26
EXP6	63	M	160	78	T	T 5	27
EXP (mean ± sd)	***52.00 ± 11.74***	***3 M – 3 F***	***170.33 ± 6.21***	***71.67 ± 9.91***			

9.2.2.2 Population

The inclusion criteria comprised chronic SCI (at least 12 months post-injury), level D on the ASIA Impairment Scale[21], the ability to maintain a standing position unsupported for at least 1 minute, and the ability to walk at least 10 meters [158]. During the study, subjects did not participate in other rehabilitation or research interventions that might have influenced the outcome of this study.
The local ethics committee approved this study, and all subjects gave informed consent to participate (Prot. CE/AG.4-PROG.231-65).

9.2.2.3 Intervention: CTRL and EXP group training

Fort CTRL and EXP patients, the rehabilitation program comprised an 8-week regimen, 5 times per week for 60 minutes each day. For the CTRL group, the entire 60 minutes was devoted to over-ground conventional rehabilitation, including balance and walking training, per Dobkin et al.[159] and Alexeeva et al.[104]. EXP participants underwent 40 minutes of the same rehab protocol as for CTRL patients, followed by 20 minutes of specific vBFB training .
In the vBFB training, patients stood on the force plate with a monitor at eye level approximately at 1.5 m away (*Figure 19*).

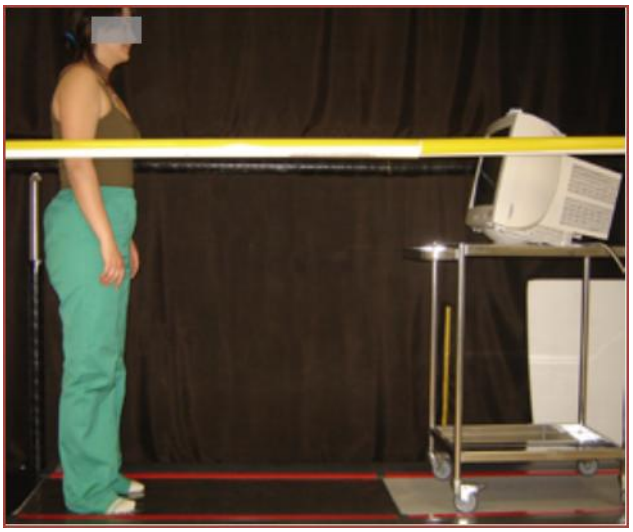


Figure 19: Patients position during vBFB training/assessment

The center of pressure (COP) position signal was used as visual biofeedback in real-time mode during the exercises. vBFB training addressed the 3 primary aspects of balance recovery for stroke patients per Nichols [160]: steadiness (the ability to maintain a given posture with minimal extraneous movements), symmetry (equal weight distribution between the weight-bearing components), and dynamic stability (the ability to move within a given posture without losing balance).

For all SCI subjects, the exercises in the vBFB protocol were the same. In particular, postural steadiness was treated with activities that required maintenance of the COP within a narrow target or shaded area on the screen as weight was transferred from one target to the next (*Figure 20*)

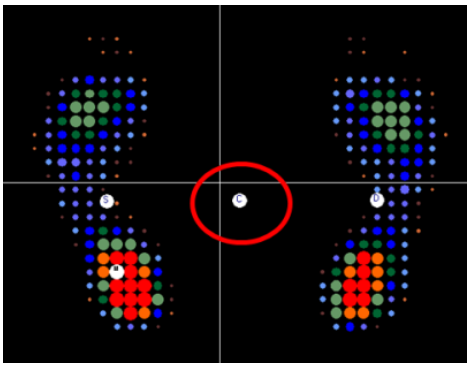


Figure 20: Postural steadiness exercise

Postural symmetry was rehabilitated by asking the subject to keep the correct weight distribution on each foot while standing to maintain the COP on the midline. Further, SCI subjects had to learn to maintain the COP on the midline during the postural and reaching tasks, such as closing/opening their eyes and reaching for an object that was in front of them (*Figure 21*).

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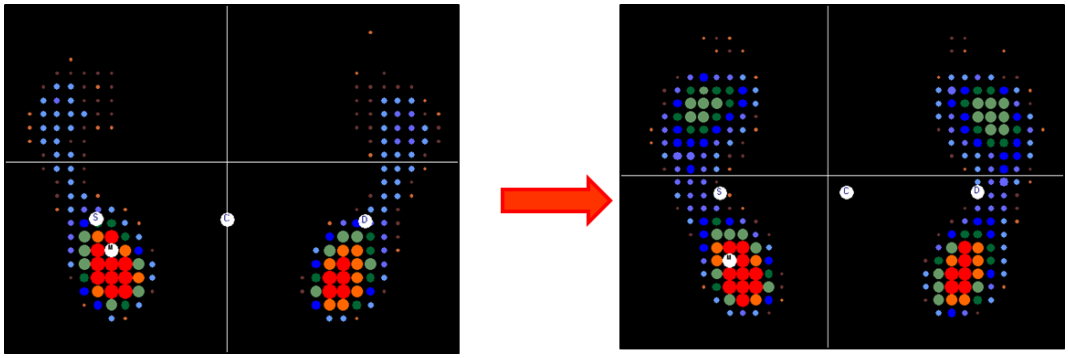

Figure 21: Postural symmetry exercise

Dynamic stability was addressed by asking patients to shift weight along the anteroposterior or mediolateral plane or follow the COP guide that appeared on the screen (*Figure 22*).

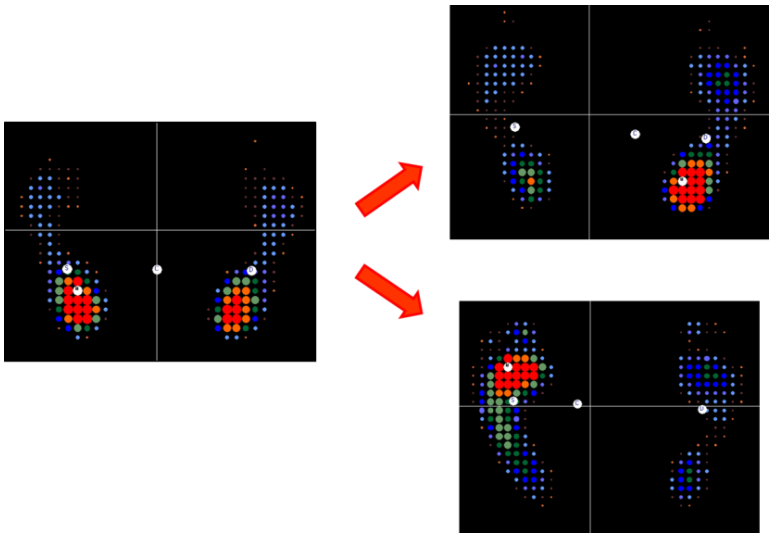

Figure 22: Dynamic stability exercise

9.2.2.4 Setup and evaluation of outcomes

At baseline (T0) and at the end of the training session (T4) and every 10 vBFB sessions (T1, T2, T3), EXP subjects underwent a battery of clinical and instrumental evaluations. Follow-up examinations were performed 1 month (C1) and 2 months (C2) after the end of the training. From our database, we extracted clinical and instrumental balance and gait data for CRTL subjects at baseline (T0) and after 8 weeks of conventional rehab (T4) (Figure 23). HEALTHY subjects underwent the same clinical/instrumental assessment once, and their data were used as a reference of physiological balance and gait parameters. For all groups, the balance and gait evaluations were performed in the following order: instrumental balance and gait examinations and clinical assessments using scales and time tests.

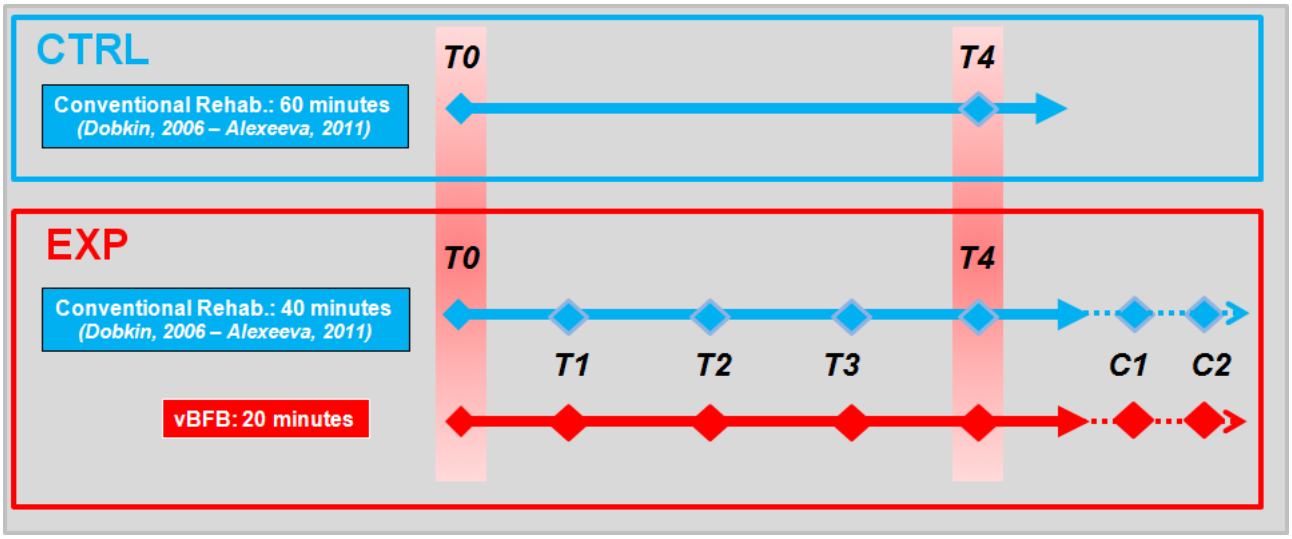

Figure 23: Rehabilitation intervention and evaluations schema for CTRL and EXP group

Neurological status was assessed using the American Spinal Injury Association (ASIA) and ASIA Impairment Scale (AIS) [161], and balance impairments were evaluated using the Berg balance scale (BBS) [115]. To examine walking level and performance, we used the walking index for spinal cord injury (WISCI) [133], 10-meter walk test (TMWT) [162], 6-minute walking test (6MWT) [163], and the timed up-and-go test (TUG) [164].

9.2.2.4.1 Evaluation of balance

Balance and vBFB training were evaluated using the same static force platform described for study "*Reliability, validity, and effectiveness of center of pressure parameters in assessing stabilometric platform in subjects with incomplete spinal cord injury: A serial cross-sectional study*" (BPM 120 - Physical Gait Software Vv. 2.66, Rome, Italy). During the assessment of static stability, as suggested by results of previous study (*see 9.1.7*) patients stood barefoot in a natural and relaxed position, arms at their sides, with the heels lined up and apart (OF) at a comfortable distance, fixed throughout the

sessions, and forefoot open to 30 degrees with eyes open (OE) facing a target 1.5 m away and eyes closed (CE). COP mean velocity (V, mm/s) was used as the highest reliable, valid and effective COP parameter to assess balance features (*see 9.1.7*). To calculate the mean V values 3 trials were performed for both OE and CE conditions, each lasting 51.2 seconds as suggested by results of previous study (*see 9.1.7*).

9.2.2.4.2 Evaluation of gait

Locomotion variables were recorded and analyzed by using the KineView Motion System® (Kineview, Hafnarfjordur, Iceland). In the experimental setup, we performed a bidimensional gait analysis of 3 strides on the sagittal plane. All subjects were instructed to walk OE at a comfortable, self-selected velocity [1], walking 2 m ahead of the mat and continuing 2 m past the end. Before data were collected, subjects performed the walking trials to familiarize themselves with the procedure. Kinematic data were recorded at 50 frames/s with a digital camera (Cyber-Shot DSC P73, Sony, Tokyo, Japan). Spatial movements of the lower extremity segments were determined, based on the position of passive markers that were placed per the Helen Hayes biomechanical model [165] modified to fit the bi-dimensional approach (*Figure 24*).

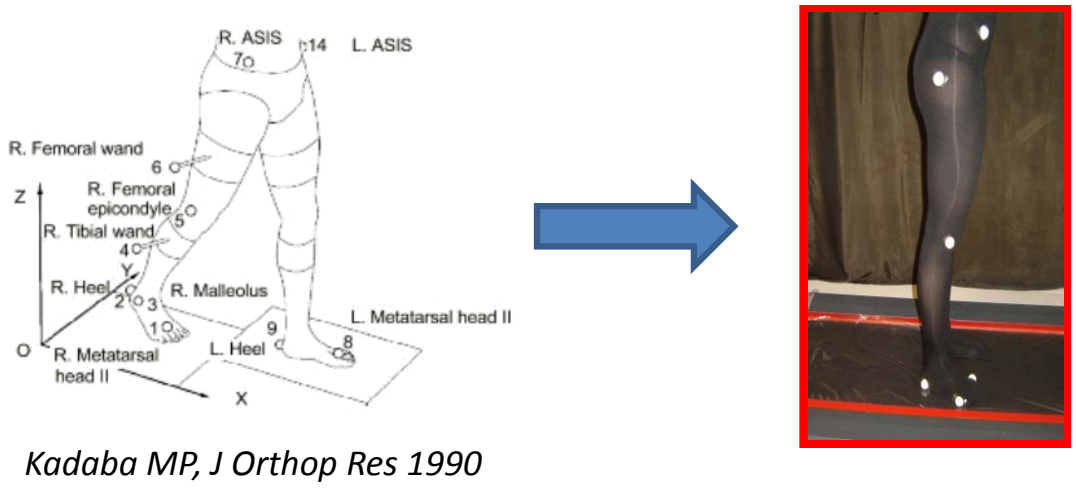

Figure 24: Passive markers position for gait evaluation by KineView Motion System®

Kinematic data were reconstructed offline using Matlab (Mathworks, Inc., version 7.1, Natick, Massachusetts, USA) after digitalization of the markers with the KineView Motion System. The following kinematic data were considered: speed (m/s); cadence (N° step/min); stride length (STRIDE: mean of right and left stride in m); stance phase (ST: mean of right and left stride); and double-time support phase (DTS: mean of right and left stride) expressed as the percentage of gait cycle. In this study, we defined STRIDE as the event between 2 successive instances of foot-ground contact, ST as the event from foot-ground contact to lift off, and DTS as the time for which both feet were in contact with the ground [166]. Foot-ground contact and lift off were assessed using KineView. All gait variables were averaged from the kinematic data of the 3 trials.

9.2.2.5 Statistical analysis

No participant withdrew from the trial, and all outcome measures were obtained for all SCI and HEALTHY subjects. For each subject, the mean values of stabilometric parameters were calculated by averaging 3 trials for each visual condition (OE – CE). Gait variables were averaged from the kinematic data of the 3 trials. Descriptive statistics were performed for all variables. Before statistical comparisons were made, Kolmogorov-Smirnov test was performed to evaluate distribution of the data.

One-way analysis of variance (ANOVA) was performed to compare balance and gait data between groups (with HEALTHY, EXP, and CTRL as independent variables) at T0 and T4. When the ANOVA results were significant, Bonferroni post hoc test was performed. K independent sample was applied at T0 and T4 to assess intergroup differences for nonparametric scale scores (BBS – WISCI).

Paired t-test was used to compare the effects of rehab approaches, evaluated as T4-vs-T0 data, for the CTRL and EXP groups. For BBS and WISCI, we used Wilcoxon test. For each balance and gait parameter, the percentage of improvement between T4 and T0 data was calculated. To compare the percentages of improvement after training between the CTRL and EXP groups, independent T-test was used. For BBS and WISCI, as nonparametric measures, group data were compared by Mann-Whitney U test.

To identify improvements during rehabilitation, the effectiveness[167] of each balance and gait parameter was calculated for both SCI groups per the following formula, using healthy data as reference scores, reflecting highest level of performance:

Effectiveness = ((SCI data T4 – SCI data T0)/(medium HEALTHY data – SCI data T0))* 100.

Differences in efficacy between the CTRL and EXP groups were analyzed by independent t-test or Mann-Whitney U test when appropriate.

One-way repeated measures ANOVA was used to compare performance at T0 versus at the vBFB training steps (T1, T2, T3, T4, C1, C2) in EXP patients, followed by post hoc comparison by Bonferroni test.

Overall comparisons of balance and gait improvement were made at each training time point (Tn) by averaging the percentage of improvement in each index across all balance or gait indices per the following formula:

Percentage of improvement = (index value at Tn / index value at T0) * 100.

Pearson R and Spearman rho correlation coefficients for continuous and ordinal variables, respectively, were calculated to quantify the relationship between the improvement in each balance index and walking index in EXP and CTRL subjects, calculated as the difference between T4 and T0 (Δ).

For all tests, the significance was set at 0.05. Statistical analysis was performed using SPSS for Windows (version 9.0, Chicago, IL).

9.2.3 RESULTS

9.2.3.1 vBFB training selectively improves balance and gait performance

Clinical and instrumental balance and gait assessment results are reported in *Table 10.*

Table 10: Data (mean and sd values) of balance and gait clinical and instrumental evaluations for HEALTHY subjects, as physiological references, and EXP and CTRL subjects at baseline (T0) and after 8 weeks of treatment (T4).

	HEALTHY		**CTRL**				**EXP**			
			T0		**T4**		**T0**		**T4**	
	Mean	***SD***	***Mean***	***SD***	***Mean***	***SD***	***Mean***	***SD***	***Mean***	***SD***
BALANCE										
BBS	*56,00*		31,00	8,97	33,00	8,00	26,00	10,69	41,00	7,80
V OE	*1,83*	*0,50*	7,24	3,11	7,12	4,61	9,54	5,54	4,58	2,66
V CE	*1,98*	*0,65*	14,11	3,33	13,84	4,94	16,86	5,84	9,95	6,99
GAIT										
WISCI	*20,00*		12,67	0,82	12,67	0,82	14,17	1,83	17,15	1,64
10MWT	*12,00*	*1,16*	28,79	15,80	27,01	12,32	21,02	9,53	19,31	9,18
6MWT	*167,33*	*20,19*	178,28	78,09	177,35	75,54	8,05	68,08	259,64	82,84
TUG	*12,67*	*1,35*	42,18	36,06	38,18	31,26	21,70	10,70	15,22	6,14
SPEED	*0,84*	*0,16*	0,36	0,17	0,36	0,19	0,37	0,14	0,46	0,15
CADENCE	*83,99*	*10,37*	55,09	21,60	54,99	23,09	56,10	12,12	65,47	16,77
STRIDE	*1,19*	*0,15*	0,72	0,14	0,73	0,14	0,78	0,17	0,85	0,13
ST	*64,03*	*1,89*	78,11	7,14	76,48	6,84	73,75	5,23	71,49	4,22
DTS	*13,92*	*2,21*	24,57	6,34	24,55	6,34	25,16	5,65	23,77	5,77

As expected by the matching criteria adopted, CTRL and EXP subjects had comparable clinical and instrumental balance and gait performance at the beginning of the training (CTRL vs EXP at T0 – *Table 10*). The 8-week treatment (T4 vs T0) had a positive effect on the EXP and CTRL groups—but

significant only in EXP patients. In the EXP group, the treatment effect was significant for all indices, except for the 10MWT and DTS (CTRL T4 vs T0 and EXP T4 vs T0 – Table 3).

