TRANS-SPINAL ELECTRICAL STIMULATION FOR IMPROVING TRUNK AND SITTING FUNCTION IN TETRAPLEGICS WITH CERVICAL CORD INJURY

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Trans-spinal electrical stimulation for improving trunk and sitting function in tetraplegics with cervical cord injury

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CERTIFICATE OF ORIGINALITY

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it reproduces no material previously published or written, nor material that has been accepted for the award of any other degree or diploma, except where due acknowledgement has been made in the text.

________________________________ (Signed)

NIRAJ SINGH THARU (Name of student)

DEDICATION

To my dear father and mother, who educated me to be sincere, caring, and have a positive attitude when dealing with overwhelming difficulties.

To my sister, brother, and friends who always put their trust in me and pushed me to develop my confidence every time throughout this journey.

ABSTRACT

The aim of this study was to examine the efficacy of trans-spinal electrical stimulation (tsES) for improving trunk control and sitting stability with task-specific rehabilitation (tsR) in people with chronic tetraplegia. Five individuals with complete (AIS-A) cervical (C4-C7) spinal cord injury were enrolled in a 32-week clinical study. This was a longitudinal cohort study, where the combined intervention of tsES and tsR was given for 12 weeks, followed by tsR alone for another 12 weeks. The stimulating sites were T11 and L1, and the electrical stimulation frequency was from 20–30 Hz with 0.1-1 ms pulse width biphasic stimulation. The functional outcome scales used were the Modified Functional Reach Test (mFRT), Trunk Control Test (TCT), Function in Sitting Test (FIST), and International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI). Moreover, the kinesiologic and electrophysiologic assessments were conducted through electromyography (EMG) and the Vicon motion capture system, followed by the assessment using 3D ultrasound imaging. The results showed that the tsES+tsR intervention improved forward reach distance from *2*.0 ± 1.58 cm to 12.3 ± 6.12 cm (p = 0.02), right lateral reach distance from 0.9 ± 0.74 cm to 4.6 ± 2.58 cm (p = 0.03), and left lateral reach distance from 1.0 ± 0.79 cm to 4.0 ± 1.69 cm (p = 0.01), respectively. Meanwhile, the TCT and FIST scores increased from 3.0 ± 0.70 to 11.6 ± 3.36 (p < 0.01) and from 12.6 ± 4.45 to 29.0 ± 8.80 (p < 0.01), respectively after tsES+tsR. In addition, motion analysis results demonstrated an increased trunk range of motion: the flexion increased from 12.2 ± 4.71º to 23.1 ± 9.0º (p = 0.01); extension from 5.7 ± 2.04º to 12.4 ± 4.48º (p = 0.01); right lateral flexion from 5.8 ± 5.63º to 9.1 ± 5.43º (p = 0.04); left lateral flexion from 6.0 ± 2.82º to 9.8 ± 2.94º (p < 0.001); right rotation from 1.7 ± 2.30º to 4.5 ± 2.67º (p = 0.01); and left rotation from 18.4 ± 13.15º to 39.6 ± 13.43º (p < 0.01), respectively. Moreover, the EMG responses were highly elevated for latissimus dorsi (LD) muscle during extension after tsES+tsR: right LD increased from 2.20 ± 1.60 µV to 8.86 ± 6.04 µV and left LD from 2.57 ±

1.81 μV to 9.94 ± 6.70 μV, whereas, for erector spinae (ES): right ES increased from 1.62 ± 0.95 μV to 6.93 ± 6.32 μV and left ES from 1.79 ± 1.25 μV to 7.53 ± 5.47 μV, respectively. Additionally, right external oblique (EO) demonstrated greater response during right rotation, the value increased from 1.75 ± 1.31 μV to 6.15 ± 4.83 μV; while left EO revealed higher response during left rotation: from 2.07 ± 1.17 μV to 13.47 ± 7.49 μV. The ultrasound imaging of the sagittal spinal curvature revealed decreased thoracic kyphosis (pre-26.6 ± 7.3º, post-16.3 ± 5.0º) and increased lumbar lordosis (pre-9.3 ± 13.9º, post-11.7 ± 8.3º). It was also found that, functional gains were maintained after the follow-up period, demonstrating long-term effects of the intervention. The findings of this study showed that the tsES+tsR intervention improved independent trunk control with increased static and dynamic sitting balance, as well as the ability to perform upper-limb activities and functional tasks while sitting.

Keywords: trans-spinal electrical stimulation, trunk control, sitting balance, tetraplegia, spinal cord injury.

Publications

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LIST OF ABBREVIATIONS

AD **-** Autonomic dysreflexia

ADL **-** Activities of daily living

AIS **-** American Spinal Injury Association Impairment Scale

ASIS **-** Anterior superior iliac spine

BP **-** Blood pressure

CoL **-** Centre of laminae

EMG – Electromyography

eSCS **-** Epidural spinal cord stimulation

ES **-** Erector spinae

EO **-** External oblique

F/U **-** Follow up

FRD **-** Forward reach distance

FES **-** Functional electrical stimulation

FIST **-** Function in Sitting Test

ISNCSCI **-** International standards for neurological classification of spinal cord injury