Table 11: Statistical comparison between CTRL and EXP groups at T0 and T4 (CTRL vs EXP) and statistical comparison between T0 and T4 (T4 vs T0) for each EXP and CTRL group are reported. Effectiveness values ± sd for CTRL and EXP gait and balance parameters and effectiveness comparison of EXP vs CTRL are also reported. Significant statistical values are underlined as bold-faced numbers. Sig: significance; n.s.: data not significant

	CTRL vs EXP		**T4 vs T0**		**Effectiveness**		
	T0	**T4**	**CTRL**	**EXP**	**CTRL**	**EXP**	**Sig.**
BALANCE							
BBS	ns	ns	ns	**0.028**	8.54 ± 8.99	51.60 ± 9,21	**0.000001**
V OE	ns	**0,0001**	ns	**0.00001**	1.81 ± 48.06	62.67 ± 26.46	**0.00003**
V CE	ns	ns	ns	**0.007**	-5.97 ± 57.70	52.78 ± 40.16	**0.003**
GAIT							
WISCI	ns	**0.020**	ns	**0.024**	0,00	59.33 ± 19.02	**0.031**
10MWT	ns	ns	ns	ns	-0.78 ± 36.82	28.67 ±62.27	ns
6MWT	ns	ns	ns	**0.017**	-1.39 ± 17.79	25.29 ±16.6	**0.023**
TUG	ns	ns	ns	**0.025**	42.54 ± 73.24	196.04 ± 183.06	ns
SPEED	ns	**0.015**	ns	**0.0003**	0.27 ± 12.60	0.19 ± 26.95	ns
CADENCE	ns	ns	ns	**0.001**	-6.75 ± 26.02	39.29 ± 51.90	**0.003**
STRIDE	ns	**0.010**	ns	**0.0001**	1.10 ± 19.50	14.93 ± 12.57	**0.007**
ST	ns	ns	ns	**0.018**	18.58 ± 31 29	3.05 ± 43.67	ns
DTS	ns	ns	ns	ns	-26.31 ± 8.94	10.12 ± 35.73	**0.026**

The CTRL-EXP group comparison at T0 by one-way ANOVA failed to reveal a group effect on any index. Conversely, at T4 group effect was significant on most gait and balance indices (CTRL vs EXP at T4 -*Table 11*).

The treatment effects on all indices, expressed as percentage of improvement from T4 to T0, are graphed in Figure 5 for the CTRL and EXP groups. EXP subjects experienced greater improvements than CTRL patients for all indices. The intergroup comparison was significant for all balance indices except V CE and the gait indices WISCI, TUG, SPEED, and CAD (*Figure 25*).

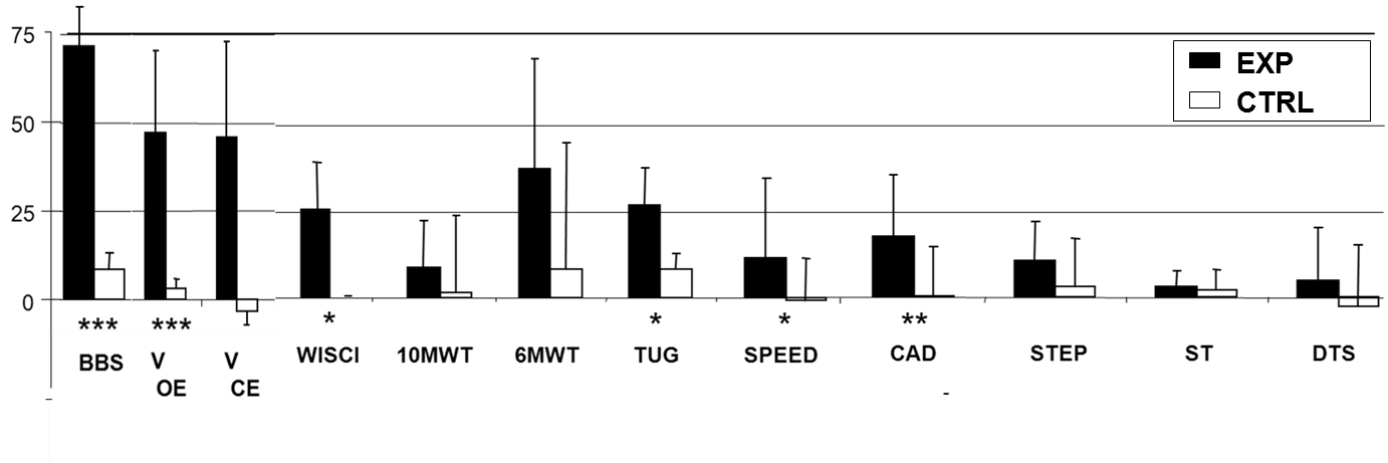

Figure 25: Percentage of balance and gait indexes improvements for EXP and CTRL groups. In the figure are reported the % of balance and gait indexes improvements, for EXP , black columns, and CTL groups , white columns. Statistical comparison between groups is reported in the figure by asterisks (p<0.05:*, p<0.005:**, p<0.001:***)

9.2.3.2 Differences between HEALTHY and SCI subjects in gait and balance indices

ait and balance indices are generally altered in subjects with motor incomplete SCI[53]. As expected, all indices in CTRL and EXP groups differed from HEALTHY data at T0 ($p<0.001$ for all EXP and CTRL data) and T4 ($p<0.001$ for CTRL data and $p<0.005$ for EXP parameters). Similarity with healthy data, expressed in terms of effectiveness [167], was used to assess the degree of recovery and improvement by rehab (*Figure 26*). We observed significant differences in treatments between the CTRL and EXP groups with regard to the improvement due to rehab (*Table 11*). The treatment effects were significant for nearly all balance indices and gait parameters.

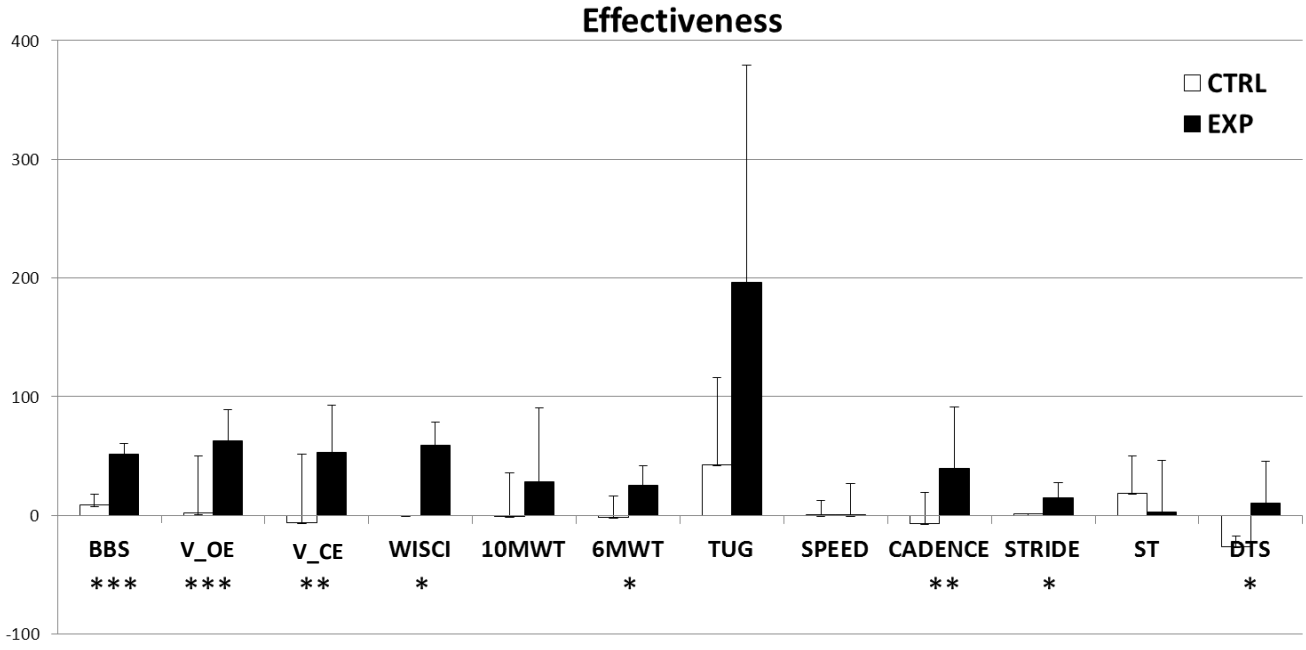

Figure 26: Effectiveness (%) of balance and gait indexes for EXP and CTRL groups. In the figure are reported the effectiveness (%) of balance and gait indexes compared between EXP , black columns, and CTL groups , white columns. Statistical comparison between groups is reported in the figure by asterisks ($p<0.05$:*, $p<0.005$:**, $p<0.001$:***).

9.2.3.3 Balance improves before gait during vBFB

Based on the gait and balance indices in the EXP group during the 8-week training period and at follow-up examinations, improvements in balance precede the amelioration of gait. The gait and balance parameters in the EXP group at all vBFB time points are reported in *Table 12*. One-way anova, with time as the main factor, demonstrated a patent effect of time on balance and gait parameters. By post hoc comparison, most balance indices reached significance before gait parameters. As detailed in Table III, most balance parameters reached significance at T1 and T2 compared with T0 already, with the remainder doing so at T3. Conversely, improvements in gait indices became significant at T3, T4, and C1 (*Table 12*)

Table 12: Balance and gait clinical and instrumental data of EXP subjects at baseline (T0) and during vBFB training (T1, T2, T3, T4, C1, C2). To compare balance and gait evaluations at T0 vs T1, T2, T3, T4, C1, and C2, repeated measures ANOVA was used (*:p <0.05, **: p <0.005, ***: p <0.001). Bold-faced numbers indicate the first significant improvement compared with T0.

	Evaluations						
Balance	**T0**	**T1**	**T2**	**T3**	**T4**	**C1**	**C2**
BBS	26.00 ± 10.69	30.00 ± 8.89	**34,67 (*) ± 8.82**	37,5 ± 8.68(***)	40,83 ± 7.78 (***)	43,67 ± 7.20 (***)	39,66 ± 9.13 (***)
V OE	9.54 ± 5.54	**7,59 ± 4.69 (**)**	6,64 ± 4.74(***)	5,77 ± 3.25 (***)	4,58 ± 2.66(***)	5,75 ± 4.26 (***)	6,21 ± 4.95 (**)
V CE	16.86 ± 5.84	**12,41 ± 6.18(***)**	12,65 ± 7.88 (*)	10,32 ± 7.30 (*)	9,95 ± 6.99 (**)	8,75 ± 6.40 (**)	7,53 ± 4.88 (**)
Gait parameters	**T0**	**T1**	**T2**	**T3**	**T4**	**C1**	**C2**
WISCI	14.17 ± 1.83	14.17 ± 1.83	15.17 ± 2.56	15.17 ± 2.56	**17.15 ± 1.64 (*)**	17.15 ± 1.64 (*)	17.15 ± 1.64 (*)
10MWT	21.02 ± 9.35	20.40 ± 11.29	20.48 ± 11.10	**19,21 ± 10.24 (*)**	19.31 ± 9 9.18 (*)	18,11 ± 8.58(*)	18,96 ± 10.25 (*)
6MWT	193.18 ± 68.08	215.67 ± 76.74	227.23 ± 79.53	**244,74 ± 88.59 (*)**	259,64 ± 82.84 (*)	238.23 ± 72.87 (*)	245.63 ± 86.95
TUG	21.70 ± 10.70	19.81 ± 9.37	21.64 ± 15.69	**17,68 ± 9.83 (*)**	15,22 ± 6.14 (*)	17,66 ± 12.29 (*)	20,30 ± 19.06 (*)
SPEED	0.37 ± 0.14	0.39 ± 0.12	0.42 ± 0.10	**0,47 ± 0.17 (*)**	0,46 ± 0.15 (***)	0,51 ± 0.13 (***)	0,51 ± 0.20 (***)
CADENCE	56.10 ± 12.12	61.12 ± 15.02	**61,08 ± 10.77 (*)**	65,25 ± 20.63 (*)	65,47 ± 15.61 (***)	68,22 ± 15.95(***)	68,12 ± 18.64 (***)
STRIDE	0.78 ± 0.17	0.79 ± 0.10	0.82 ± 0.11	0.83 ± 0.13	**0,85 ± 0.13 (***)**	0,89 ± 0.08(*)	0,88 ± 0.18 (*)
ST	73.75 ± 5.53	73.38 ± 34.70	71.66 ± 4.18	**72,88 ± 4.12 (*)**	71,49 ± 4.22(*)	71,38 ± 3.01 (**)	70,96 ±5.93 (**)
DTS	25.16 ± 5.65	29.26 ± 13.06	23.65 ± 5.32	25.37 ± 5.64	23.77 ± 5.77	**19,6 ± 6.02 (*)**	25.39 ± 7.03

To examine the relationships between changes in balance performance and gait indices during vBFB training, we calculated the overall percentage of improvement in balance and gait (see statistical analysis section for details) for all time points of vBFB (*Figure 27*) and noted parallel improvements in balance and gait indices. Further, balance indices reached significance earlier than improvements in gait.

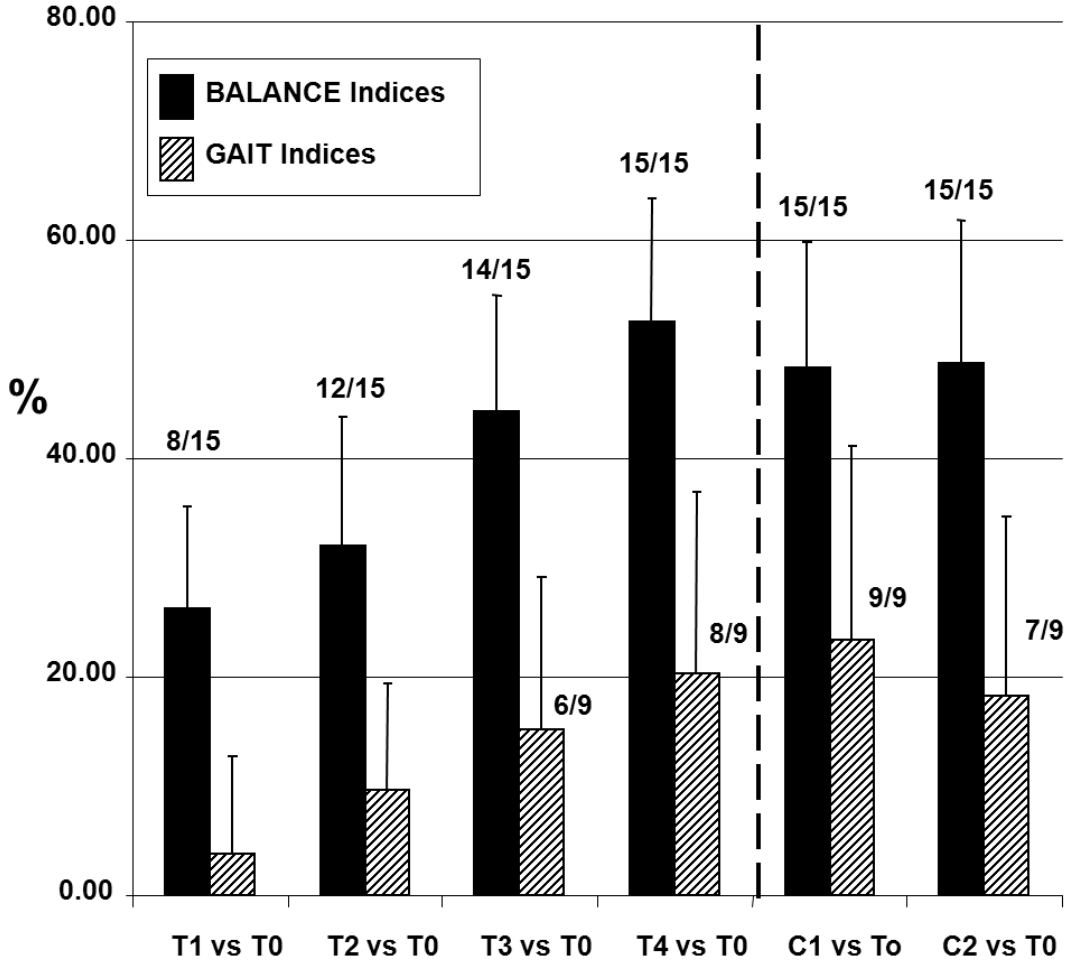

Figure 27: EXP Group: Percentage of improvement at T1, T2, T3, T4, C1, and C2 compared with T0 values.

9.2.3.4 vBFB training: enhancements in balance and gait correlate

The relationships between improvements in balance and gait over time are not conclusive of a direct influence of balance on gait. To identify the indices that predict improvements in both areas better, we analyzed the correlation factors for the T4/T0 improvement (Δ) for balance and gait data. There were no significant relationships in the CTRL data, but in the EXP group, several significant correlations were observed, especially for BBS and length parameters of balance data and DTS, 10MWT, and WISCI scores for g ait *(*Table 13).

Table 13: EXP group: Pearson's and Spearman's correlations for continuous and ordinal variables (BBS and WISCI) respectively, between gait *a*nd balance improvements calculated as T4/T0 differences (Δ). Bold-faced numbers indicate coefficients having p <0.05 (*), p <0.005 (**) or p <0.001 (***).

Correlations between improvements in balance and gait										
		Δ SPEED	**Δ CAD**	**Δ STRIDE**	**Δ ST**	**Δ DTS**	**Δ WISCI**	**Δ 10MWT**	**Δ 6MWT**	**Δ TUG**
Δ BBS	**C.C.**	**.569(*)**	.276	-.117	.330	**.599(**)**	**.828(**)**	**-.943(**)**	.314	.086
	Sig.	.014	.268	.644	.182	.009	.000	.000	.204	.735
Δ V OE	**C.C.**	**.678(**)**	**.534(*)**	.040	.379	**.589(*)**	**.772(**)**	**-.606(**)**	.240	-.248
	Sig.	.002	.022	.875	.120	.010	.000	.008	.337	.322
Δ V CE	**C.C.**	.286	**.529(*)**	-.036	.131	.445	**.818(**)**	**-.872(**)**	.378	.301
	Sig.	.250	.024	.887	.605	.064	.000	.000	.122	.225

9.2.4 DISCUSSION

Our open case study with a prospective control indicates that vBFB training improves balance and gait in chronic motor incomplete SCI subjects. Further, inclusion of vBFB training effected greater improvements in gait than conventional gait rehabilitation alone.
In the past 10 years, stabilometric platforms have been used widely to evaluate and rehabilitate balance. vBFB protocols have been used to rehabilitate individuals with neurological and non-neurological disorders, including multiple sclerosis [168], stroke [160], cerebellar ataxia [169], cerebral palsy [170], Parkinson disease [169], and ankle instability [171]. In these pathologies, vBFB training has been effective in improving balance.

The effects of vBFB training on SCIs have only recently been addressed [113]. SCI subjects learn to use visual cues and sensory inputs from the body and improve their standing balance [113]. Our data, consistent with those of Sayenko [113], indicate that vBFB training promotes balance in chronic SCI subjects. Clinical and instrumental evaluation tools concur in demonstrating significant improvement in balance after training only in the vBFB-treated group (EXP), compared with minor changes in conventionally treated subjects (CTRL), highlighting the value of task-specific balance training in increasing balance in chronic SCI subjects.

Classically, leg paralysis, reduced interlimb coordination, and impaired balance are the chief limitations to overground ambulation in SCI subjects [70], of which balance has recently been proposed to be highly predictive of gait recovery in SCI subjects [5], meriting specific targeting.

Balance vBFB training is effective in improving gait in various pathologies. vBFB training also has beneficial effects on walking speed in multiple sclerosis subjects [168], and gait parameters in chronic ankle instability [171]. In stroke, improvements in walking function after vBFB training was reported in one study [172] but not in another [173]. Our study is the first to examine the effects of vBFB training on gait in SCI subjects.

One of the chief problems in determining the efficacy of a rehabilitation protocol is the presence of spontaneous recovery. Spontaneous recovery from SCI has been well documented in subacute patients [62], whereas it seldom occurs in chronic lesions patients more than 1 year after development of the lesion [18].

Tefertiller et al. recently reviewed 19 studies that reported the lack of efficacy of task-specific gait training in chronic SCI [174]. Our data on the CTRL group are consistent with these findings. Subjects with chronic SCI who were treated with a conventional gait rehabilitation protocol without vBFB (CTRL group) experienced minor, insignificant improvements in gait. Conversely, the implementation of vBFB in the rehabilitation protocol drastically altered the effectiveness of the therapy. In the group that followed the rehabilitation protocol with vBFB training (EXP group), significant post-treatment improvements were observed for most gait parameters. The difference between the presence and absence of vBFB in the rehabilitation protocol was evidenced by the disparity in gait values at the beginning (T0) and end (T4) of training between groups, reaching

significance in most parameters only in the EXP group (*Table 11*). Worthy to note that only EXP group reached a reliable improvement of balance parameters (i.e BBS, V OE and V CE) and WISCI score not due to errors in measurement, as detailed by Tamburella et al. [175].

The lack of efficacy of conventional rehabilitation alone and the effectiveness of balance and gait training plus vBFB in chronic SCI subjects requires further analysis. Our study focused on walking AIS D subjects. Based on the WISCI values (*Table 10*), all subjects relied on some type of aid for walking. These aids, in addition to supporting attenuated muscle strength, substitute for balance. Thus, we hypothesize that at the chronic stage, subjects learn to adapt while performing everyday activities, progressively decreasing the need to maintain their balance unassisted [46]. If this hypothesis is true, at this stage, there might be little opportunity to improve muscle strength after traditional gait rehab, whereas balance training might compensate for the lack of balance exercises due to the use of aids.

Nevertheless, the value of good balance for gait in SCI is well established. Better balance enables one to have better functional gait at a higher speed with fewer aids [5;115]. Thus, we assume that task-specific vBFB training, although it acts on motor programs for balance control strategies in training regimens, is also effective for gait motor programs.

This link between balance and gait improvement has been confirmed by correlation analyses, based on T4/T0 differences. In the overall assessment of balance, improvement in COP parameters appears to be strictly linked to improvements in gait. In particular, with regard to instrumental balance and gait assessment, COP length indicators correlate with improvements in SPEED and DTS. These findings are supported by data on older, healthy subjects that have demonstrated the link between COP length and gait SPEED [176] or DTS [176]. With regard to improvements during training, Nardone et al. [124] reported correlation between COP length and DTS recovery in stroke subjects.

That improvements in balance precede the amelioration in gait also links vBFB to gait . Clinical and instrumental evaluations have demonstrated that EXP subjects improved balance after 10 days of vBFB treatment, whereas gait data improved significantly after 30 vBFB sessions (

Figure *28*, *Table 12*). Although parallel improvements in balance and walking have been observed in acute [47] and chronic SCI subjects [177], no study has examined the interdependence of these functions. We can not conclude that there is a causal relationship between improvements in balance and gait, but we have demonstrated that static stability improves before walking in chronic SCI subjects and thus propose that improvements in walking depend in part on those in balance.

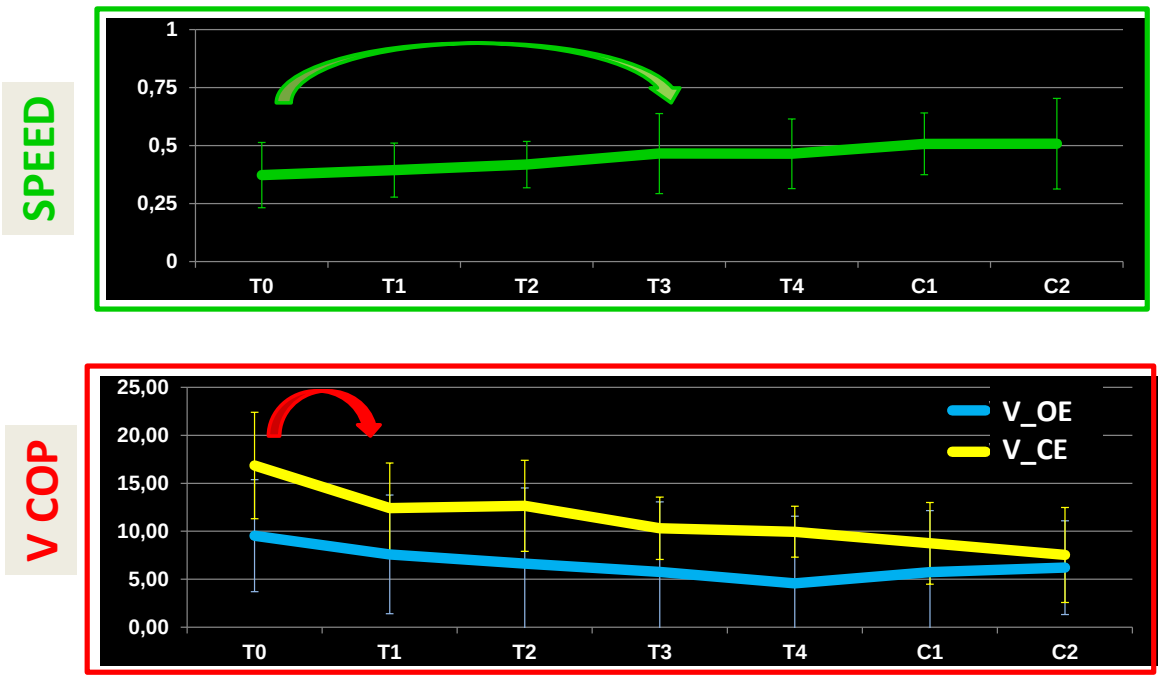

Figure 28: V and SPEED improvements in relation to vBFB training steps. Green and red arrow, point out respectively significant improvements of gait SPEED and V values in comparison to T0 assessment for EXP group.

Although improvements in balance and gait might be unrelated with recovery in spontaneous SCI subjects, all SCI subjects in both groups were chronic (> 12 months) with stable gait and balance parameters. Further, the groups performed similarly with regard to gait and balance for all parameters at baseline. This stability in functional status is supported by the not significant response after 8 weeks of conventional gait training in the CTRL group.

The intensity of rehabilitation, a significant factor of the effectiveness of rehabilitation, might be related to improvements in gait [178]. In our study, both SCI groups were treated 60 min daily, 5 times per week. In this regiment, the treatments differed only in the type of training—ie, vBFB—which was implemented only in the EXP group.

Thus, vBFB improves gait parameters, but it is unknown whether these improvements are related to physiological gait. To this end, we compared EXP and CTRL data with balance and gait data from matched HEALTHY subjects. As expected, at baseline, the performance on balance and walking differed significantly in all SCI patients compared with healthy subjects [53]. Confirming the matching procedure, the gap in performance versus healthy data was similar in both SCI groups at T0. At the end of the training, the parameters in both groups remained different from those of healthy subjects. Nevertheless, balance and gait indices more closely approximated those of healthy ones than the CTRL group. By statistical comparison of the effectiveness between conventional rehab and vBFB trainings with regard to balance and gait data, we noted a significant difference between CTRL and EXP group (Effectiveness - *Table 11*).

For gait, significance was not reached in the one-time test and 10MWT and for one kinematic parameter, DTS, after vBFB training. The WISCI and 10MWT results are related. WISCI is a scale that was developed to include device use in the evaluation of gait for a distance of 10 meters and should thus be effective in scoring balance-related changes in gait. Nevertheless, most AIS-D subjects are at the same WISCI level, rendering it nearly useless in this group [179]. Further, Burns proposed that an improvement of one WISCI level in chronic SCI subjects has clinical relevance [146]. Thus, the significant improvement of 3 WISCI levels that was associated with the insignificant improvement in the 10MWT only in the EXP group suggests that vBFB training is effective.

DTS values, although they were insignificant at T4, became significant at C1 (*Table 12*), a finding for which we have no clear explanation. Nevertheless, the correlation between DTS and balance is well documented [124;176], and the lack of changes in DTS in the CTRL group further support our findings on the efficacy of vBFB.

The reliability of our findings and their clinical significance is strengthened by our follow-up data. At 2 months after the end of treatment, the improvements in balance and gait were maintained, underscoring the value of vBFB in the chronic stages of spinal lesions but highlighting the effects of balance feedback practice with regard to relearning motor skills and the ability to modulate skill retention with long-lasting effects [180].

9.2.5 Study limitations

This study was not double-blinded. The CTRL group was epidemiologically, clinically and eurologically matched with the EXP group but was structured as a historic group. Thus, successive prospective studies in a larger group of subjects are required to confirm our observations. The results of this trial merely reflect the response of chronic SCI patients to training intervention, due to the inclusion of only those with chronic SCI to reduce variability in data and increase the statistical power [181]. Thus, our study does not apply to a population of acute and subacute SCI subjects.

9.2.6 CONCLUSION

Our results indicate that vBFB training improves balance and gait in chronic motor incomplete SCI subjects. Further, inclusion of vBFB training in a rehabilitation protocol effected greater improvements in gait than conventional gait rehabilitation alone, also maintained at follow-up examinations.

10 *Study 2:*

Somatosensory inputs by application of KinesioTaping: Effects on spasticity, balance, and gait in chronic spinal cord injury

10.1 INTRODUCTION

In designing effective gait rehabilitation programs after SCI, knowledge of the neuronal mechanisms that mediate and, in particular, influence the afferent feedbacks in the function of the damaged spinal cord is paramount [11]. Locomotion requires continuous modulation of spinal CPG circuits to adapt to the everchanging environment. Feedback from a variety of sources, such as visual, vestibular, somatosensory, and proprioceptive circuits, must be interpreted and integrated into CPG activity to generate locomotion that is effective under all conditions [11]. In this complex framework, sensory feedback and context-specific gait requirements interact in affecting muscle synergies [182].

As detailed above, cortical re-organization occurs after SCI due to re-organization may be attributed to pre-existing and new neural circuits. Additionally recovery function can be also related to the re-activation of parts of sensory motor system that are still intact [98]. Delwaide and Crenna [183] suggested that it is possible to activate the supraspinal centers by exteroceptive afferents. In line with this hypothesis Nakazawa [184] et al recently proposed that during standing disrupted plantar pressure sensation resulted in balance deficits, implying that cutaneous afferents might not only contribute to the control of locomotion, but also to posture. It is generally assumed that the sensory information projecting to the spinal cord and brain serves to correct errors in movement, i.e., provides corrective feedback in response to the activation of sensory receptors from a wide range of tissues and tissue environments that change in a predictable way. One approach to re-activate nervous system, particularly in the context of sensorimotor system, is to use rehabilitation strategies that include somatic sensory afferent and activating functional movements [185].

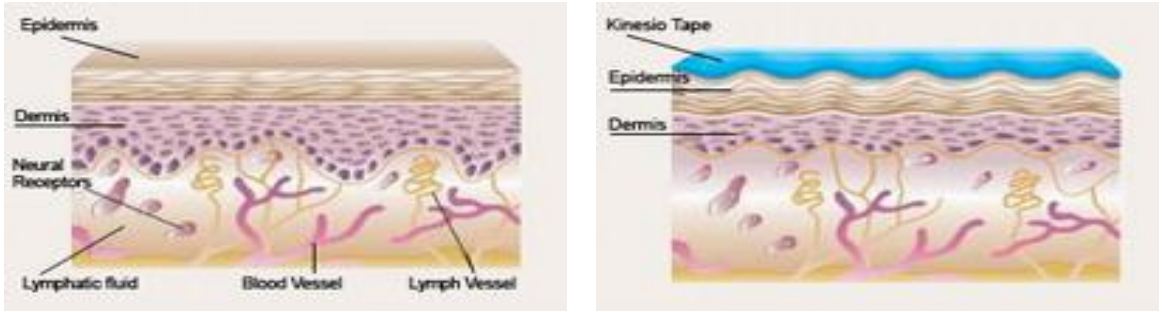

Figure 29: General representation of skin with and without Kinesio Taping over epidermis.

In recent years, increasing cutaneous stimuli through neuromuscular KinesioTaping (KT) (Figure 29) has been proposed to enhance somatosensory inputs [186]. Alexander et al. reported decreased H-reflex amplitude after KT of the trapezius, suggesting that it influences muscle tone [187]. This KT-dependent H-reflex decline indicates that it is inhibitory and adjusts muscle activity through proprioception feedback [188]. KT has been used in neurological pathologies[189-191], including stroke and multiple sclerosis, and various orthopedic disorders[20-22;68], generally improving muscle tone, range of motion, center of pressure balance parameters, and pain symptoms.

Major gait impairments in incomplete SCI are caused by ankle spasticity[6;9] and decreased balance[5;6], both of which are positively affected by KT in neurological[189] and non-neurological disorders[21-23]. Thus, we examined KT treatment in controlling ankle muscle tone in subjects with incomplete SCI, determining its effects on spasticity, balance, and gait by clinical and instrument-based evaluations.

10.2 MATERIAL AND METHODS

10.2.1 Study design - Population

A randomized crossover case control design was used to compare the effects of KT and conventional nonelastic silk tape (ST) on ankle muscles in subjects with chronic incomplete SCI**.** Patient selection was based on the clinical assessment, per the American Spinal Injury Association (ASIA) standards for neurological status, and on the degree of ankle spasticity [21], per the modified Ashworth scale (MAS). The inclusion criteria were chronic SCI lesion (ie, at least 12 months postinjury), AIS level D, and MAS higher than 2 bilaterally in the soleus/gastrocnemius muscles. The exclusion criteria were the presence of other neurological or orthopedic impairments, participation in other studies, and pharmacological treatment for spasticity in the previous 4 weeks. This study was approved by the local ethics committee.

From January 1, 2013 to April 30, 2013, 33 consecutive patients who were admitted to the Spinal Cord Rehabilitation outpatient service of Santa Lucia Foundation were examined by an experience neurologist (G.S.), of whom 11 subjects met the inclusion criteria. The demographics and clinical features of the SCI subjects are reported in *Table 14*.

Table 14: Patients' clinical and epidemiological data

Patients	Sex	Age	Weight (Kg)	Height (cm)	Etiology	Lesion Level	Years since SCI	MAS	WISCI level
PT1	M	34	85	1.82	Traumatic	C6	4	3	13
PT2	M	69	75	1.65	Traumatic	C6	8	2	18
PT3	F	35	60	1.76	Non traumatic (Degenerative)	T9	4	5	19
PT4	M	51	74	1.73	Non traumatic (Vascular)	C6	3	2	18
PT5	F	41	60	1.64	Non traumatic (Vascular)	T6	4	2	19
PT6	M	52	80	1.78	Traumatic	C6	3	2	20
PT7	F	77	67	1.66	Non traumatic (Vascular)	T10	7	2	19
PT8	M	58	66	1.73	Non traumatic (Tumoral)	T11	2	4	19
PT9	F	41	55	1.7	Non traumatic (Tumoral)	T7	10	4	20
PT10	M	72	81	1.64	Non traumatic (Degenerative)	C7	6	3	13
PT11	F	38	64	1.6	Traumatic	T8	12	3	20
Mean		***52***	***70***	***170***			***5.72***	***2.9***	***18***
S.D.		***16***	***10***	***0.07***			***3.19***	***1.04***	***2,57***

10.2.2 Intervention: KT and ST treatment

After enrollment, SCI subjects were randomized into 2 treatment groups. Group A (n = 6) underwent 48 hours of KT, followed by 48 hours of ST 1 week later. Group B (n = 5) received 48 hours of ST treatment, followed by 48 hours of KT treatment after 1 week (*Figure 30*). All subjects underwent clinical and instrumental evaluations before (T0) and immediately after treatment (T_{48h}). Electromyography (EMG) was performed only in Group B before, during, and after KT treatment. A certified KT practitioner (F.T.) administered all taping procedures. Clinical and instrumental outcomes were measured at T0 and T_{48h} after removal of the KT by a different researcher (L.M.) who was blinded to the treatment.