LD **-** Latissimus dorsi

LK **-** Left knee

LLF **-** Left lateral flexion

LLRD **-** Left lateral reach distance

LR **-** Left rotation

LPIS **-** Left posterior iliac spine

LSHO **-** Left shoulder

µV **-** Micro-volt

mA **-** Milliampere

mFRT - Modified Functional Reach Test

NLI - Neurological Level of Injury

PSIS - Posterior superior iliac spine

ROM - Range of motion

RA - Rectus abdominis

RK - Right knee

RLF - Right lateral flexion

RLRD - Right lateral reach distance

RPIS - Right posterior iliac spine

RR - Right rotation

RSHO - Right shoulder

RMS - Root mean square

SCI - Spinal cord injury

SpO2 - Oxygen saturation

SD - Standard deviation

tsR -Task specific Rehabilitation

TCT - Trunk Control Test

tsES -Trans-spinal electrical stimulation

VICON - Vicon motion capture system

Chapter 1 Introduction

1.1 Spinal cord injury overview

Spinal cord injury (SCI) refers to the "loss of motor, sensory, or autonomic functions below the level of injury, resulting in persistent neurologic impairment and disability" [1]. The worldwide incidence and prevalence of SCI ranged from (8.0 – 246.0) to (236.0 – 1298.0) per million people each year [2]. The American Spinal Injury Association Impairment Scale (AIS) divided SCI into two categories: complete and incomplete. The sacral region (S4-S5) that lacks sensory and motor functioning is defined as complete (AIS-A), while the sacral region (S4-S5) with some sensory and motor function maintained is called incomplete (AIS-B, C, D, or E) [3, 4]. Moreover, SCI has been classified into two types based on the nature of the injury: traumatic SCI, which occurs when the spinal cord nerves are damaged in an accident or through violence; and non-traumatic SCI, which occurs as a result of infection or tumour [5]. Additionally, depending on the severity of the neurological damage, SCI is classified as tetraplegia or paraplegia. Tetraplegia is defined as neurological damage occurring at or above the thoracic vertebrae (T1) level, and paraplegia is described as injury occurring below the T1 level [6]. The most common type of SCI is cervical injury, accounting for 60% of all cases [7], with C5 (cervical vertebrae) being the most often affected level [8]. One-third of SCI sufferers are tetraplegic, meaning they have a complete lesion 50% of the time, with a male to female ratio of 3.8/1 [9]. For people with SCI, the potential for regaining stability during sitting is minimal [10]. Moreover, motor or sensory recovery is often restricted to minimal success in people with tetraplegia, but restoration of function is more often substantial and highly variable in those with paraplegia [11, 12].

SCI is a devastating condition that causes functional impairments affecting a person's mobility, self-care activities, and emotional, personal, familial, and social life, etc. [13, 14]. SCI has a significant impact on young people's lives, lowering their productivity and resulting in economic consequences [15]. In 2010, Furlan et al. stated that over the last decade, the incidence and prevalence of SCI had increased globally [2]. In the majority of cases, SCI has long-term consequences that last a lifetime, and the individual is at risk of developing a variety of secondary complications that may even result in premature death [16]. SCI's most evident consequences are paralysis and diminished mobility [17]. Restoring paralysis lessens the severity of subsequent problems, and enhances the quality of life for those with SCI [18]. As a result, motor recovery and functional improvement are essential rehabilitation goals [17, 19]. Although motor restoration does not occur below the lesion in those with complete SCI [19], research has indicated that individuals with complete or incomplete SCI exhibited motor and sensory improvement after one year of follow-up [20]. SCI is associated with substantial abnormalities in a variety of physiological systems, the most prevalent of which are muscular atrophy and sensory motor disorders [21]. Tetraplegics reported significantly more limitations and restrictions in terms of quality of life than paraplegics, therefore, developing an appropriate treatment plan on a priority basis and considering the degree of damage is important [22]. For people with complete SCI, functional activities, bed mobility, and self-care tasks are difficult and problematic in the absence of trunk control [23]. Similarly, individuals with SCI are also more prone to instability and fall-related injuries [10]. As a result, trunk recovery is a primary priority for restoring motor function and lowering the risk of falling [23, 24]. Moreover, individuals who have sustained SCI live with impaired function, emphasizing the critical nature of restoring motor function [25]. In contrast, developing neuromodulation techniques has demonstrated motor improvement in SCI by activation of spinal sensory circuits [26], and with advancements in science and technology, new therapy approaches aimed at improving function and quality of life are being developed [25].

Spinal cord injuries are both debilitating and fatal [27], resulting in not only motor and sensory impairments [1], but also a financial burden on the individual and the healthcare system, which is relatively double for tetraplegia than for paraplegia [28]. Although expected lifespan and survival rates have increased over the years, notably in paraplegia, mortality rates in tetraplegia remain high [29]. Individuals with tetraplegia or paraplegia place a higher priority on trunk stability than on mobility [30]. Therefore, trunk improvement is important for developing functional independence and overcoming emerging problems. According to Yeo et al., individuals with complete tetraplegia are expected to live 70% of their lives compared to the lifespan of the general population [31]. As a result of the severity of their SCI, their functional ability has been significantly reduced [32, 33]. A recent study reported that a person with complete C6 tetraplegia may have the potential to drive independently, increasing their participation in social events and sports [33]. There is still a need to investigate trunk and seated control functions, both of which are necessary for driving. Furthermore, appropriate trunk stability is required when performing upper-limb tasks while seated [34]. Thus, further study is required to fully explain the trunk motor improvement associated with sitting for SCI. Previous research has mostly concentrated on rehabilitating upper and lower limb motor function [35-37], with just a few studies investigating trunk motor recovery in individuals with lower levels of injury [10]. Motor and sensory abilities have improved for the majority of SCI survivors. Tetraplegia, on the other hand, has a low rate of recovery [38]. Yet, studies on tetraplegia involving the trunk have been rarely conducted, and current knowledge remains insufficient, leaving a research gap to be filled. In addition, the majority of research has focused on limb muscles, with less attention paid to trunk muscles [39]. The current study is aimed at investigating the effects of trans-spinal electrical stimulation (tsES) in combination with task-specific rehabilitation (tsR) for regaining trunk control and sitting function in individuals with tetraplegia. To achieve this aim, research was done to obtain three specific objectives: (1) to examine the efficacy of tsES for improving trunk control and sitting function with tsR in people with tetraplegia; (2) to investigate the effect of tsES on motor and sensory functions; and (3) to compare the spinal sagittal curvature changes before and after the intervention. Furthermore, the significance of this study lies in its potential to improve trunk control and sitting function, and the outcomes may change the rehabilitation paradigm for individuals with complete tetraplegia and facilitate their transition towards a more independent life.