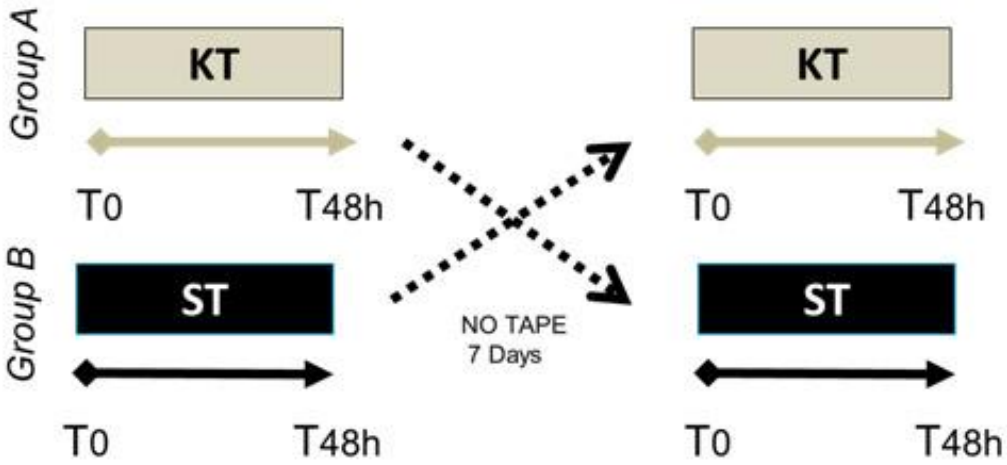

Figure 30: Randomized crossover case control study schema.

KT and ST were applied bilaterally to the plantar-flexor ankle muscles, soleus (S), and gastrocnemius (G), per Luque-Suarez et al. [192]. Standard 5-cm single-strip nonelastic silk tape and Cure© tape were used for the ST and KT, respectively. Y-strip tapes were applied to the S and G muscles with the subject in a prone position, the with knee extended and the ankle in 90° passive dorsiflexion. Both tapes were applied directly to the skin using a decompressive muscle technique, with 0% stretch, from the calcaneus to the medial and lateral femoral condyles (*Figure 31*). To maximize their adhesion, the tape strips were warmed by rubbing them in the hands several times on the application zone [192].

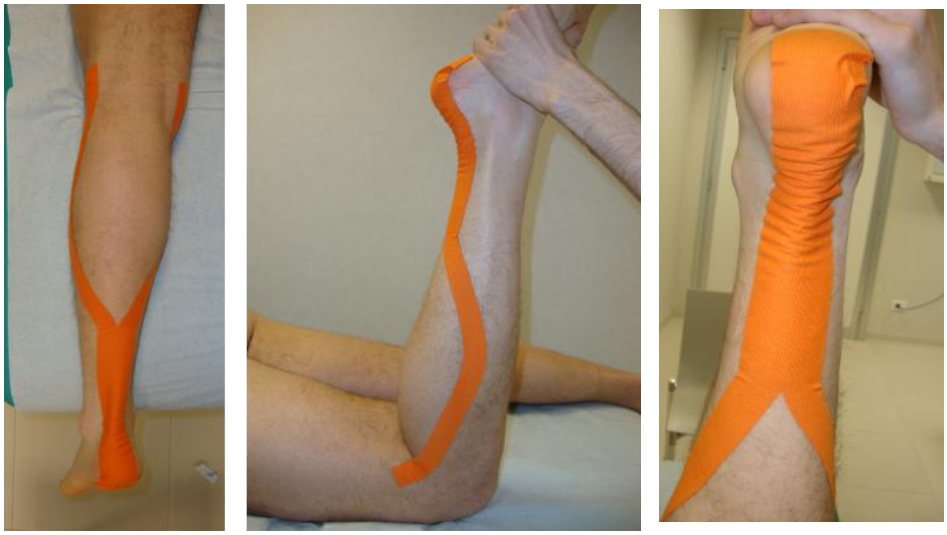

Figure 31: KT application for calf muscles

10.2.3 Setup and evaluation of outcomes

All assessments were performed by the same examiner at the same time each day before application of the tape (T_0) and after 48 hours (T_{48h}) of KT or ST treatment. Neurological status was assessed using the American Spinal Injury Association (ASIA) and ASIA Impairment Scale (AIS) [21]. Active and passive range of motion (ROM) was measured using a standard manual goniometer [193].

The Modified Ashworth Scale (MAS) [194] was used to evaluate ankle spasticity. Spasms, clonus, and pain were scored using the Penn modified Spasm Frequency Scale (PSFS)[195], Spinal Cord Assessment Tool for Spastic Reflexes subscale for clonus assessment (SCATS) [196], and Global Pain Scale (GPS) [197], respectively. Balance and gait were assessed using the Berg Balance Scale (BBS) [115], Walking Index for Spinal Cord Injury (WISCI) [133](21), 10-meter walk test (10MWT) [162], 6-minute walking test (6MWT) [163], and timed up and go test (TUG) [164]. Walking time tests were performed using a self-selected walking device, if needed [198] and scored using the WISCI, as reported in *Table 14*. All subjects we subjected to instrument-based balance and gait analyses as detailed below.

The visual analog scale (VAS) was administered at T_{48h} to assess perception of reductions in spasticity and tape's acceptance. Patients were asked to quantify the reduction in spasticity due to the tape, on a scale from 0 (no reduction in spasticity) to 10 (maximum reduction in spasticity). EMG analyses were performed only for KT-treated subjects in Group B.

10.2.3.1 Evaluation of balance

Balance was evaluated using the same static force platform described for Study 1 (BPM 120 - Physical Gait Software Vv. 2.66, Rome, Italy). As detailed for Study 1 static stability was assessed per protocol defined above (see *9.1.7*) by COP mean velocity (V, mm/s) analysis in OE and CE visual assessment conditions.

10.2.3.2 Evaluation of gait

Locomotion kinematic gait data were recorded and analyzed using the bidimensional KineView Motion System ® (Kineview, Hafnarfjordur, Iceland) per the protocol for chronic SCI subjects already described for Study 1 (see *9.2.2.4.2*) based on 3 strides at a self-determined velocity. The following kinematic data were considered: speed (m/s), cadence (N° step/min), stride length (m), stance phase (STANCE, %), and double-time support phase (DTS, %).

10.2.3.3 EMG assessment

For Group B patients, surface EMGs of tibialis anterior (TA), extensor hallucis longus (EHL), S, and G muscle activity were analyzed. Recordings were made before (T_0), 5 minutes after KT was applied (T_1), and after the KT was removed (T_{48h}). EMG data were acquired through 4 wireless EMG sensors (Figure 32), 1 for each muscle, affixed per SENIAM recommendations [199] using EMG Delsys. EMG data were processed using EMG Works Analysis (Delsys, Boston, USA) using a pass-band filter between 10 and 450 Hz, and successively a 50-Hz notch filter. Root mean square (RMS) values, with a window of 0.250 and an overlap of 0.0625, were obtained from the filtered data. Data on each muscle were then imported into Matlab (Mathworks, Inc., version 7.1, Natick, Massachusetts, USA) to analyze muscle coactivation by calculating the coactivation index (CI) [200]

$$CI = \frac{\int EMG(S+G)}{\int EMG[(TA+EHL)+(S+G)]} \cdot 100$$

CI is a relative measure of antagonist (S and G) contribution to total activation (S and G + TA and EHL) during the dorsiflexion task (30). Thus, an increase in CI reflects a rise in co-contraction. CI ranged from 0% to 100%, with 100% indicating full muscle coactivation, defined as coactivation (ie, simultaneous activity) of all ankle muscles. EMG data were recorded while patients were asked to perform maximal voluntary contraction (MVC) during 5 dorsiflexion active movements lying down with knees flexed and extended. Data were averaged across the 5 active tasks.

Figure 32: EMG wireless sensors

10.2.3.4 Statistical analysis

No participant withdrew from the trial, and all outcome measures were obtained for all SCI subjects. Descriptive statistics were generated for all variables. Prior to the statistical comparisons, normal distribution of the data was confirmed by Kolmogorov-Smirnov test.

Treatment effects were analyzed by grouping the KT and ST data on Group A and B subjects. Paired t-test was used to compare the effects of treatment, evaluated as T0 versus T_{48h}, for each KT or SK treatment groups. At T0 and T_{48h}, KT and ST were compared by independent t-test and Mann-Whitney U-test for ordinal and non ordinal variables, respectively.

For each clinical and instrument-based parameter, the percentage of improvement due to KT and ST was calculated as follows:

$$\textit{Percentage of improvement} = [(T_{48h}\ \text{data} - T_0\ \text{data}) / T_0]*100.$$

Treatment effects on percentage of improvement data were analyzed by independent t-test or Mann-Whitney U-test when appropriate.

CI data on KT-treated Group B patients were analyzed by repeated measures ANOVA, with time (T0 vs T_1 vs T_{48h}) as the main within-group factor, followed by Bonferroni post hoc test when the ANOVA results reached significance.

Statistical significance was considered at $p < 0.05$ (*:$p < 0.05$, **: $p < 0.005$, ***: $p < 0.001$) . All statistical tests were performed using the Statistical Package for the Social Sciences Software (SPSS), version 12.0 (Chicago, IL).

10.3 RESULTS

No clinical or instrument-based assessment differed significantly between Groups A and B at T_0 (*Table 15*) (p >0.05).

10.3.1 Clinical Assessment

The clinical assessment results are shown in*Table 15*. As expected, almost no changes were observed between T_0 and T_{48h} in the ST group. Conversely, versus T_0, KT treatment at T_{48h} significantly improved passive (p <0.005) and active ROM (p <0.001), SCATS score with the knees flexed and extended (p <0.001), PSFS (p < 0.001), BBS (p <0.001), and 6MWT (p < 0.001). Compared with ST, KT had significant treatment effects T_{48h} on SCATS with the knees flexed and extended (p <0.05) and on MAS (p <0.05).

Based on percentage of improvement values, we noted significant treatment effects on active and passive dorsiflexion ROM (p< 0.001), pathological reflex with the knees flexed (p <0.005) and extended (p <0.001), PSFS (p <0.001), GPN (p <0.001), BBS, and 6MWT (p <0.001).

With regard to perception of spasticity, VAS score was 7.9 ± 1.2 after KT and 2.5 ± 1.3 after ST (p<0.05).

Table 15: Clinical and instrumental assessment. Into KT T48h column is reported statistical comparison of T0 vs T48h data. Comparison between KT and SHAM data at T0 and T48h, and percentage of improvements' comparisons between KT and ST groups are reported in the last columns of the table (**p* <0.05, ** *p* < 0.005, *** *p* <0.001). Grey cells indicate significant p values. n.s.: not significant; for clinical scales abbreviation see List of abbreviation.

Clinical data	KT Mean (sd)		ST Mean (sd)		*P* KT vs ST		
	T_0	T_{48h}	T_0	T_{48h}	T_0	T_{48h}	Percentage of improvement
Passive ROM (°)	88,64 (11,63)	**78,64 **** (10,88)	85,27 (13,07)	85,27 (13,07)	n.s.	n.s.	**0,001*****
Active ROM (°)	90,18 (13,47)	**80,45 ***** (12,41)	87,27 (14,55)	87 (14,21)	n.s.	n.s.	**0,001*****
SCATS (flexed knee)	2,18 (0,82)	**1,55***** (0,82)	2,09 (0,91)	2,09 (0,91)	n.s.	**0,008***	**0,002****
SCATS (extended knee)	2,18 (0,82)	**1,09***** (0,54)	2,09 (0,91)	2,09 (0,91)	n.s.	**0,008***	**0,001*****
MAS	3,82 (1,17)	1,82 (0,75)	3,6 (0,84)	2,45 (0,93)	n.s.	**0,05***	**0,001*****
PSFS	2,73 (1,35)	**1***** (1,26)	2,09 (1,51)	2,09 (1,51)	n.s.	n.s.	**0,001*****
GPS	2,45 (3,3)	1 (2,49)	2 (3,26)	2 (3,26)	n.s.	n.s.	**0,04***
BBS	39,64 (7,7)	**42,82***** (7,15)	40,36 (7,68)	40,55 (8)	n.s.	n.s.	**0,001*****
WISCI	18 (2,57)	18 (2,57)	18 (2,57)	18 (2,57)	n.s.	n.s.	n.s.
6MWT (m)	231,65 (106,479)	**259,63***** (116,13)	253,63 (125,16)	251,25 (125,02)	n.s.	n.s.	**0,001*****
10MWT (s)	24,62 (17,07)	19,94 (14,28)	22,97 (18,11)	21,94 (17,32)	n.s.	n.s.	n.s.
TUG (s)	25,69 (17,50)	20,45 (13,30)	22,11 (14,34)	21,27 (13,92)	n.s.	n.s.	n.s.

10.3.2 Evaluation of balance

For both visual conditions, V significantly improved between T0 and $T_{48h,}$ (p<0.05) as well as the percentage of improvement of V values between T0 and T_{48h} (p<0.05). Furthermore KT comparison with ST at T_{48h}, had significant treatment effects on V for both visual conditions (p <0.05) (*Table 16*).

Table 16: Balance assessment. The KT T48h column lists the statistical comparison of T0 vs T48h data. Comparisons between KT and SHAM data at T0 and T48h and percentage of improvement between KT and ST groups are reported in *the* last columns of the table (*: p <0.05, **: p < 0.005, ***: p <0.001). Grey cells indicate significant p values. n.s.: not significant; for abbreviation of COP parameters, see List of abbreviation.

CoP parameters		**KT Mean (sd)**		**ST Mean (sd)**		***P***		
						KT vs ST		
		T_0	**T_{48h}**	**T_0**	**T_{48h}**	**T_0**	**T_{48h}**	**Percentage of improvement**
Open Eyes	**V (mm/s)**	3,78 (2,04)	**3,08*** (1,49)	(3,64) (1,92)	3,66 (2,1)	n.s.	**0,01***	**0,02***
Closed Eyes	**V (mm/s)**	5,53 (3,68)	**4,82*** (3,22)	4,77 (2,80)	5,21 (3,92)	n.s.	**0,03***	**0,02***

10.3.3 Evaluation of gait

The effects of KT on STRIDE, STANCE and DTS at T_{48h} versus T0 were significant (p <0.001). Further STRIDE (p <0.001), STANCE, and DTS (p <0.005) improved with KT at T_{48h} compared with ST. Comparison of percentage improvement values demonstrated significant treatment effects for all kinematic parameters (speed, cadence, and DTS: p <0.05; STRIDE and STANCE: p < 0.001) (*Table 17*).

Table 17: Gait assessment. The KT T48h column lists the statistical comparison of T0 vs T48h data. Comparisons between KT and SHAM data at T0 and T48h and percentage of improvement between KT and ST groups are reported in the last columns of the table (*: p <0.05, **: p < 0.005, ***: p <0.001). Grey cells indicate significant p values. n.s.: not significant; DTS: double-time support phase.

Kinematic gait data	KT Mean (sd)		ST Mean (sd)		*P* KT vs ST		
	T_0	T_{48h}	T_0	T_{48h}	T_0	T_{48h}	Percentage of improvement
Speed (m/s)	0.54 (0.2)	0.56 (0.24)	0.51 (0.18)	0.50 (0.19)	n.s.	n.s.	**0.02***
Cadence (steps/min)	69.67 (22.61)	71.09 (24.80)	66.47 (20.52)	65.79 (20.55)	n.s.	n.s.	**0.04***
STRIDE (m)	1.04 (0.15)	**1.15 ***** (0.19)	1 (0.13)	0.97 (0.13)	n.s.	**0.001*****	**0.001*****
STANCE (%)	72.42 (24.39)	**64.99 ***** (21.63)	69.94 (23.81)	65.49 (23.66)	n.s.	**0.005****	**0.001*****
DTS (%)	27.44 (11.05)	**24.46 ***** (9.20)	26.66 (10.93)	24.64 (10.52)	n.s.	**0.005****	**0.05***

10.3.4 Assessment of EMG CI

CI, as assessed with the knees flexed or extended, declined significantly immediately after application of KT (p <0.001 – F [19.046]). After 48 hours of treatment, this effect was maintained only with the knees flexed (p <0.001 – F [0.820]) (*Figure 33*).

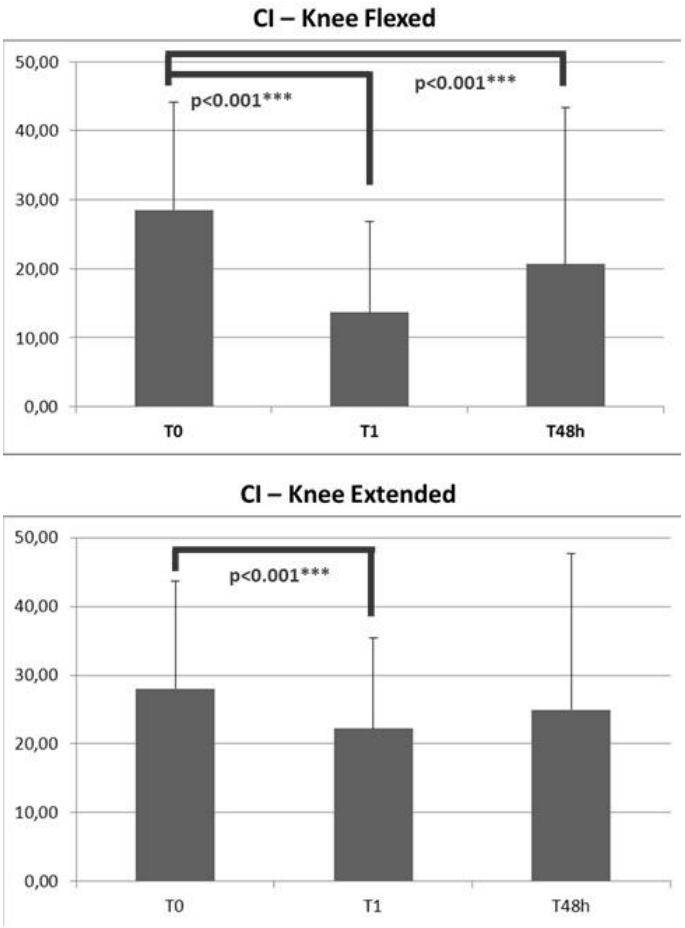

Figure 33: CI index at T_0, T_1, and T_{48h} for EXP group

To determine the most notable effects of KT, the results were divided into primary and secondary outcome measures, as reported in *Table 18*. MAS, BBS, COP V, 6MWT, STRIDE, and STANCE were identified as the most important outcomes, and the remaining data were considered secondary outcomes and used to evaluate additional effects of the intervention.

Table 18: Primary and secondary outcome measures. Clinical and instrumental data on spasticity, balance, and gait have been divided into primary and secondary outcome measures. The KT T48h column lists the statistical comparison of T0 vs T48h data. Comparisons between KT and SHAM data at T0 and T48h and percentage of improvement between KT and ST groups are reported in the last columns of the table (*: p <0.05, **: p < 0.005, ***: p <0.001). Grey cells indicate significant p values. n.s.: not significant; for abbreviations, see see List of abbreviation.

			KT Mean (sd)		ST Mean (sd)		*P:* KT vs ST		
			T_0	T_{48h}	T_0	T_{48h}	T_0	T_{48h}	% of improvement
PRIMARY OUTCOMES	**MAS**		3.82 (1.17)	1.82 (0.75)	3.6 (0.84)	2.45 (0.93)	n.s.	**0.05***	**0.001*****
	BBS		39.64 (7.7)	**42.82***** (7.15)	40.36 (7.68)	40.55 (8)	n.s.	n.s.	**0.001*****
	V (mm /s)	**OE**	3.78 (2.04)	**3.08*** (1.49)	(3.64) (1.92)	3.66 (2.1)	n.s.	**0.01***	**0,02***
		CE	5.53 (3.68)	**4.82*** (3.22)	4.77 (2.80)	5.21 (3.92)	n.s.	**0.03***	**0,02***
	6MWT (m)		231.65 (106.479)	**259.63***** (116.13)	253.63 (125.16)	251.25 (125.02)	n.s.	n.s.	**0.001*****
	STRIDE (m)		1.04 (0.15)	**1.15 ***** (0.19)	1 (0.13)	0.97 (0.13)	n.s.	**0.001** ***	**0.001*****
	STANCE (%)		72.42 (24.39)	**64.99 ***** (21.63)	69.94 (23.81)	65.49 (23.66)	n.s.	**0.005****	**0.001*****
SECONDARY OUTCOMES	**CLINICAL DATA**		Passive / Active ROM, SCATS, PSFS, GPS, WISCI, 10MWT, TUG (for details, see Table 15)						
	INSTRUMENTAL DATA		**BALANCE:** A, X, Y, L, V_{LL}, V_{AP} for both visual conditions: OE and CE (for details, see Table 16)						
			GAIT: Speed, Cadence, DTS (for details see Table 17)						

10.4 DISCUSSION

In this study, we examined the effects of KT treatment in chronic incomplete SCI subjects compared with nonelastic ST on functional relevant aspects of the post-SCI condition—ie, ankle muscle spasticity, balance, and gait. By MAS and analysis of functional balance and gait, 48 hours of KT treatment improved MAS, BBS, V CoP, 6MWT, STRIDE, and STANCE (*Figure 34*), indicating better functional status after KT, with reduced spasticity and improved balance and gait.

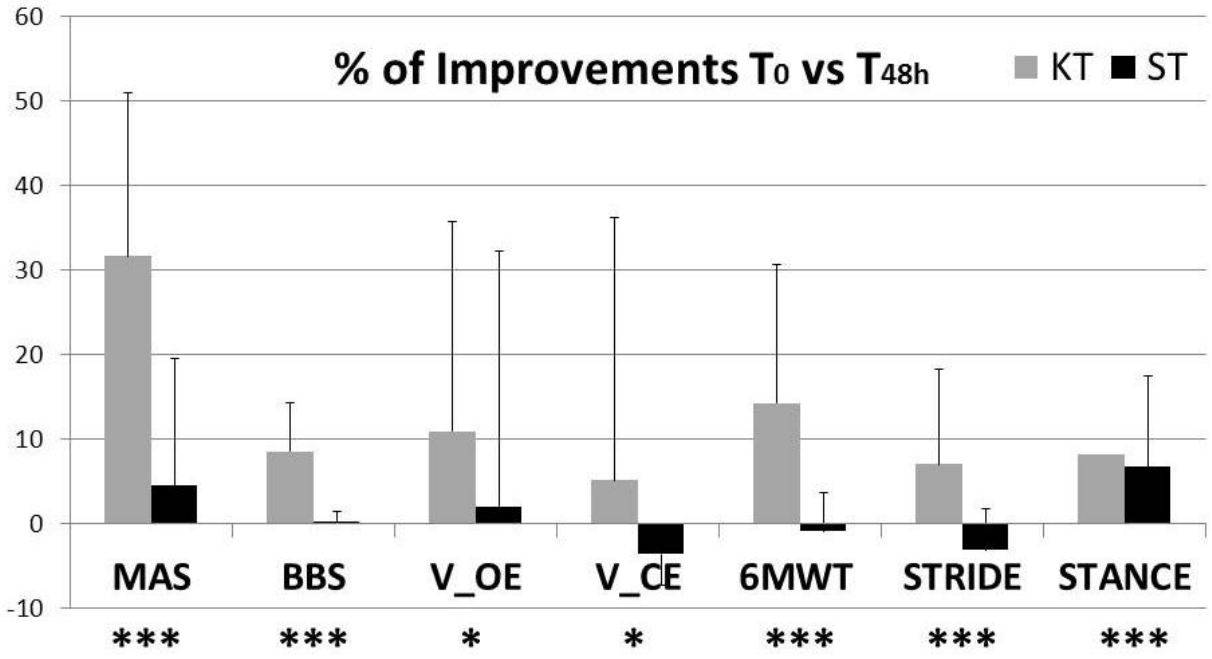

Figure 34: Percentage of improvements T0 vs T48h assessment of spasticity, balance and gait features

In general no adverse events were observed, and subjects reported no discomfort during KT treatment.

KT is used to enhance sensory inputs, decreasing spasticity through proprioception feedback and relieving abnormal muscle tension, in healthy athletic subjects [188;201]. Few studies have examined KT in neurological lesions, such as multiple sclerosis [189] and stroke [190;191]. In multiple sclerosis, Cortesi et al. observed positive effects of KT of the ankle on COP balance parameters, suggesting that ankle taping helps stabilize body posture immediately [189]. In stroke patients, KT of the gluteus muscles increases hip extension during gait, suggesting that muscle activation improves through cutaneous stimuli [190], whereas no positive effects were obtained by combining ankle KT and botulinum toxin to reduce plantar flexor spasticity [191]. No data are available on the effects of KT in SCI subjects.

The crossover paradigm that we used allowed us to blind subjects to the treatment allocation and limit the risk of compliance in analyzing the effects of KT versus ST [202]. To prevent overflow effects of KT, an interval of 7 days separated application of the tapes [203;204].

Although significant differences were observed in passive/active ROM, clonus, spasms, BBS, 6MWT, and most COP parameters and kinematic gait data after 48 hours of KT, almost no changes were observed after 48 h of ST treatment, as expected, due to the chronic condition. Treatment effects were analyzed by comparing improvements after 48 hours of KT and ST treatments. KT reduced MAS and improved active and passive ankle ROM, which was paralleled by a decrease in spasticity-associated symptoms, clonus, and pain. Control of ankle spasticity is paramount in improving balance and gait in SCI subjects [6]. KT had significant therapeutic effects on balance and gait, both of which improved with regard to the clinical scales and stabilometric and kinematic data. After KT treatment, there was better control of balance, as confirmed by the decline in V and L COP parameters [189], as well as an improvement in kinematic gait parameters. Decreases in STANCE and DTS reflect improved dynamic postural stability, which has been suggested to specifically influence gait in subjects with chronic motor incomplete SCI [5] (*Table 18*).

To determine the possible mechanism of these improvements, EMG data were collected in Group B patients before, during, and after KT treatment. CI has been proposed as an index of spasticity in stroke subjects [205] and is indicative of fatigue-induced decreases in muscular co-contraction in healthy athletic subjects [206]. In this study, we used the CI to evaluate EMG activity of agonist versus antagonist ankle muscles. A high degree of CI reflects excessive antagonistic muscle contractions during dynamic activities compared with agonist muscle activity, impairing function and increasing the metabolic cost of performing the task [207]. Our EMG data demonstrated a significant reduction in CI with KT, suggesting improved motor outcome [205] and confirming our clinical data on spasticity.

Notably, CI improved immediately after application of KT—an effect that was maintained, although slightly reduced, after 48 hours. The lack of significance of the CI data at 48 hours with the knee extended confirm the high variability of spasticity measurements in this posture compared with the knee flexed (*Figure 33*). The significant reduction in CI due to KT might be explained by 2 reasons: the increase in EMG activation of the TA and EHL and the decreased co-contraction phase of the antagonist S and G muscles. Considering the findings of Alexander et al. [187], in which amplitude of the H-reflex decreased after KT of the trapezius in healthy subjects, it is conceivable that KT also adjusts muscle activity by inhibiting proprioception feedback [188] also in SCI subjects.

To improve outcomes and methods of applying the tape, it is necessary to understand the mechanism that leads to better upright balance and gait. The effects of KT were clinically significant immediately after its application, implying that the changes were not due to long-term learning, as reported in multiple sclerosis [189]. In addition to the secondary effects of spasticity changes, the alterations in the balance control system might be explained by changes in skin receptor inputs due to application of KT [208]. The mechanical effects of applying tape to the skin might increase skin receptor output, stimulating supraspinal centers and thus enhancing kinesthetic and joint position sense [186;209] and improving balance.

In analyzing the effects of KT on gait, sensory components can not be dismissed. Applying pressure to and stretching the skin with KT can stimulate cutaneous mechanoreceptors and enhance signal information of joint movement or joint position [210;211]. The importance of sensory inputs in influencing the activity of gait central pattern generators (CPGs) is highlighted [212]. In SCI patients,

changes in CPG circuits are well documented [212;213] and are learning-dependent, primarily through rhythmic peripheral influences that imposed by the exercise—for instance, during robotic gait training [62;214]. The importance and effectiveness of sensory input in modulating stepping in SCI has been demonstrated in a wide range of experiments [91]; for example, modulation of sensory information influences spinal circuit reorganization to be effective from milliseconds to months [213]. Thus, sensory modulation through KT might not only influence spasticity but also intervene in longlasting reorganization of spinal gait circuits. In this theoretical framework, the influences of KT on gait merit studies not only in subjects with SCI but in all neurological gait pathologies.

Subjectively, the VAS results indicate a significant reduction in perception of spasticity after KT treatment and that spasticity is negatively associated with quality of life after SCI [215].

The significance of the sensory effects of KT must also be considered in analyzing its effects on pain. In our study, despite the short-term treatment, GPS declined significantly after KT and but not with ST. Treatment significance was present when comparing KT and ST GPS improvements. Although this study did not aim to evaluate the effects of KT on pain, our results are consistent with data in chronic low back pain patients [216] and merit dedicated studies, possibly with longer application times of KT.

In conclusion, KT is a valid technique to reduce spasticity and related symptoms in the short term and improve balance and gait in chronic incomplete SCI subjects. Further studies are needed to determine its long-lasting effects.

10.5 Study limitations

The sample size of SCI subjects (n = 11) was small, which might have limited the statistical relevance of the study. Nevertheless, the statistical differences were large, rendering the statistical error that was caused by sample size negligible. Further, as suggested by Friston [217], significant results that are based on a small sample indicate a greater treatment effect than equivalent results in a large sample

A follow-up study with a longer KT application is necessary to confirm these preliminary data, and a theory on the neurophysiological effects of taping would facilitate the generation of experimental hypotheses.

10.6 CONCLUSION

Short term application of KT reduces spasticity and pain and improves balance and gait in chronic SCI subjects. These promising data, require confirmation in a larger cohort of patients.

11 *Study 3:*

Walking in Water and on Land after an Incomplete Spinal Cord Injury

11.1 INTRODUCTION

Even if hydrotherapy is often used in the rehabilitation protocols of different pathologies [218-220], few studies analyzed the effects of water environment on gait and only in regard to orthopedic diseases [221;222]. In the case of spinal cord injuries (SCIs), a single study demonstrated the positive effects of hydrotherapy in decreasing the amount of medications required for the treatment of spasticity [7]. At present, no data are available on the characteristics of gait in water after SCI, although walking in water (WW) is commonly used as a low-impact exercise for training and rehabilitation [223;224]. From a biomechanical point of view, there are several reasons to support the hypothesis that WW is helpful for gait rehabilitation. Because of the buoyant force, the lower apparent body weight simulates a microgravity environment, allowing standing and ambulation with less muscular strength while providing increased postural support [225]. Indeed, the apparent body weight in water (the gravitational force minus the buoyancy force) decreases to approximately one-third of the body weight when subjects walk in chest-deep water; and to one-half, in waist-deep water[223].

Water environment also provides a sort of body-weight support as other novel gait therapies do on the basis of complex and expensive body-weight support robotic assisted devices that have been the objective of several group studies [226]. In comparison to these approaches gait arehabilitation in water represents a low cost thepary. In addition, because of the drag force exerted by water on the human body, the increased resistance to movement provides a helpful environment for progressively increasing muscle strength [227]. Another benefit of hydrotherapy is the reduced level of joint loading and impact; moreover, warm water relaxes the muscles and temporarily decreases pain [227]. Water is also a supportive, low-risk exercise environment that may reduce the likelihood of acute injury and the fear of falling while improving participation and adherence [228;229]. Furthermore, comfortable walking speed in water is slower than on land [230], suggesting that exercises in water may be able to reduce the speed of falling because of the properties of viscosity and density. This allows individuals with impaired balance to have more time to detect postural errors that might lead to the fall [231]. Evidences from different pathologies supported the efficacy of hydrotherapy. Water environment exercise improves postural capabilities in healthy elderly people [231]. Positive effects on muscular strength, cardiovascular function, and gross motor skill performance have been observed in children with cerebral palsy [220]. Pain reduction in patients with knee osteoarthritis [218] and positive changes in balance and qualityof-life in older subjects with a diagnosis of osteopenia or osteoporosis [232] by hydrotherapy have also been reported. None of these studies addressed the effects of hydrotherapy on kinematic variables of gait or analyzed the differences between walking on land (WL) or WW. Furthermore, quantitative and detailed evidence concerning the effects of WW on gait in comparison with on-land activity in SCI subjects is absent. In regard to on-land condition, even if

many studies addressed electromyographic activity in SCI subjects [233;234], kinematic variables have been seldom analyzed [53]. In comparison with healthy subjects, a reduction in cadence and knee angular velocities was present in subjects with thoracic injuries, whereas reduced stride and ankle velocity were associated with lumbar injuries[53]. As regards water environment, only few studies address walking in healthy subjects from a kinematic point of view [7;224;230;235-239], and only three provided a full description of a complete gait cycle in healthy young and old subjects [7;239]. In water condition, speed has been reported to be approximately 36% of the speed on land; and stride length, approximately 10% of land values [7;230]. The range of motion (ROM) of the ankle, knee, and hip joints has been reported to be similar in both conditions[7;230] even if a decrement in knee ROM during stance in water has also been indicated[230;239-241]. Given the lack of information related to WW of SCI subjects, the goal of the present matched case-control study was to characterize kinematic gait parameters of adults with incomplete SCI WW and WL, in comparison with the gait characteristics of matched healthy subjects walking in the same environments, to identify specificities of WW for SCI subjects. This knowledge will help to correctly plan hydrotherapy rehabilitation protocols after SCI.

11.2 MATERIAL AND METHODS

11.2.1 Study design - Population

This study included 15 patients with chronic or subacute SCI (SCI group [SCI-gr]), level D at the American Spinal Injury Association Impairment Scale [161], with a mean TSD time from lesion of 157.04 ± 186.83 days and 15 healthy controls (CTRLs). The SCI-gr patients and the CTRL subjects were matched according to demographic features. The SCI-gr was composed of seven women and eight men with incomplete SCI, without any limitation in ROM or presence of orthopedic diseases, affected by traumatic (eight patients) and nontraumatic lesions (seven patients); seven had cervical injuries (tetraplegia group "TETRA-gr"); and eight had thoracic or lumbar lesions (paraplegia group "PARA-gr"). The CTRL group was composed of seven female and eight male volunteers without any known physical or mental illness. SCI-gr age (43.53 ± 17.43 yrs), height (173.93 ± 8.95 cm), and body weight (66.6 ± 9.80 kg) mean ± SD values were not statistically different from those of the CTRL group (age, 38.6 ± 15.42 yrs; height, 167.90 ± 7.67 cm; and body weight, 66.27 ± 10.39 kg). Before their participation, all subjects signed an informed consent form in accordance with article 616 of the Italian criminal code and law 196/03 on the privacy of personal data. This study was approved by the ethical committee and conducted in accordance with the Declaration of the World Medical Association.

Neurologic status was assessed using the American Spinal Injury Association standards by applying the American Spinal Injury Association Impairment Scale[21]. Walking level was assessed by trained examiners using the Walking Index for Spinal Cord Injury [133]. Spasticity of the lower extremities was measured using the Modified Ashworth Scale [194]. To obtain a single score, the authors calculated the mean of the scores of each joint examined, as in the composite Modified Ashworth Scale [242]. The patients' demographic and clinical features are reported in *Table 19.*

Table 19: SCI patients' demographic and clinical data. AIS LEMS indicates lower extremity motor score of the American Spinal Injury Association Impairment Scale; F, female; M, male; MAS, Modified Ashworth Scale; PT, patient; WISCI, Walking Index for Spinal Cord Injury.