1.2 Conventional rehabilitation in SCI

Conventional rehabilitation is a basic, inadequate therapeutic strategy with minimal standards, although rehabilitation experts have addressed some specific aspects despite the lack of universal principles [18]. Due to the limited availability of inpatient services and high expenditures, health care experts prepare to release SCI sufferers once it is feasible and focus on emergence-based therapy for functional independence. Acute treatment based on traditional methods may vary by location or even practitioner [18, 40]. Furthermore, due to the limits of health care providers, the number and duration of therapeutic training sessions have been drastically decreased, demanding that clinicians focus on current patient requirements in preparation for discharge [41]. SCI rehabilitation has been linked to the severity of the damage and the level of disability in recent years, and focuses on the most optimal restoration after a lesion and helps an individual reintegrate into society as independently as possible [42, 43]. Traditionally, SCI management aimed to teach compensatory skills. However, with modern technological developments and research, rehabilitation has undergone a paradigm shift and, after the emergence of neuromodulation, the focus has changed to neuromuscular re-education, improving muscle strength, restoration of lost function, and enhancing functional ability [44, 45]. Moreover, different forms of neuromodulation may be used in conjunction with traditional rehabilitation procedures to improve rehabilitation results, and integrating techniques that are not yet in clinical use may provide additional benefits [46]. In addition, conventional rehabilitation is gradually shifting to neural restoration through the use of innovative, intensive therapy strategies that target pathophysiological alterations and regeneration concepts effectively [47]. As a result, management and care of people with SCI has improved dramatically, and is primarily focused on improving quality of life rather than just prolonging their lifespan [48]. Previously, SCI has been treated as an inpatient procedure, but now it is progressively becoming a life-long process. Hence, the traditional belief that improvement is restricted to the first two years after SCI is changing and providing hope that functional recovery might be possible after many years [49].

1.3 Neuromodulation in SCI

Neuromodulation is defined as a technique that uses electrical interfaces via stimulation devices [50] to modify neuronal activity and alter human sensorimotor function [51]. It includes both invasive and non-invasive methods, and it is also used in therapeutic treatments [50, 51]. Additionally, neuromodulation has been successfully implemented in SCI rehabilitation to reduce long-term complications, regain volitional motion and hand dexterity, and has demonstrated the potential for activating confined neural circuits below the lesion [46, 52]. Invasive and non-invasive spinal stimulations have both been demonstrated to enhance motor control in people with SCI [53]. Simultaneously, non-invasive neuromodulation of the spinal cord has been shown in recent research to have the capacity to restructure supraspinal connections and modify spinal networks [12]. It is safe and appropriate for all SCI individuals [54], also easier to use for clinical purposes [55]. Again, non-invasive methods have been adopted commonly to replace the surgeries required during invasive stimulation [56]. On the other hand, invasive stimulation installation poses more considerable surgical risks in the cervical spinal area compared to the lumbar region [57]. The bulk of current investigations on neuromodulation has focused on increasing locomotion ability [58-60], while restoring trunk function is underestimated. Recently, among various neuromodulation techniques, tsES has been found to be promising for SCI [61]. Recent research has put a lot of emphasis on analysis and modelling of abled-body trunk function and SCI has received little attention [62]. Moreover, few investigations have explored the effect of non-invasive tsES in the lumbosacral region on trunk stability, and the results are limited and incomplete [10, 63]. Some commonly used neuromodulation methods in SCI rehabilitation have been described.

1.3.1 Epidural spinal cord stimulation

Epidural spinal cord stimulation (eSCS) is an invasive neuromodulation technique that helps to relieve chronic pain, decrease spasticity, tends to increase particular rhythmic muscle activity in the lower extremity, induces respiration, enhances urinary function, and improves sensorimotor neural activity and the ability to influence various organs in the sympathetic nervous system, or viscero-somatic reflexes [64-66]. The eSCS has progressed from a simple two-electrode array to modern, integrated applications. Recent multielectrode computers have updated electrode designs with many active connections that enable more precise control of the electric current, as well as larger energy output and high-power electronic processors that provide a wide variety of stimulation settings [67]. There are various technical and clinical difficulties with eSCS, such as failure of equipment, power leakage, battery charger limitation, connection malfunction, etc. [68]. On the other hand, eSCS requires surgery for insertion of the stimulator [37], and have higher adverse effects [69]. The equipment has presented approximately five percent of operational problem [70]. The medical consequences include tissue injury, haemorrhage, hematoma, infection (4%-10%) and headache [69, 71, 72]. In order to maximize the advantages of eSCS while eliminating the drawbacks, a non-invasive tsES has been invented and studied recently [73-76]. A new wave of neurorehabilitation therapies is emerging, based on current developments in neurology and manufactured biodevices. These methods have been shown to be effective in causing long-term modifications in neuronal networks [77].

1.3.2 Functional electrical stimulation

Functional electrical stimulation (FES) is both invasive and non-invasive [78] and is a neurorehabilitation technique that uses rapid electrical impulses to produce movements during walking or biking [79, 80]. It may be used on many parts of the body by applying it to the skin above the particular muscle and peripheral nerve. Moreover, it is recommended to administer FES to specific muscle groups instead of nerves since it causes minimal harm to tissues and has a greater success rate while using a smaller amount of electrical energy [81]. Due to the fact that FES has both direct and indirect effects, it may be applied in a variety of ways in rehabilitation [82]. The FES method has a number of advantages in SCI treatment, including improved residual motor strength, enhanced mobility and joint range for extremities, and lower spasticity, all of which contribute to improved sensorimotor capabilities [81]. Additionally, FES improves upper and lower extremity motor performance [80, 81], enhances cardiorespiratory endurance by increasing pulmonary airflow, elevating flow rate and lung volume [83], and reduces neuropathic or nociceptive discomfort and stiffness, which are common following SCI [84]. Pressure ulcers are a familiar consequence occurring in SCI, and FES plays a significant role in improving the speed of pressure sores' recovery [85]. In addition, FES also assists in the management of bowel and bladder malfunctions, including the improvement of erection and ejaculation problems. Moreover, it was shown that FES enhances blood flow and metabolic health, which leads to increased muscular mass, stabilizes equilibrium, and better posture control [86]. Simultaneously, invasive FES, when delivered continuously, has the ability to adjust kyphotic sitting postures, modify lateral vertebral alignment, increase respiration and breathing flow, and change interface pressures [87].