	Sex	Age (Years)	Height (cm.)	Weight (Kg)	Lesion level	Etiology	AIS LEMS	WISCI	MAS
PT 1	M	49	181	84	T12	Non traumatic (Postactinic)	42	16	0
PT 2	F	64	174	66	C4	Non traumatic (Spondilogenic myelopathy)	48	19	0
PT 3	M	53	179	75	C7	Non traumatic (Arthrosis)	50	20	0
PT 4	M	51	159	68	C5	Traumatic	45	19	0.33
PT 5	M	26	167	70	L2	Traumatic	34	16	0
PT 6	M	24	193	80	C7	Traumatic	49	16	1
PT 7	M	34	175	61	T11	Traumatic	47	16	1
PT 8	F	69	165	66	L1	Ischemia	40	19	0.66
PT 9	M	28	184	58	T10	Non traumatic (Arteriovenous fistula)	40	19	0.5
PT 10	F	23	178	53	L4	Traumatic	44	16	0
PT 11	M	45	175	72	C5	Traumatic	50	20	1
PT 12	F	66	175	56	T9	Non traumatic (Ischemia)	46	19	0
PT 13	F	32	174	72	T12	Traumatic	41	19	1
PT 14	F	23	170	49	C6	Traumatic	44	20	0
PT 15	F	66	160	69	C5	Non traumatic (Ischemia)	45	20	0

The inclusion criteria were as follows: American Spinal Injury Association Impairment Scale level D; ability to walk at least 3 m without aids between parallel bars at a comfortable speed; absence of any hydrotherapy treatment before or during the study; and a score of 7 in communication, expression, memory, and problem solving on the Functional Independence Measure[243]. The exclusion criteria were cardiac or respiratory failure; infective skin conditions; excessively low, high, or uncontrolled blood pressure; urinary tract infections; urinal or fecal incontinence; or morbid hydrophobia [244].

11.2.2 Experiment Settings

Experimental setup and procedure used to collect data were similar to those reported elsewhere[223]. Both groups of SCI and healthy subjects walked at self-selected comfortable speeds, first on a walkway in the laboratory, on-land condition (WL), and subsequently on a walkway in the swimming pool, water condition (WW). Both on-land and water conditions were examined by the same operator on the same day. In WL, the patients were asked, for safety reasons, to walk between the parallel bars without contact. As regards WW, no device was used, and the participants were instructed to keep their arms on the water surface. The walkway in the swimming pool was set according to the participant's height, in such a way that they all walked with the water at the xiphoid process level. This allowed the subjects to walk in the water environment with an equivalent energy expenditure to gait on land8 and with an apparent weight of 34.7% ± 3.2% of their body weight on land [223]. Water temperature was maintained at 35° C.

11.2.2.1 Motion Analysis

Locomotion variables were recorded and analyzed using the KineView Motion System (Kineview, Hafnarfjordur, Iceland), as for Study 1 and 2. The experimental setup was the same for WL and WW. Specifically, the authors performed a two-dimensional gait analysis of three consecutive strides on the sagittal plane, the main plane of movement [245], captured from both sides of the body. All subjects were instructed to walk with open eyes at a comfortable, self-selected velocity [1], walking 2 m ahead of the mat and continuing 2 m past the end. The first right foot-ground contact was considered the starting point for video recording. Before data collection, the subjects performed walking trials to familiarize with the procedure. Movies were captured with a sampling hertz of 50 frames per second with a digital camera (Cyber-Shot DSC P73; Sony, Tokyo, Japan) enclosed in waterproof housing (MPK-PEA; Sony, Tokyo, Japan) for underwater recordings (Figure 35).

Figure 35: waterproof housing for underwater recordings

For both conditions, especially for WW, to eliminate size and depth visual distortions caused by water, the KineView System was carefully calibrated each time for offline analysis. Spatial movements of the lower extremity segments were determined on the basis of the position of the markers, placed as per the Helen Hayes biomechanical model [165], modified to fit the bidimensional

approach according to the requirements of the KineView Motion System software. The following bone landmarks were used for the markers' placement: the first and the fifth metatarsal head, external and internal side of the calcaneus, the femoral epicondyle, the greater trochanter, and the anterior superior iliac spine (*Figure 24*). As regards joint angles, hip angle was defined by the anterior superior iliac spine, greater trochanter, and lateral epicondyle markers; knee angle was defined by the greater trochanter, lateral epicondyle, and lateral calcaneus markers; and ankle angle was defined by the lateral epicondyle, lateral calcaneus, and lateral fifth metatarsal head markers (*Figure 36*).

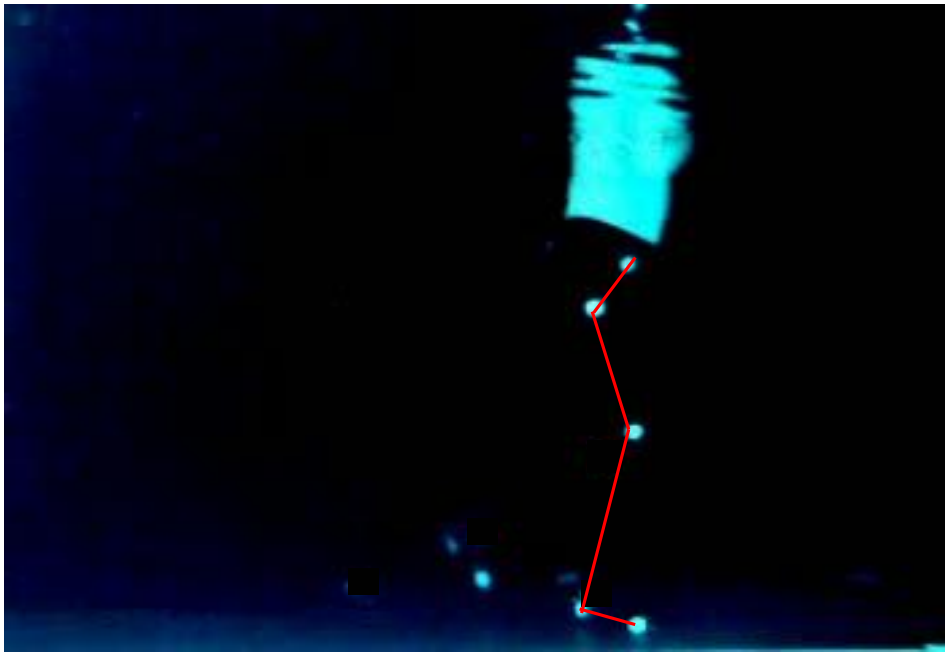

Figure 36: Gait assessment in water environment.

The following kinematic data were considered: speed (m/s); stride length (STRIDE: mean of right and left stride in m); stance phase (Stance: mean of right and left stride) expressed as the percentage of gait cycle and overall duration of gait cycles (gait cycle time in seconds). Stride and stance phase were defined as for Study 1 and 2 [166]. From the position of the markers, the position of the hip, knee, and ankle joints on the sagittal plane was calculated, to obtain ROM data (degrees) for each joint, as the peak-to-peak angular displacement during the complete gait cycle.

11.2.2.2 Data Analysis

Reconstruction, filtering, and offline analyses of kinematic data were performed offline using Matlab (version 7.1; Mathworks, Inc, Natick, MA) after digitalization of the markers with the KineView Motion System (Kineview, Hafnarfjordur, Iceland). Digitized data were smoothed using a moving average low-pass filter with a frequency of 10 Hz. For each subject, kinematic data of three strides were analyzed for each condition, WL and WW, then averaged to obtain the mean value for each participant. These cycles were then averaged across the groups (CTRL, SCI-gr, PARA-gr, and TETRA-gr) and conditions (WW and WL).

For each kinematic gait parameter, differences between the CTRL subjects and the different groups of SCI subjects (SCI-gr, PARA-gr, and TETRA-gr) were assessed by means of delta (Δ) calculation from absolute values according to the following formula: Δ =(SCI data - CTRL data).
As regards the position of the markers in the sagittal plane, the three strides from each participant in each environment were normalized in time from 0% to 100% and averaged across the groups (CTRL, SCI-gr, PARA-gr, and TETRA-gr) and conditions (WW and WL). Furthermore, to point out data dispersion from the average, mean and standard deviation values across gait cycles were also obtained for each group (CTRL, SCI-gr, PARA-gr, and TETRA-gr) and condition (WW and WL).

11.2.2.3 Statistical Analysis

Descriptive statistics were performed for all variables. Before statistical comparisons, the Kolmogorov-Smirnov test was performed to evaluate normal distribution of the data. For each group, statistical comparisons between the two different environments, WW vs. WL, was made by independent t test. Furthermore, to point out differences between the groups for each environment condition, WW and WL, analysis of variance evaluation was used. When analysis of variance reached significance, the Bonferroni post hoc test was selected.
Statistical significance was accepted for p <0.05 (*: p<0.05, **: p <0.005, ***: p <0.001). All statistical tests were performed using the Statistical Package for the Social Sciences software (version 12.0; Chicago, IL).

11.3 RESULTS

No participants withdrew from the trial, and all outcome measures were obtained for all SCI and healthy subjects.

11.3.1 Kinematic Data

In *Table 20*, the mean (standard deviation) values of kinematic gait parameters for the CTRL and SCI subjects WL or WW are reported. Statistical comparisons between WW and WL are also reported for each group. As regards WW data, the CTRL group presented, as expected [230;239], a significant reduction in speed and stride with a coherent gait cycle time increment in comparison with WL (p < 0.001 for all parameters). No significant changes were present in the stance/swing percentage relationships.

	CTRL			SCI-gr		
	WW	WL	WW *vs.* WL	WW	WL	WW *vs.* WL
Speed (SD)	0.33 (0.05)	0.95 (0.21)	$P < 0.001$	0.17 (0.09)	0.27 (0.22)	$P < 0.05$
Stride length (SD)	1.02 (0.15)	1.25 (0.24)	$P < 0.001$	0.69 (0.20)	0.67 (0.21)	
Stance phase (SD)	63.98 (3.25)	65.13 (2.71)		60.60 (15.48)	71.49 (7.52)	$P < 0.05$
Gait cycle time (SD)	3.15 (0.73)	1.34 (0.2)	$P < 0.001$	3.78 (1.11)	2.75 (1.37)	$P < 0.005$

	PARA-gr			TETRA-gr		
	WW	WL	WW *vs.* WL	WW	WL	WW *vs.* WL
Speed (SD)	0.15 (0.09)	0.23 (0.24)		0.19 (0.09)	0.32 (0.19)	$P < 0.05$
Stride length (SD)	0.74 (0.20)	0.68 (0.24)		0.74 (0.20)	0.68 (0.21)	
Stance phase (SD)	59.87 (20.01)	72.16 (9.13)		61.43 (9.5)	70.72 (5.78)	
Gait cycle time (SD)	4.28 (1.20)	3.40 (1.58)		3.20 (0.69)	2.02 (0.55)	$P < 0.05$

Table 20: Kinematic gait parameters. Reported mean (standard deviation) kinematic gait data on water (WW) and on land (WL) of the healthy subjects (HEALTHY), the subjects with SCI (SCI-gr), and the following lesion-level subgroups: thoracolumbar lesion group (PARA-gr) and cervical lesion group (TETRA-gr). Statistical comparison between WW and WL conditions (WW vs WL) are reported on the last grey column for each group as *p* values.

For the SCI-gr, comparisons between WW and WL indicated that gait in water was characterized, similarly tothe CTRL group, by significant speed reduction ($p < 0.05$) and gait cycle time increment ($p < 0.005$). In contrast to what was observed in the CTRLs, the SCI patients presented a significant reduction in the stance percentage ($p < 0.05$) associated with an invariance of the stride. The general pattern of gait in water was maintained also after grouping the patients according to the lesion level. Both the PARA-gr and the TETRA-gr presented a reduction in speed and in stance phase percentage, together with stride invariance. Similarly, both groups presented a gait cycle total time increase in water. Interestingly, despite the similar general trend, land vs. water statistical comparisons in the PARA-gr and the TETRA-gr were different. No statistical significance was observed in any of the parameters analyzed in the PARA-gr, whereas WL vs. WW significant differences for speed ($p < 0.05$) and gait cycle total time ($p < 0.05$) were recorded in the TETRA-gr.

Statistical comparison between the groups for each environment is reported in Figure 1. On land, the SCI subjects, in comparison with the CTRLs, presented a gait characterized by a reduction in speed ($p < 0.001$) and stride ($p < 0.001$) and by a significant gait cycle time increment ($p < 0.001$) in agreement with previous observations.18 The CTRL and SCI subjects also presented gait differences in the WW condition. The SCI patients walked significantly slower (p <0.001), presented significant reduced stride ($p < 0.001$), and presented a longer gait cycle total time, with similar values of stance phase percentages. Both the PARA-gr and the TETRA-gr presented significant differences from the gait of the CTRL group similar to those observed for the SCI-gr for WW and WL (*Figure 37*), with a notable exception for gait cycle total time. For both environments, statistical comparisons with the CTRL data demonstrated significance for both the PARA-gr and the TETRA-gr as regards speed (PARA-gr: WL and WW, P < 0.00; TETRA-gr: WL and WW, $p < 0.001$) and stride (PARA-gr: WL, $p < 0.001$; WW, $p < 0.05$; TETRA-gr: WL and WW, $p < 0.001$). As regards WW gait cycle total time, significant differences between the CTRL and the PARA-gr evidenced in WL ($p < 0.05$) were maintained in WW ($p <$ 0.05), whereas the TETRA-gr data were significantly different from the CTRL data only in WL ($p < 0.05$). CTRL vs. PARA-gr and TETRA-gr statistical comparisons show significant differences as regards stance phase percentage in WL (PARA-gr: $p < 0.05$; TETRA-gr: $p < 0.005$), which were abolished while WW.

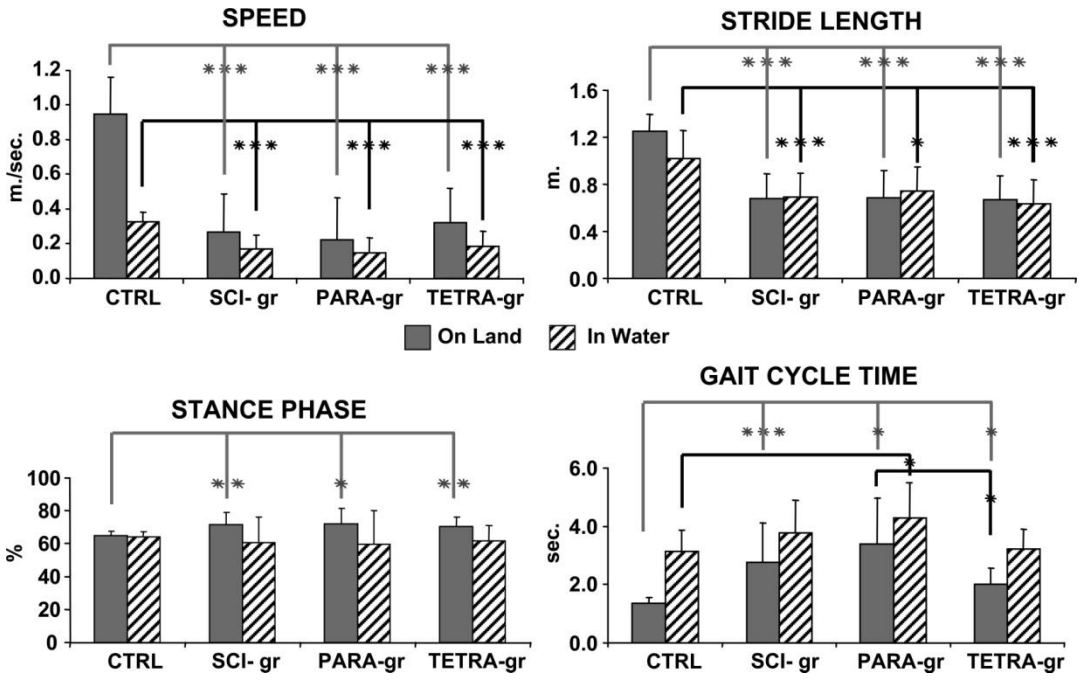

Figure 37: Kinematic gait parameters. Histograms of kinematic gait data (mean T standard deviation) on land (gray columns) and in water (striped columns) in the healthy CTRLs, in the subjects with SCI (SCI-gr), and in the following lesion-level subgroups: thoracolumbar lesion group (PARA-gr) and cervical lesion group (TETRA-gr). Statistical comparisons of the CTRL subjects vs. the SCI-gr, the PARA-gr, and the TETRA-gr are pointed out by lines above the graphs: gray line as regards WL and black line as regards WW (*$p < 0.05$, ** $p < 0.005$, *** $p < 0.001$)

Delta (Δ) between kinematic data of the healthy CTRLs and the SCI subjects for WL and WW were assessed to point out the possible influence of walking environment on kinematic gait parameters (*Figure 38*).

As regards WW, compared with WL, Δ was reduced for all parameters. Specifically, Δ differences reached significance for speed ($p < 0.001$) and stance phase percentage ($p < 0.05$) for all groups. Stride length Δ between WL and WW were significant for the SCI-gr ($p < 0.05$) and the TETRA-gr ($p < 0.05$) but not for the PARA-gr. This data analysis stressed the higher similarity of gait parameters between the CTRL and SCI subjects for WW in comparison with those for WL. This enhanced similarity is also maintained when the SCI subjects are grouped according to the lesion level, especially for the TETRA-gr. It is worth noting that, as regards stance phase duration, the enhanced similarity between the SCI and healthy subjects is accompanied by an inverse trend of differences: in comparison with CTRL data, the SCI subjects presented an increased stance phase for WL condition, whereas in WW, a reduction is observed.

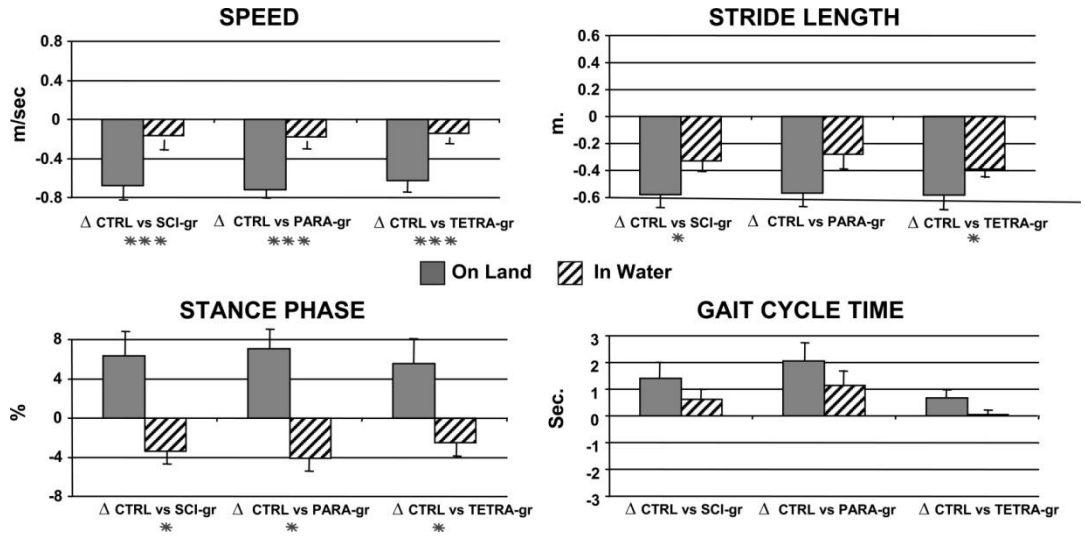

Figure 38: Group differences in kinematic gait parameters. Histograms of kinematic gait parameters during the stride cycle on land (gray columns) and in water (striped columns), reported as the groups' difference (Δ)between the healthy CTRLs and the SCI(Δ CTRL vs. SCI-gr), thoracolumbar lesion(Δ CTRL vs. PARA-gr), or cervical lesion(Δ CTRL vs. TETRA-gr) groups. Statistical comparisons between WL and WW are reported on abscissas for each group (*$p < 0.05$, ** $p < 0.005$, *** $p < 0.001$).

11.3.2 Joint Segmental Angles

Figure 39 depicts the mean joint angle values of the hip, the knee, and the ankle during the stride cycle of the CTRL group and of the different SCI groups WL or WW. In the healthy subjects, the hip in water tended to hyperflex with a peak, not present on land, at the end of the swing phase; similarly, a hyperflexion was observed in knee parameters for the overall gait cycle. This hyperflexion was highlighted at the beginning of the stance phase and during the swing phase, in which a delay in the peak of flexion was observed. Regarding ankle behavior, plantarflexion was enhanced in water, and both plantarflexion and dorsiflexion peaks were anticipated.

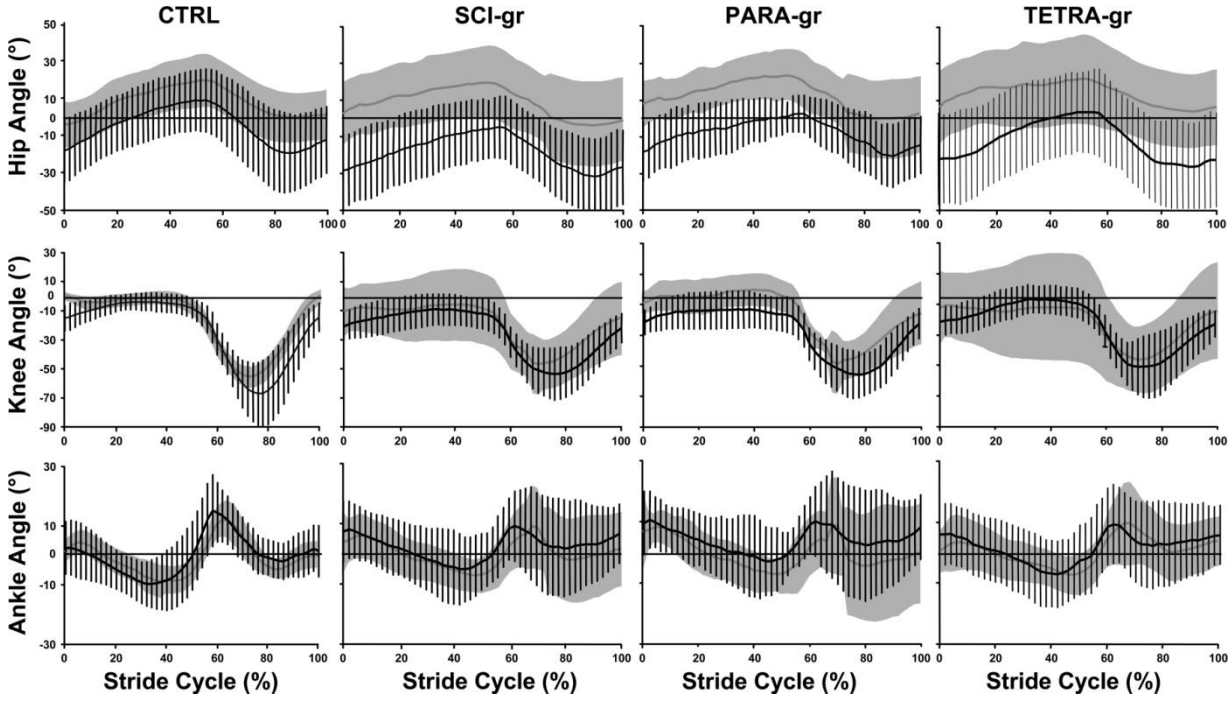

Figure 39: Values of joint angles during gait cycle. Hip, knee, and ankle joint angles (mean ± standard deviation) during gait cycle on land (gray area) and in water (line) in the healthy CTRLs, in the subjects with SCI (SCI-gr), and in the following lesion-level subgroups: thoracolumbar lesion group (PARA-gr) and cervical lesion group (TETRA-gr). Stance phase: 0%-60%; swing phase: 60%-100%. Positive values indicate ankle plantarflexion and knee and hip extension; negative values indicate ankle dorsiflexion and knee and hip flexion.

In the SCI subjects, the greatest difference between the water and land conditions was observed as regards hip values. In water, the hip was hyperflexed throughout the overall gait cycle. Regarding knee data, the land and water traces tended to overlap almost completely, even if the joint tends to be more flexed in water than on land. A little delay of the swing flexion peak in water was recorded. The ankle behavior tended to present a slightly enhanced plantarflexion in water, more evident at the end of the stance and throughout the swing. This pattern was associated with an anticipation of both dorsiflexion and plantarflexion peaks. Similar trends were

also observed after grouping the subjects according to the lesion level (PARA-gr and TETRA-gr; *Figure 39*).

On the other hand, key differences among the lesion-level groups were observed, taking into account the standard deviation values of the joint angles' overall gait cycles for both environments (*Figure 40*). In the CTRL subjects, the standard deviation values for the hip, knee, and ankle angles were significantly reduced during WL than WW ($p < 0.001$ for all joints). In the SCI subjects, the pattern was completely reversed as regards the hip and knee joints. The joint angles' standard deviation values were significantly lower in water than on land (hip: $p < 0.005$; knee: $p < 0.001$). As for the CTRL subjects, an increment was present in water for the ankle standard deviation values ($p < 0.001$). Interestingly, by grouping the SCI subjects according to the lesion level, some differences were revealed between WW and WL. In the WW condition, the standard deviation values were significantly reduced as regards the knee joint for the TETRA-gr ($p < 0.001$) and as regards the hip joint for the PARA-gr ($p < 0.05$). In line with the CTRL and SCI-gr data, the ankle standard deviation values were significantly increased for WW ($p < 0.001$).

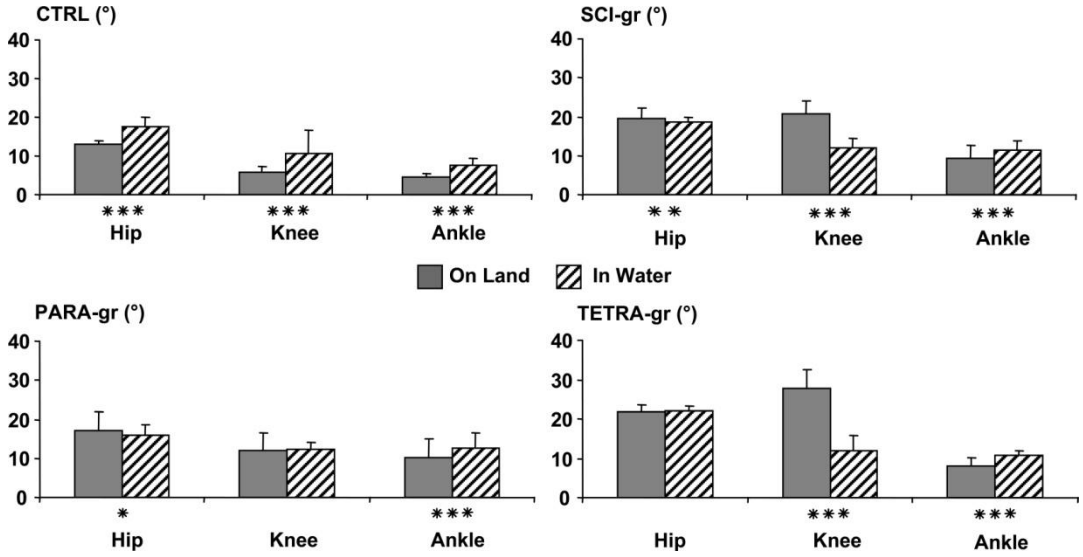

Figure 40: Standard deviations of joint angles. Histograms of standard deviations of the hip, knee, and ankle joint angles (mean ± standard deviation) during gait cycle on land (gray columns) and in water (striped columns) in the healthy CTRLs, in the subjects with SCI (SCI-gr),and in the following lesion-level subgroups: thoracolumbar lesion group (PARA-gr) and cervical lesion group (TETRA-gr). Statistical comparisons between WL and WW are reported on abscissas for each joint (*$p < 0.05$, ** $p < 0.005$, *** $p < 0.001$).

11.3.3 Range of Motion

Figure 41 presents ROM mean values for the hip, the knee, and the ankle on land or in water for the CTRL group, the SCI-gr, the PARA-gr, and the TETRA-gr. Comparison between WW and WL for each group showed that water environment did not modify ROM values, either in the CTRL or in the SCI subjects. The only exceptions were the CTRL and the TETRA-gr hip values, which presented enhanced ROM in water. These latter differences were statistically significant (CTRL, $p < 0.05$; TETRA-gr, $p < 0.05$).

For both WL and WW data, statistical comparison among the groups indicated that the CTRL and SCI subjects differed significantly only in the knee values (WL: $p < 0.05$; WW: $P < 0.05$). The knee ROM values also differed between the CTRL and the TETRA-gr but only as regards WL ($p < 0.05$).

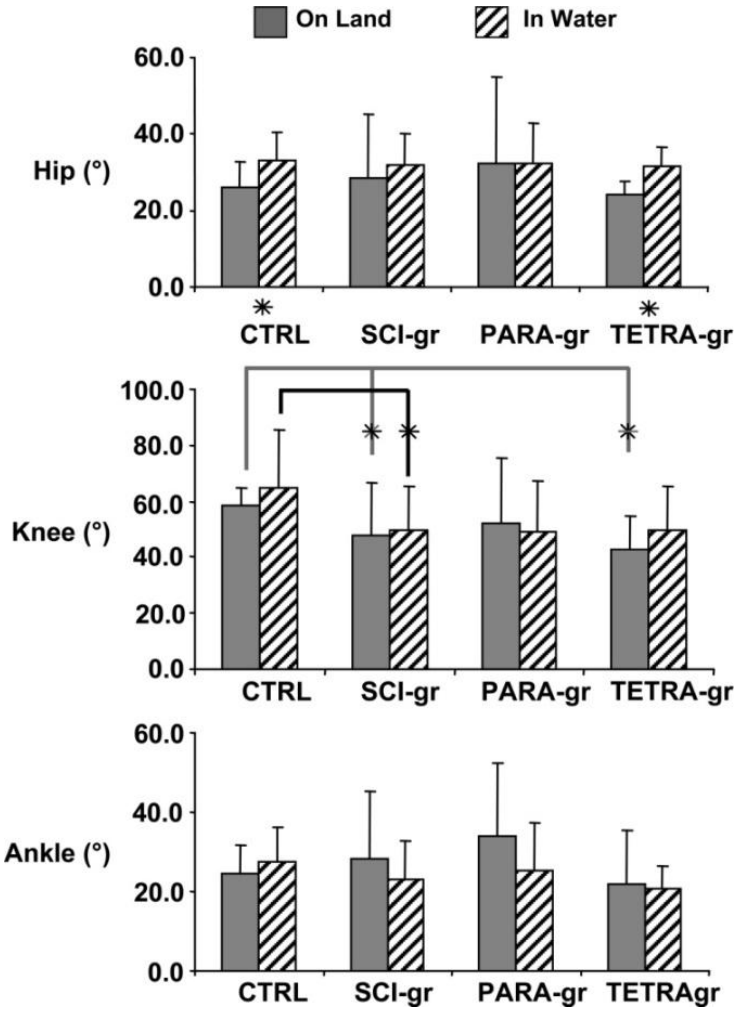

Figure 41: ROM of joint angles during gait cycle. Histograms of ROM of hip, knee, and ankle joint angles (mean ± standard deviation) during gait cycle on land (gray columns) and in water (striped columns) in the healthy CTRLs, in the subjects with SCI (SCI-gr), and in the following lesion-level subgroups: thoracolumbar lesion group (PARA-gr) and cervical lesion group (TETRA-gr). Statistical comparisons of the CTRL subjects vs. the SCI-gr, the PARA-gr, and the TETRA-gr are pointed out by lines above the graphs: grey line as regards WL and black line as regards WW. Statistical comparisons between WL and WW conditions are reported on abscissas for each group (*$p < 0.05$, ** $p < 0.005$, *** $p < 0.001$).

11.4 DISCUSSION

This study analyzed complete gait cycles of the SCI subjects WL and WW at a self-selected comfortable speed, reporting new kinematic data that support water environment to reduce gait differences between SCI and healthy subjects.

As regards the results of this study, kinematic gait data of WL in the SCI subjects are in line with previously published data [53] in demonstrating, after SCI, a total gait cycle time increment associated with stride length and speed reduction (*Table 20*). These differences were more evident in the subjects with thoracic or lumbar damage compared with those with cervical lesions, as previously reported [53].

As regards the effects of water environment on gait in healthy subjects, in this study and in those of Barela et al. [230;239] and Orselli and Duarte [223], WW presented, compared with WL, an increment of the gait cycle time and a reduction in gait speed and stride length. Despite slower speed, stance phase percentage was not modified, as also previously reported [223;230;239] (*Table 20*).

It has been proposed that in water stance phase, duration remains unmodified because of a double effect of water: an increase, caused by speed reduction, and a decrease, caused by body-weight unloading increment [239]. Consequently, for the healthy subjects, the two effects cancel each other and the temporal organization of gait stride is approximately the same in water and on land [239]. For the SCI subjects, the data of this study demonstrate that

WW, in comparison with WL, is characterized by a reduction in gait speed and an increase in gait cycle time, as observed in the healthy subjects, and, differently from the CTRLs, by an invariance of the stride and a reduction in stance phase duration (*Table 20*). These differences in the effects of water environment induce the SCI subjects to walk in water with a gait more similar to the healthy one than when WL (*Figure 38*), supporting the idea that water may represent a good training environment for gait rehabilitation. It can be argued that speed reduction alone might induce a more physiologic gait independent from environmental changes. Present data do not allow to completely rule out this criticism. To establish the rehabilitative efficacy of WW, approach-devoted studies are needed.

Qualitative analyses of traces of joint segmental angles indicated that water induces the same trend in the CTRL and SCI subjects. As reported for the healthy subjects, because of buoyancy [230;238;239;241], the hip and knee joints are more flexed and the ankle is more plantarflexed in water than on land in both the CTRL and the SCI-gr (*Figure 39* and *Figure 42*). It has been hypothesized that in water, because of reduced support forces caused by apparent body weight reduction, there is a diminished need for the ankle to provide support in healthy subjects [223]. The same principle might well be applied also to SCI subjects.

The data of the standard deviation values of the joint segmental angles allow further considerations. The standard deviation of the ankle segmental angle increased in water in both the healthy and SCI subjects, whereas the knee and hip values behaved differently in the two groups, namely, in the healthy controls, water induced an increment in the knee and hip standard deviation values, whereas in the SCI subjects, water induced a decrement (*Figure 40* and *Figure 42*).

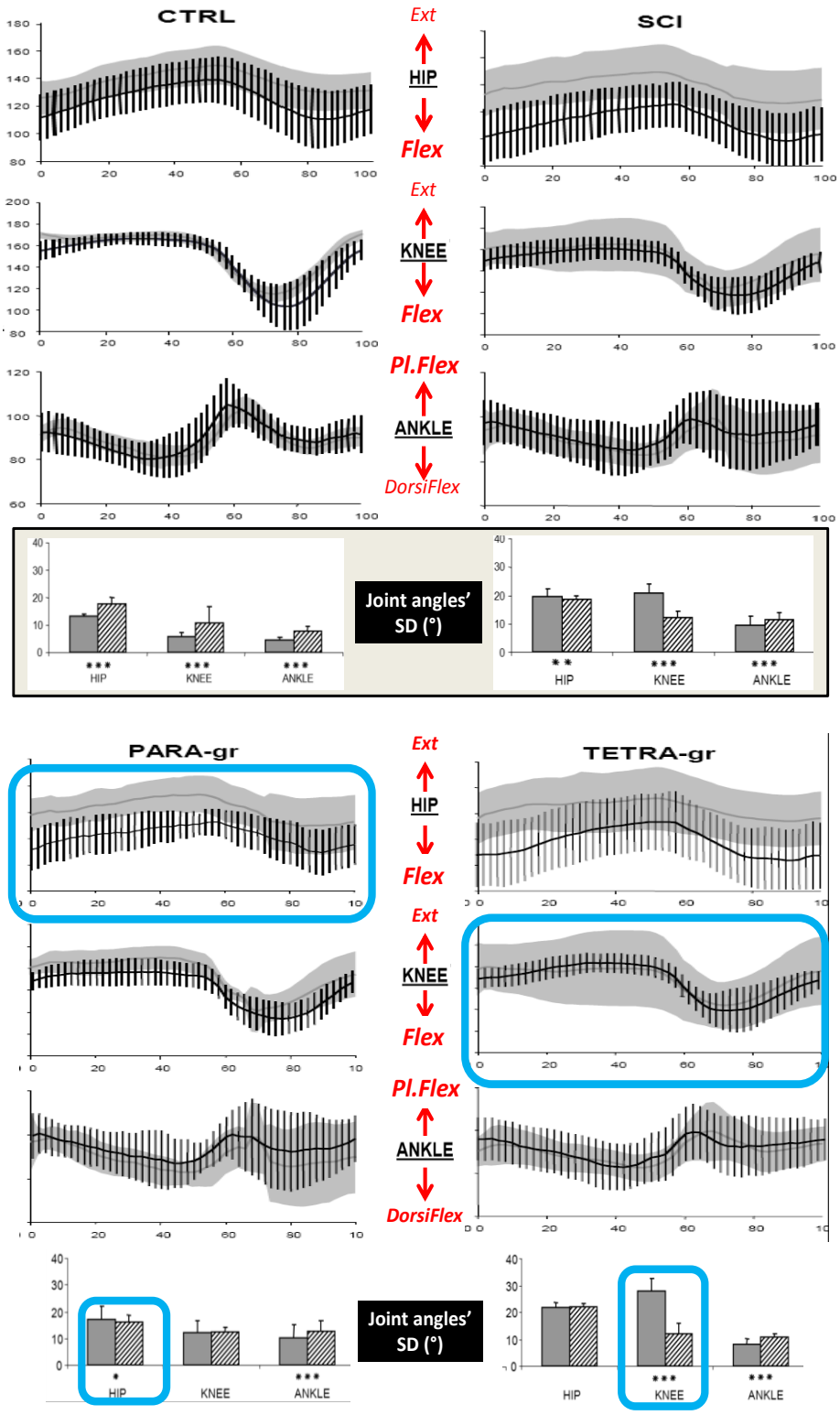

Figure 42: General schema of hip, knee, and ankle joint angles for SCI groups on land and in water. Hip, knee, and ankle joint angles (mean ± standard deviation) and joint angles' SD data during gait cycle on land (gray area) and in water (line) in the healthy CTRLs, in the subjects with SCI (SCI-gr), and in the following lesion-level subgroups: thoracolumbar lesion group (PARA-gr) and cervical lesion group (TETRA-gr).