1.3.3 Trans-spinal electrical stimulation

Trans-spinal electrical stimulation (tsES) is an emerging neuromodulation technique in which electric current is administered to the spinal cord using stimulating pads superficially positioned on the skin surface over the spine to generate therapeutic benefits. The tsES is a non-invasive method [35] that modulates the activities of neural pathways through spinal stimulation [88] and is used for electrophysiological and therapeutic examinations [89]. Its basic method of operation is through spinal cord activation via sensory pathways in the dorsal roots, which provides subthreshold excitation to interneurons and motor neurons distal to the injury. Motor neurons near to the threshold are then more rapidly triggered by the brain's intact but inactive residual descending pathways, restoring volitional control of movement [90] to the same structures targeted by eSCS [91]. Previously, it was utilized mainly for treating pain, but it is now widely employed in rehabilitation for motor function restoration [92] in people with neurological impairments [93] caused by SCI [94]. Similarly, the tsES can be used alone or in conjunction with functional therapy [54] and has the therapeutic potential to improve voluntary motor control, extremity muscle strength, posture, locomotion, spasticity, trunk stability, and overall spinal function [52, 95, 96] in people with chronic paralysis [97]. It generates a variety of currents at a frequency of (5-50 Hz) delivered at varying intensities (10 - 200 mA) via a carrier frequency of 5 and 10 kHz, resulting in therapeutic benefits [98]. Similarly, the tsES functioning process has been investigated in recent years. It produces an electrical field that activates the neurological connections [99], and the constant stimulus increases excitatory transfer in nerve fiber cells while restricting neural activity interplay, which aids in the release of endogenous neurotrophic materials that improve motor control [100]. To improve rhythmic motor output, tsES stimulates the proximal afferent fibers of the posterior roots [101]. Due to higher technical and clinical complication rates of eSCS [69], as an alternative, non-invasive tsES has been developed and is advantageous over the invasive method [10, 76]. Alternatively, the restriction of tsES is the anatomical space around the stimulating location, as this may result in alterations in the delivery [102] and duration of stimulation [103] owing to the possibility of scorching the skin. According to certain investigations, skin breakdown in the stimulation zone results in an increase in systolic blood pressure of more than 60 mmHg [63]. Besides, it has been found that tsES can achieve comparable outcomes to eSCS without affecting residual motor function [104]. As a result of eSCS and tsES stimulation, people with total paralysis are able to perform voluntary actions, stand, and walk more effectively [63]. Similarly, it was reported that the interneuronal spinal circuits may be neuromodulated by a non-invasive tsES, similar to what occurs after complete SCI with eSCS [105]. Furthermore, a 20-minute delivery of tsES at rest has been shown to alter neural activity and motor function in people with SCI, much like previous neuromodulation techniques that target spinal synaptic connections or the primary motor cortex [98]. Although eSCS is considered as a revolutionary therapy for permitting mobility after SCI, non-invasive tsES is an emerging method of activating comparable target neural structures [105]. Previous studies using tsES showed it could decrease spasticity [106], modify neuronal connections [107], assist locomotion [108] and stepping [101], and initiate volitional movement [37]. However, tsES has not been evaluated in the restoration of motor function of the trunk in quadriplegia. Simultaneously, the impact of tsES on improving sitting control in SCI has been open to question [10]. Therefore, it would be of interest to study the restoration of trunk function for complete SCI. At present, only limited therapeutic progress in this approach has been documented in individuals with a high severity of cervical damage [109]. The immediate effects of the tsES on postural control make it possible to construct a rehabilitation plan for improving balance [10]. Therefore, it is suggested that further research is needed to determine the long-term effectiveness of adjunct treatments, such as task-specific trunk control training and neuromodulation, in individuals with SCI [63].

1.4 Neurorehabilitation for SCI

Neurorehabilitation is a branch of rehabilitation with the goal of assisting in the recovery of neural damage as well as the restoration of any functional changes that may have occurred as a result of it [110]. At present, there is no cure for SCI; meanwhile, the current therapy aims to minimize secondary complications and increase residual function [111]. Even though, in the absence of treatment for tetraplegia, rehabilitation is the choice of treatment available that has emphasized conservative approaches for regaining function [11, 25, 38]. Traditional rehabilitation treatments focused on compensatory measures that prioritized the use of non-paralyzed muscles over the restoration of function in paralyzed muscles, so such methods were not able to achieve motor and sensory improvement [112]. Aside from the fact that the advantages of rehabilitation programs are too small to be clinically meaningful, they also take too long and cost too much money [12]. There is little that could be done to improve the functions of peoples with SCI [61]. In addition, previous animal and human research expanded the rehabilitation concept, resulting in the devolvement of motor learning-based rehabilitation, also known as task-specific rehabilitation [112].

1.4.1 Task-specific rehabilitation

Task-specific rehabilitation (tsR) is a therapeutic intervention where the participant focuses on realistic and precise motor activities with uniformity for the purpose of attaining a particular skill. The training is based on practical activity through targeted and repeated specific exercises that regain muscle strength and advance functional skills. The tsR is based on the idea that motor output can be shaped and re-trained in response to specific sensory inputs. Thus, it focuses on regaining muscular strength and improving functional abilities through targeted and repeated specific exercises [113]. It emerged from animal study, and has been refined within the psychological literature on motor function and learning, and subsequently used in clinical studies for both normal and injured individuals [113]. The importance of repetition in initiating and sustaining brain changes cannot be overstated. However, in the absence of new relevant skill development, repeated performance of a task is unlikely to result in significant brain modifications [114]. Less rigorous tsR regimens with the more affected limb (e.g., 30–45 minutes) may elicit brain reconfiguration and associated significant functional benefits [114].

According to a prior study, when sensory stimulation is paired with motor training, the benefits of tsR may be boosted even further [115]. Moreover, continuous independent sitting training combined with upper limb activities has been shown to promote sitting stability in chronic SCI [116]. Therefore, in order to decrease dependency and maintain quality of life in SCI survivors, sitting control is an important part of rehabilitation that may be efficiently accomplished by goal-oriented and tsR exercises [117]. In addition, attempts have been made in tsR paradigms to increase motor performance by adding complexities to the individual motor tasks being taught. It was discovered that teaching people with incomplete SCI, with a range of tasks in a variety of circumstances and settings is more beneficial for enhancing their competence [118]. Correspondingly, the tsR is a commonly used approach and is expected to help people with chronic SCI regain postural control in the rehabilitation context to improve sitting [119]. The tsR has been shown to be more beneficial than other types of exercise training for motor recovery and physical output in people with chronic SCI [120, 121]. Alternatively, the motor responses elicited by tsES were increased when treated with tsR [122]. As a result, tsR is suggested as a key component in rehabilitation [123]. However, there is still much to be learned about its effectiveness, specifically for higher levels of SCI. It is feasible that tsR targeted at enhancing particular mobility goals, like walking, may also produce stability benefits. More study is needed in order to explain the precise elements of tsR necessary for increasing sitting balance function in SCI [124].

1.5 Trunk control and sitting function in SCI

In the sitting position, the trunk plays an essential role for spinal posture alignment and functional tasks accomplishment of the upper limbs [117, 125]. More than 60% of SCI survivors considered trunk control with functional hand movements an important factor in performing daily living tasks [116]. Moreover, people who have lower thoracic SCI have been observed to have superior static or dynamic balance than those with higher thoracic SCI [126].

Likewise, people with higher levels of injury have very minimal sitting function and trunk control is almost diminished. Therefore, individuals at such a level of injury require maximum trunk strength to maintain the stability of their head and neck in a sitting position [127]. Trunk control contributes to the functional activities involving the upper extremities and assists in decreasing the compensatory actions during those functional tasks. Hence, trunk control should be combined with upper extremity function restoration as it assists in controlling the upper limbs [128]. The paresis of trunk musculature in SCI leads to compromised sitting that interrupts the normal posture [129]. Similarly, sensory impairment and trunk muscle weakness in SCI survivors are significant causes of postural instability and sitting imbalance [130], and they are at greater risk of falling and related injuries due to poor trunk control and balance [10]. Nevertheless, trunk balance is a key factor when performing static and dynamic functional tasks and is considered the main aim for regaining postural control [131].

Sitting function is one of the greatest required skills in SCI individuals who want to live an independent life by performing their functional tasks of daily living [117], and its failure or imbalance can result in serious fall injuries [132]. Muscle weakness and sensory disturbances impair sitting capacity, increasing reliance on others to perform activities of daily living (ADL) [133]. People with tetraplegia have severe trunk muscle weakness that impairs their sitting and upper extremity functions, limiting their overall functional activity and necessitating the use of a wheelchair [129], and they have higher challenges than people with other conditions [134]. Therefore, specific muscle strength training for trunk and sitting balance is required in such individuals [135] and is one of the important goals in the rehabilitation of SCI [136]. The dynamic sitting ability and capacity to sit independently in people with SCI, along with the function of the upper limbs, determine their quality of life [130]. Furthermore, trunk strength and sitting control are predicted to reduce the fatigue of upper limbs while operating a manual wheel chair and prevent musculoskeletal problems [137]. Simultaneously, postural instability due to motor and sensory impairments results in muscular weakness and sitting control difficulties [136]. As a result, sitting has been considered as an essential function in people with SCI in order to maintain posture and perform purposeful tasks [117, 137].

1.6 Trunk stability and instability in SCI

Trunk stability refers to an individual's ability to maintain an erect sitting position while performing other motions by adjusting the spinal alignment and accompanying muscular activity [138]. It is essential for human activity and movement [139], everyday tasks, including sitting, standing, walking, and reaching, are impossible unless the trunk is stabilized [140]. Spinal abnormalities create trunk instability and raise the likelihood of falling, resulting in physical deterioration and a decreased quality of life [141]. In addition, people who have sustained complete or incomplete SCI often have trunk impairment. As a consequence, affected people are often unable to maintain independent sitting balance, resulting in trunk instability, decreased independence with ADL, etc. [136, 142]. Trunk instability and compensatory efforts may lead to serious health issues such as bed sores, kyphosis, breathing difficulties [143] and upper limb musculoskeletal pain [144]. Therefore, achieving trunk stability is among the most important goals for people with SCI because of the functional and long-term health consequences [145].

The capacity to perform skilful action lies in individual's potential to make proper postural modifications in order to maintain postural stability during segment displacements [142]. There have been a number of initiatives to increase the stability of people with SCI when they are sitting, wheeling, or reaching [146]. Although several studies have focused on increasing trunk stability in SCI by modifying wheel chairs and using chest harnesses, footrests, etc., these passive adjustments are supported only in the forward direction, and sideways movements are still compromised [147, 148]. Correspondingly, there is some evidence to support the claim that these modifications do little more than passively improve seating stability in people with

SCI [149]. Because of their failure to stabilize the trunk, people with SCI employ non-postural musculature such as the neck and shoulders to make compensatory motions or positions that help them manage their stability when sitting and wheeling [129]. In addition, people with SCI often place one hand over the back of their wheelchair in order to provide the required force to keep their body from sliding forward excessively while attempting to grab an item in front of them [150]. There remains a research gap which necessitates voluntary trunk stability in all movement directions. In cervical SCI, the severity of muscle dysfunction below the neural damage is essential because it affects the level of functional deficits in both postural stability and breathing [151]. However, it remains to be investigated how trunk stability and sitting balance increase the functional capacity in chronic SCI. The capacity of people with SCI to execute most activities is much reduced when they are seated in a wheelchair. Thus, to carry out ADL, people with SCI need a steady and appropriate sitting position [152]. For this reason, it is reported that quadriplegics and paraplegics choose to focus on regaining trunk stability rather than walking ability [143, 145]. The restored ability to control the trunk and sitting balance will assist in improving ADL performance, contributing to an overall enhanced quality of life for those with tetraplegia.

1.7 Trunk posture and spinal curvature in SCI

Posture is essential for SCI individuals who have been disabled for a long time because of their condition, and the position of the spine plays an important role in spinal stability [153]. Around 70 - 80 percent of people with SCI are confined to a wheelchair and must rely on it for all of their mobility and functional needs. Their muscles need to be strong so that they can lean forward or backward while maintaining their posture. Thus, posture is an important consideration for those with sitting and trunk problems [154-156]. Individuals with SCI may find it more difficult to maintain good posture due as their trunk strength decreases, but this assumption is debatable [136]. Therefore, regaining control of one's sitting posture is one of the goals of rehabilitation in SCI [136]. SCI individuals have considerable limitations in many aspects of their lives. Preventing, diagnosing, and treating such problems is crucial for improving lifespan, community involvement, and health-related quality of life [17]. There has been a lack of research on how an SCI individual's posture affects their recovery from motor and functional impairments. Also, the compensatory postural muscle activity and alterations in postural motor control during reaching tasks have been an important area of research to study seated postural control in SCI individuals [136]. There is a need to investigate and monitor the posture of chronic SCI individuals. This helps to prevent people from sitting in uncomfortable positions and reduces the chances of developing complications [157].