As regards ROM data on land, CTRL vs. SCI group differences were observed only in knee ROM, and this difference was a result of the TETRA-gr data (*Figure 41*). Knee ROM reduction in tetraplegia has been previously reported[246], and it has been interpreted as a consequence of the altered knee agonist antagonist muscles coupling with flexion reduction during swing phase. In line with this interpretation in WW condition, knee ROM improvement may be the consequence of the buoyant force supporting knee flexion during swing. Consequently, group differences in knee ROM between the healthy and TETRA-gr subjects, evidenced on land, disappeared in water. On the other hand, considering the effects of water environment in comparison with on-land gait, in line with previous reports of healthy subjects [223;230] no significant differences for hip, knee, and ankle ROM in the CTRL group, the SCI-gr, and the PARA-gr were observed. This suggests that the relationship between these adjacent segments did not change during stride cycle for land or water conditions.

Water effects on joint segmental angles allow some speculations of rehabilitative relevance. Bodyweight unloading reduces the need of hip extension for body forward propulsion and of both knee extension and ankle dorsiflexion needed for support. In SCI patients, limited hip and knee flexion, especially during swing phase, are considered two specific targets for overground gait rehabilitation [247]. Thus, water environment's effects that favor a generalized flexion pattern can support the flexion improvement needed for SCI gait rehabilitation.

The second interesting speculation derives from group differences in the water effect on standard deviation of joint segmental angles. Overall, it is intriguing that water has opposite effects on standard deviation of the hip and knee joint segmental angles in healthy (increased) and in SCI (reduced) subjects. In particular, the highest significant decrease in standard deviation of segmental angle was observed for the knee joint in the TETRA-gr and for the hip joint in the PARA-gr. It can be hypothesized that for healthy subjects in a water environment, the increased effort to move the limbs would induce a gait less automatic than on land, as suggested by the reduction of the stereotypy of leg movements. On the other hand, the SCI subjects in both environments present a gait less automatic than that of the CTRLs, as indicated by the higher variability. In WW, the reduced load might help to regain, at least partially, a better control of leg movements, thus reducing the variability of the hip and knee joint angles. Although it is evident that a definite conclusion cannot be drawn from the present data, it can be speculated that in water, both the healthy and SCI subject walk in a "new" environment in which a more "voluntary/explicit" effort is needed. On land, although healthy gait is "automatic/implicit", SCI gait is based on voluntary/explicit effort. It is generally believed that an automatic movement is more stereotyped than a voluntary one. Therefore, at least for implicit/voluntary differences, the SCI subjects would control gait with the same mechanism in WW or WL conditions, whereas the healthy subjects would shift from an automatic gait in WL to a more voluntary one in WW. On the other hand, the reduced weight in WW would allow an easier control for the SCI subjects, thus allowing a more regular gait. The knee and hip joints represent key rehabilitation points for subjects with tetraplegia [246] and paraplegia[235], respectively. Interestingly, water specifically targets these crucial joint problems according to lesion level by reducing the variability of the knee joint angles in tetraplegia and the variability of the hip joint angles in paraplegia, in association with more physiologic ROM of the joints.

The present findings support some clinical considerations for SCI rehabilitation. Reduction in joint angles' standard deviation, in speed, and in stance phase duration allow SCI subjects to walk in water with a gait more similar to that of healthy subjects, allowing a training of stride temporal organization more physiologic than on land. In the framework of motor learning, functional-related plasticity can be considered as the guiding rule for rehabilitation, and it is generally agreed that repetition of a movement would strengthen related neural connectivity [248]. In this study, water environment stimuli reached a more physiologic response of the locomotion skill than on-land condition. Therefore, the exercise of a task-specific locomotion motor pattern associated with physiologic parameters would support the circuits that allow such movement. Thus, because of functional plasticity principles, WW may favor more than WL the strengthening of physiologic circuits, according to the task-specific acquisition, retention, and transfer principles of motor learning[57]. Furthermore, swing phase duration increment increases dynamic postural stability requests, favoring balance training. This latter training has been suggested to specifically improve gait in subjects with chronic motor incomplete SCI, as reported in Study 1.

Finally, it is worth noting that gait training in water provides a sort of body-weight support as other novel gait therapies do on the basis of complex and expensive body-weight support robotic assisted devices that have been the objective of several group studies [226]. No studies ever attempted to compare gait rehabilitation in water vs. body-weight support approaches. Ad hoc studies are needed to experimentally test the efficacy of hydrotherapy for rehabilitation protocols after SCI and to evaluate the similarities and the differences between this and other approaches proposed to enhance gait recovery.

11.5 Study Limitations

A possible limitation of the present study is the sagittal plane two-dimensional analysis used to estimate kinematic data during WW and WL. Although kinematic data are usually acquired with sophisticated three-dimensional gait analysis systems when addressing WL, most studies addressing WW are based, as in the present study, on two-dimensional systems [223;230;239].Two-dimensional systems provide data only as regards the sagittal plane of movement, which is considered the main plane of movement [245]. On the other hand, the complete lack of available data regarding gait in water by the subjects with SCI also renders two dimensional data quite relevant.

Another possible limitation is the relative small sample size of the SCI subjects (n = 15), which may reduce the statistical relevance of this study. It should be stressed that most studies addressing gait in water are based on even smaller samples and that the statistical differences reported here are quite large, thus making the statistical error caused by sample size negligible.

Furthermore, all SCI subjects enrolled presented a high degree at the Walking Index for Spinal Cord Injury assessment; thus, the present data can apply only to a fraction of subjects with SCI. It could be interesting to enlarge the study to subjects with lower walking capacity.

Finally, it should be stressed that this study is not intended to and does not provide clinical indications on the efficacy of gait training in water for walking recovery in SCI. Data support water

environment as useful in inducing a more physiologic gait for subjects with incomplete SCI. Future research should estimate whether this type of exercise is capable of supporting gait recovery in SCI and to what extent.

12 CONCLUSIONS

As stated above gait control mechanisms are multifarious and in incomplete SCI subjects they might be lesioned in different degree. Present data demonstrate that isolate intervention on single aspects of the gait functional impairments may help in improving gait function (*Figure 43*).

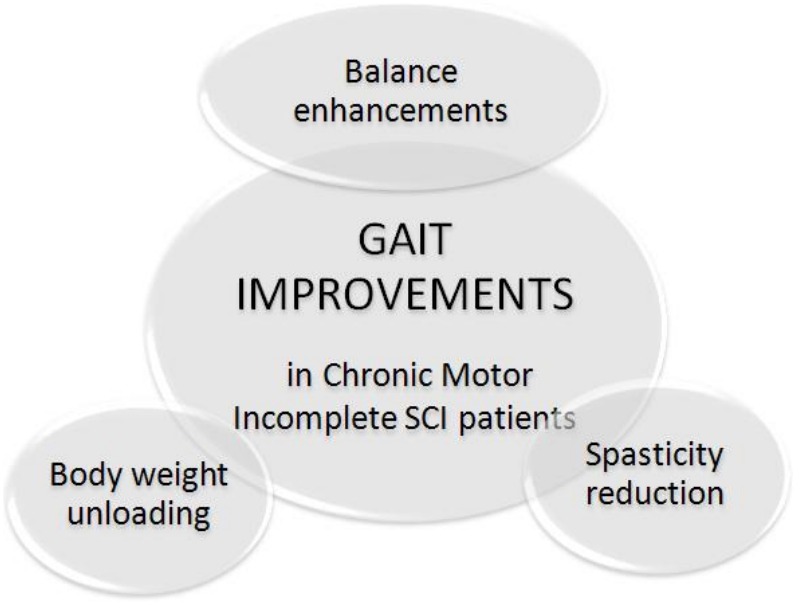

Figure 43: General schema of specific treatments used in the three studies to influence SCI gait.

Classically, functional gait training is considered the most effective approach to recover gait function[25]. Present data, broaden this vision suggesting that, besides task specific training, ad hoc protocols aimed at specific impaired functions involved in gait control might help to boost recovery. Specifically we demonstrated that isolate balance training without any specific task oriented gait exercise is effective in improving gait in subjects with chronic motor incomplete SCI (*Table 21*). That, enhancement of somatosensory inputs by KT is effective in reducing spasticity an in improving both balance and gait functions. Finally that, compared to overground, water environment allows chronic motor incomplete SCI subjects to walk with a gait pattern more similar to the physiological one*Table 21*. These evidences support water environment as training condition for SCI rehabilitation.

Table 21: Overview of studies' results.

STUDIES' RESULTS			
Study N°	**State of the Art**	**Results**	**Rehabilitation Impact**
1 vBFB for Balance and Gait	*Task specific training is considered the gold standard for rehab. If balance improvement can be transferred to gait remains to be ascertain.*	*vBFB training is effective in improving balance and gait in chronic motor incomplete SCI subjects.*	*Inclusion of vBFB training in a rehabilitation protocol for chronic incomplete SCI subjects is more effective than conventional rehabilitation alone.*
2 KT and spasticity	*Spasticity highly influence gait. Kinesio Taping has been proposed to treat spasticity but its efficacy in SCI subjects has to be verified.*	*Short-term application of Kinesio Taping reduces spasticity and pain and improves balance and gait in chronic SCI subjects.*	*Kinesio Taping application is a valid technique to reduce spasticity in the short term improving balance and gait in chronic incomplete SCI subjects.*
3 Walking in Water	*Hydrotherapy is a traditional approach for SCI gait rehabilitation although kinematic effects of water environment on SCI gait have not been defined.*	*In water Gait of SCI subjects is more similar to the physiological one than during overground walking.*	*Walking in a water environment may be of rehabilitative significance for SCI subjects.*

In *study 1* task-specific sensory cues by means of vBFB technique have been used to improve balance and gait. Re-education of balance function in SCI patients by task-specific oriented training [155] has been previously examined, focusing on sitting balance recovery [155 156 110] or standing balance [113;157]. There are no data on the efficacy of task-specific biofeedback balance training in supporting walking functions in chronic motor incomplete SCI patients. Our results demonstrated that in chronic motor incomplete SCI subjects:

- Task specific vBFB training improves balance and gait;

- The inclusion of vBFB training effects greater improvements in gait than conventional gait rehabilitation alone.

We assumed that task-specific vBFB training, although it acts on motor programs for balance control strategies in training regimens, is also effective for gait motor programs. In the overall assessment of balance, improvement in COP parameters appeared to be strictly linked to improvements in gait. The key point is that these improvements in balance preceded the amelioration in gait, suggesting that improvements in walking depend in part on those in balance. Although parallel improvements in balance and walking have been observed in acute[47] and chronic SCI subjects[177], no study previously examined the interdependence of these functions.

For *study 2*, KinesioTaping approach has been used to re-activate nervous system, particularly in the context of sensorimotor system, including somatic sensory afferent inputs and activating functional movements [185]. Our results highlight that KT had significant immediately therapeutic effects on spasticity and related symptoms in the short term and improved balance and gait in chronic incomplete SCI subjects. KT treatment facilitates:

- A significant spasticity reduction, suggesting improved motor outcome;
- A better control of balance and an improvement of dynamic postural stability, associated with a positive enhancement of kinematic gait parameters.

These results interpret considering somatosensory effects due to increasing skin receptor output through tape application. This in turn, stimulates supraspinal centers and thus enhances kinesthetic and joint position sense [186;209]. Applying pressure to and stretching the skin with KT can stimulate cutaneous mechanoreceptors and enhance signal information of joint movement or joint position[210;211]. Thus, sensory modulation through KT might not only influence spasticity but may also intervene in long-lasting reorganization of spinal gait circuits.

As concern *Study 3* it demonstrated that, in SCI motor incomplete subjects, water environment allows a more physiological gait pattern than on-land condition. Therefore, it can be hypothesized that performing a task-specific locomotion exercise in an environment that allows a more physiological gait would reinforce correct gait pattern inhibit pathological ones. Because of functional plasticity principles, WW may favor more than WL the strengthening of physiologic circuits, according to the task-specific acquisition, retention, and transfer principles of motor learning[57]. Furthermore water environment increases dynamic postural stability requests, favoring balance training. This latter training has been suggested to specifically improve gait in subjects with chronic motor incomplete SCI, as reported in Study 1.

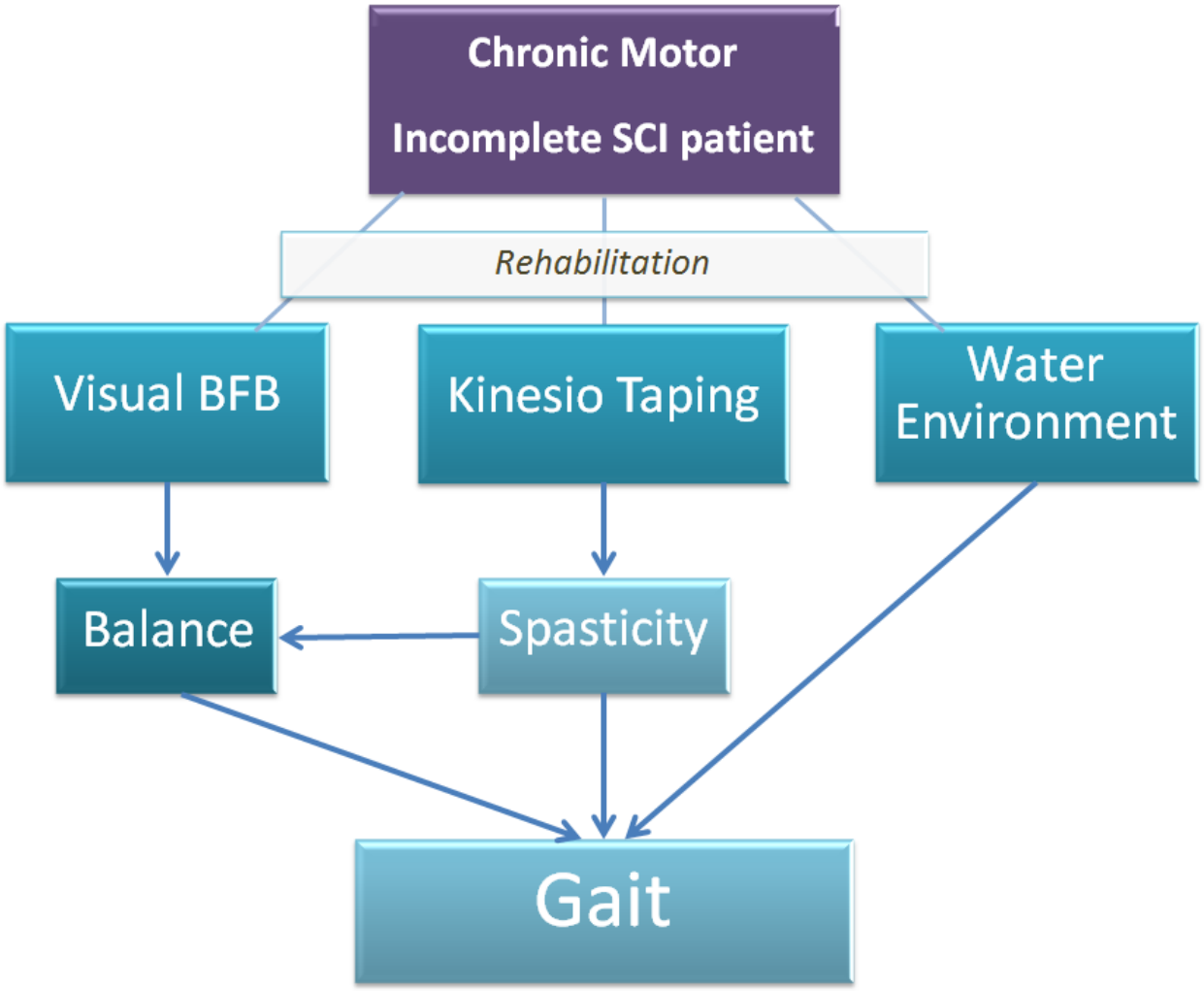

Figure 44: Overview schema of the effects of specific rehabilitation treatments on gait in chronic incomplete SCI subjects

In conclusion, present results demonstrate that for chronic incomplete SCI subjects gait rehabilitation might take advantage of integrating different approaches aimed at balance rehabilitation by vBFB, at somatosensory inputs enhancement by KT, as well as at body weigh support by water environment (*Figure 44*) .

An interaction among the different rehabilitation approaches is a topic that still needs to be verified. Functional tasks, by definition address all the systems involved in a given task, but they do not consider possible differences among impairments. Therefore, in a holistic approach both spared and impaired functions will be treated equally. In a more selective approach, like the ones here analyzed, each function is addressed specifically. These two approaches are by no means in opposition. Better knowledge of the pathophysiological mechanisms determining gait impairment in SCI and a better understating of the effects of the different rehabilitation protocols on gait control systems will help us in progressing and in improving the efficacy of gait rehabilitation after SCI (*Figure 44*).

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