Due to prolonged sitting in a wheel chair and abnormal sitting posture, a curved spine (C-shaped) develops, increasing the risk of spinal curvature deformities. This also results in a variety of complications, including pressure ulcers, functional difficulties with ADL, and wheel chair falls [23, 127, 154]. People with SCI who sit with extended lower limbs and with no trunk stabilization have a hyperkyphotic thoracic spine, decreased lumbar kyphosis, and posterior pelvic tilt [152]. As a result, SCI sufferers must be prioritized in preventing the advancement of spinal deformity [158]. There are two main elements that affect the extent of trunk function impairment for people with SCI: severity and level of damage [159]. Simultaneously, those who have suffered cervical injuries at the C5 - C8 level may be able to utilize their upper limb as an external support to keep their sitting posture upright. Also, kyphotic curvature is formed as a result of this compensatory movement in the trunk, which has a negative impact on everyday activities and quality of life [127]. Little attention is given to the postural alignment and spinal curvature abnormalities in higher level SCI, which means there is a need for studies to examine the curvature changes.

It is widely accepted that maintaining a sense of equilibrium when sitting is essential for doing most daily tasks. The balance and movement of the trunk are closely connected to the individual’s capacity to complete functional tasks [136]. The curvature of the spine from the cervical to the lumbar helps to distribute the body's weight evenly and avoids excessive movement [160]. Ligaments, muscles, and neurological signals all contribute to the maintenance of the spinal curvature [161]. A properly curvatured spinal sagittal posture provides strength and stability to the spine, allowing it to remain in alignment with minimum muscular effort [162]. Similarly, individuals with spinal curvature that is out of alignment are more susceptible to injury because of a loss in muscular strength and higher body sway [163]. Additionally, individuals with SCI who rely on a wheelchair or have poor trunk stability usually acquire a deformity of sagittal curvature [158]. Furthermore, sagittal curvature decreases around the age of 40, and it is also associated with health-related quality of life [164]. A decrease in the sagittal curvature leads the body to become unstable and need external support to maintain its equilibrium [165]. Also, lordosis is among the most common spinal curvature abnormalities, and it is influenced by several factors, such as head and sitting position, backrest shape, etc. [166]. Spinal curvature is essential for maintaining proper posture, but alterations in spinal alignment result in high loading and reduced motion, causing a variety of spinal ailments [165]. Individuals with SCI had a significant 15° reduction in pelvic angle, indicating a posterior pelvic tilt when seated in the same chair as those without SCI [167]. Therefore, spinal curvature assessment and monitoring may play an important role in the prevention and management of spinal abnormalities [168].

1.8 Functional motor recovery using tsES in SCI

Recent developments in tsES have paved the way for a new era of treatment outcomes after SCI [104]. It generates motor actions by descending drive and sensory signals from the periphery onto spinal neuronal networks [100]. When a broken spinal linkage reacts to a stimulus, this implies the possibility of reverting to a functioning condition sufficient to restore and enhance motor capabilities [105]. The tsES delivery at a frequency of 30 Hz improved the volume of rhythmically responsive muscles, boosted leg muscle activation, and reduced clonus [101]. It also enhanced lower extremity muscular coordinated rhythms, resulting in smoother walking motions [105]. On modulation of the lumbar region during walking, it showed regulated flexion, whereas sacral stimulation demonstrated extension during stepping [109]. Simultaneously, the tsES stimulus at 15 or 30 Hz could successfully enhance locomotion function with lower limbs in a gravity neutral stance. Moreover, both invasive and non-invasive stimulation have been found to trigger spinal locomotion regions to elicit non-voluntary stepping actions [169]. It was instantly apparent that the highly impaired leg was able to perform greater dorsiflexion during the rhythmic ankle mobility, resulting in a greater range of motion [95]. Again, an increase in the volitional activation of specific lower limb muscles was observed during sit-to-stand training [55] in chronic SCI [37]. And, a significant grade of limb muscle activation occurred during self-weight shift while standing [36]. It was reported that using tsES on the rostral area improved locomotor function, whereas stimulating the caudal region assisted in recovering extensor action of the trunk muscles [36]. Additionally, tsES over the L1-L2 region at 15Hz allowed trunk extension, resulting in improved postural control [10]. Simultaneously, trunk muscle activation was facilitated by using higher intensities (> 80 mA), which aided in postural maintenance [55], and the duration of stimulation was noted to be at least 20 minutes to generate therapeutic benefits [170]. The stimulation of the enlarged lumbar spinal cord enhanced self-control after persistent paralysis with a more steady, upright sitting position [10] and quickly restored the ability to sit up straight [63]. Previous research has shown that tsES had benefits for muscles innervated distal to tsES delivery site and its effects were beyond targeted regions segments, leading to improvements in hand and arm performance [98]. The tsES application to the cervical level demonstrated that proximal arm and shoulder muscles were activated [57] with an increase in purposeful hand movement [171]. Correspondingly, tsES stimulation at 50 Hz for 30 minutes reduced spasticity. It was also recommended that instead of using systemic drugs or ablative therapies, which have long-term adverse effects, this therapeutic strategy may be adopted [106, 172].

1.9 3D ultrasound imaging

3D ultrasound imaging is a radiation-free scanning device [173], convenient and affordable [174] that has presently been used as a practical musculoskeletal imaging modality [175]. Moreover, it is a non-invasive technique used for detection, diagnosis, tracking growth, and evaluating the efficacy of therapy [176]. In addition, it generates a three-dimensional image of the spine by recording its actual form [176] and helps to measure real 3D parameters, such as Cobb angle on the planes of the maximal curve, by providing a clearer view of the degree of the structural changes [177]. 3D ultrasound imaging has been shown to be equivalent to radiological measures [173], showing the possibility of being extensively used for evaluation of spine-related disorders such as scoliosis [174]. Similarly, medical researchers are increasingly interested in 3D ultrasound because it provides doctors with immediate output that aids in the acquisition of high-quality imaging and quick spatial information of the examined region [178]. As long as clients are regularly monitored, therapists and physicians may determine if they need to have their sagittal spinal curvatures restored in order to enhance their clinical outcomes and prevent further issues [179]. Furthermore, 3D ultrasound imaging may be used to identify pathologies that would otherwise go undetected in a two-dimensional perspective by using volume reconstruction and rendering methods [180]. Therefore, it is undeniably a time-saver for healthcare practitioners since it minimizes the amount of time spent analyzing pictures [178]. This enables healthcare practitioners to immediately evaluate factors, such as spinal rotational movement, which would otherwise require estimation techniques that use a single posteroanterior radiographic image [173]. Since it is non-radioactive, 3D ultrasound could be utilized even for children to continuously evaluate their sagittal spine profile over lengthy periods of time [179]. It is a promising imaging technique for assessing and monitoring the sagittal spinal profile growth in people with spine problems [179]. This quick 3-D ultrasound technology might be utilized to scan other bones in the future with the progress of this approach [181]. In addition, people with scoliosis can benefit from the use of this new technology, which provides a rapid and efficient 3D ultrasound evaluation. It has been used to measure the spinal curvature and create coronal view pictures of the spine anatomy [174]. The people with SCI experience anatomical alignment changes with the progression in the chronic stage that result in musculoskeletal deformities [182]. They generally adopt abnormal posture due to prolonged wheel chair use developing a C-shaped sagittal spinal profile [127]. As the current study hypothesized trunk control and sitting function improvement after the combinational treatment. The researcher also expected alignment changes in the sagittal spinal curvature with improved sitting posture. Therefore, the researcher used 3 D ultrasound to measure the sagittal spinal curvature differences pre and post intervention.

1.10 Summary

Spinal cord injury results due to damage of the spinal connections in the spinal cord. Overall functions of the body below the damage are impaired, and most people have long-term paralysis as a consequence. The neck is the most commonly injured body part, which causes paralysis of both the upper and lower limbs. As stated earlier, this condition is called tetraplegia, where loss of hand and arm function makes it difficult to carry out even the most basic of everyday tasks. As a result, one's level of freedom and overall well-being are drastically diminished. SCI has a devastating impact that extends beyond the person to their family, community, and country as a whole. Additionally, the rate is growing year after year, escalating the situation to a worldwide scale. The stability of the trunk is essential for human motion and mobility, and common functions such as sitting, standing, walking, and reaching are difficult without it. The ability to sit is one of the most important skills for people with SCI who want to lead a more independent life. Approximately 70 to 80 percent of people with SCI are wheelchair bound and must rely on it for all of their mobility and functional requirements. Spinal curvature abnormalities are more likely to occur in people who sit for extended periods of time in a wheelchair in an improper sitting position. In order to avoid spinal deformities, SCI survivors must give special attention to trunk stability. Tetraplegics suffer from significant trunk muscular weakness, which affects their ability to sit and use their upper limbs. As a consequence, they are confined to a wheelchair. SCI sufferers whose trunk muscles have been paralyzed sit more awkwardly, increasing their risk of injury from falls and other accidents. Therefore, it is important for both paraplegic and tetraplegic individuals to have a functioning trunk. It is expected that strong trunk and sitting stability would decrease upper extremity fatigue and avoid muscular injuries when using a manual wheelchair. With the help of a stable trunk, functional tasks involving one's upper limbs may be performed more efficiently and with less need for compensatory measures.

There is currently, no effective therapeutic method for SCI after the chronic stage. According to previous studies, muscular strength could not be regained below the level of damage. As a result, conservative management has been the preferred plan of treatment. Traditional therapies tended to concentrate on acute care and early release, while rehabilitation was aimed at teaching compensating abilities. On the other hand, prior studies have primarily concentrated on upper limb or lower limb recovery, yet trunk rehabilitation is necessary for both categories of therapy, since trunk control is linked with upper extremity movement, and locomotor training, therefore with a compromised trunk those training is unimaginable. Thus, trunk control restoration takes precedence over all other functions. For those who have suffered SCI, new therapies under development hold great promise for improving function. Scientists have recently discovered that neuromodulation enables paralyzed muscles to work. SCI individuals may benefit from both invasive and non-invasive stimulation methods. The majority of the investigations were conducted to restore locomotion function. However, recovery of trunk ability is the primary therapeutic aim in people with tetraplegia. Using neuromodulation methods, motor gains have been shown in individuals with SCI, and these approaches have the potential to be a new therapeutic treatment option. Invasive neuromodulation was a ground-breaking procedure that exhibited several advantages, mostly in lowering stiffness. Because of surgical need, there were more clinical and technical issues. Alternatively, a non-invasive technique has been developed that has been shown to be effective in SCI, delivering comparable outcomes to invasive stimulation. Since it is non-invasive and has fewer side effects, it has been a popular treatment option in recent years. It was also shown that traditional rehabilitation treatments did not enhance motor skills enough to be clinically useful. Studies, on the other hand, suggest that functional rehabilitation might benefit from specific and focused training. Furthermore, tsR was shown to be more advantageous for motor recovery and physical outcomes compared with other forms of exercise training. Thus, the tsES can be an alternative treatment for chronic SCI that can be used alone or in conjunction with rehabilitation training. Previously, SCI therapy was centered on avoiding secondary problems and extending life expectancy, but with the advent of neuromodulation, the paradigm has shifted to enhancing quality of life. However, relatively very few studies on improving trunk control, particularly in tetraplegia, have been undertaken. The research question focuses on "could a combined intervention of tsES and tsR have a long-term impact on trunk recovery in tetraplegia?" in comparison to studies reporting improved upper and lower limb function. Furthermore, recent developments in tsES have paved the way for a new era of treatment outcomes after SCI. The tsES produced immediate trunk self-control with a more steady and upright sitting position and quickly restored the ability to sit up straight [10, 63]. These previous studies on trunk control have only been conducted on subjects with paraplegia or incomplete cervical SCI. Moreover, motor or sensory recovery is often restricted to minimal success in people with tetraplegia. Therefore, further research is warranted for long-term treatment effects on motor recovery in individuals with complete tetraplegia. Conventional SCI rehabilitation focused on teaching compensatory skills. However, tsR has shown some benefits over the conventional rehabilitation, but it has little evidence to support claims in clinical prognosis. Furthermore, it was hypothesized that the combination of tsES with tsR may recover adequate function in SCI. As a result, the findings of this research might transform the rehabilitation paradigm for people with complete SCI and help them adapt to a more self-sufficient lifestyle.

1.11 Outline of thesis

The hypothesis of the present study was that the combined intervention of tsES and tsR could improve trunk control and sitting functions in people with complete chronic tetraplegia and maintain the improvements for a longer period of time. This thesis describes the methodology with the experimental procedures and outcome measures in Chapter 2. Chapter 3 presents the results and findings of the study. Chapter 4 includes the discussion related to the findings of the present study. Chapter 5 summarizes the findings and provides concluding remarks and recommendations for future work.

Chapter 2 Methodology

2.1 Study subjects

This research includes five people with SCI who have had impaired trunk and sitting function. Each participant had sustained a traumatic cervical SCI. The characteristics of the injury were chronic and with complete tetraplegia (AIS-A). Two out of the five SCI subjects lack grasping ability. None of them could propel themselves independently in manual wheel chairs, leaving them completely reliant on carers. The study subjects had never been stimulated in any way never participated in any research project. Each participant rode in a motorized wheel chair that was properly cushioned and supported in the back. The SCI subjects' availability for research was lower due to the pandemic, which resulted in the recruitment of a smaller sample size. Participant consent was obtained prior to the start of the experiments, which were approved by the Human Subjects Ethics Sub-Committee of The Hong Kong Polytechnic University (Reference no: HSEARS20190201002-01).

2.1.1 Study timeline and assessment

As shown in Fig. 1, the total study period was 32 weeks, which included six assessment sessions. A study revealed that an eight-week training program on trunk muscles using invasive stimulation developed the endurance to tolerate stimulation for more than two hours and showed improvements in seated balance [183]. Though the investigators assume that treatment delivery for a longer duration could have better outcomes. Therefore, 12 weeks of treatment were selected for each phase of therapy with 6 weeks of follow-up period. No stimulation was used during the overall assessments. A professional, experienced physiotherapist delivered the sessions and assessed the participants. Initially, the first two weeks were spent screening subjects and testing tsES, which included determining the optimal stimulation settings and doing some tsR training. This was performed to study the effects of tsES since it was discovered that tsES increased systolic blood pressure [23]. Additionally, vital signs such as blood pressure

(BP) and oxygen saturation (SpO2) were monitored regularly. Individuals with tetraplegia are more likely to have autonomic dysreflexia, which may occur as a result of an increase in BP [23] or changes in posture during tsR training. This screening phase assisted us in minimizing potential dropouts. A baseline assessment was conducted after two weeks, followed by five further assessments at six-week intervals. The experiment lasted 24 weeks and was separated into two different phases: intervention phase and the training phase of 12 weeks each: tsES+tsR and tsR respectively. In each phase of tsES+tsR and tsR alone, two assessments were carried out at a 6-week interval. Lastly, a follow-up assessment was conducted six weeks after the completion of tsR training. The functional assessment was conducted using the following outcome measures: (1) Modified Functional Reach Test (mFRT) - to determine the reaching distance; (2) Trunk Control Test (TCT) - to assess static and dynamic equilibrium; (3) Function in Sitting Test (FIST) - to measure functional sitting balance; and (4) and International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) - to assess sensory and motor level injury characteristics. These four outcomes measures selected in this study are standardized tools used for assessment of sensorimotor, trunk and sitting function in SCI. The mFRT [184], TCT [185], and FIST [186] have proven reliability and validity in SCI. Similarly, kinesiologic and electrophysiologic assessments were performed using the Vicon motion capture system (VICON) to assess the trunk range of motion parameters and electromyography (EMG) to measure the responses of the main muscles (rectus abdominis, external oblique, erector spinae, and latissimus dorsi) involved in trunk and sitting control function. Moreover, a 3D ultrasound scan was used to get a radiographic evaluation of the sagittal curvature of the spine. Additionally, kinematics and kinetics assessments were performed beginning in the 8th week, i.e. after 6 weeks of tsES+tsR delivery. Because the subjects lacked full trunk control and were seated with assistance, these factors might have influenced the outcome. As a result, after achieving static control, these assessments were conducted and considered as a baseline.

2.1.2 Inclusion and exclusion criteria

This research included participants in stable medical conditions of both genders. Each subject was required to sign a consent form and abide by the research study's rules and regulations. The following are the inclusion and exclusion criteria:

Table 1: lists the study's inclusion and exclusion criteria:

Inclusion criteria	Exclusion criteria
1. The subject must be tetraplegic as a result of cervical injury.	1. In the prior six months, received injections (Botox or Dysport).
2. Must be at least 19 years of age.	2. Had infections or sores due to pressure.
3. At least one year after the injury.	3. Had severe spasticity and/or contracture of the muscles.
4. Subject with a cervical injury (C4-C8) and some voluntary control of the upper limb.	4. Had internal fixations at the site of the injury.
5. **U**nable to sit independently due to lack of trunk control; needs assistance in activities of daily living.	5. Those with transplants, including cardiac pacemakers and defibrillators.
6. Cooperative and with stable respiratory parameters.	6. Had received any kind of stimulation therapy or treatment.
7. Non-neuromodulated subjects.	7. Suffering from diseases such as asthma, hypertension, etc.

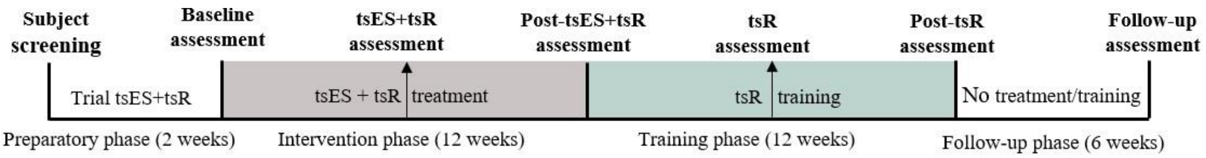


Figure 1: The outline of the study. The participants were enrolled and screened to ensure they were suitable for the research. After completing a baseline assessment, participants had two phases of therapy, each phase lasting 12 weeks, with two assessments completed every six weeks. Intervention phase: trans-spinal electrical stimulation (tsES) combined with task-specific rehabilitation (tsR), and Training phase: tsR alone. Six weeks following the completion of the tsR training period, assessments were repeated (follow-up).

2.2 Study protocols

2.2.1 Study design

This was a longitudinal cohort study and the participants were recruited through convenience sampling method. The study subjects participated in this research at different points of time; therefore, they were conveniently recruited based their availability. The study was categorised into four different phases. The first phase included two weeks of preparation training (trial) prior to the intervention (tsES+tsR), followed by a baseline assessment. During this phase the subjects were treated with different protocols to identify the individual's response to the stimulation. The frequency of 20 Hz to 30 Hz were tested on each individual. It was reported that stimulating at 30 Hz facilitates voluntary movement while at 15 Hz results in facilitation of tonic extensor activity specific for postural control [10]. During this period, their response to tsES was tested and optimal stimulation settings were also determined. The pain intensity scale (VAS) was used to record their response to the stimulation. After the placement of stimulating electrodes, the stimulation parameters were set and the intensity was gradually increased till the individual's maximum tolerance was reached. The participants were asked to experience the extension of the trunk (straightening of the spine) and an increase in the trunk stability in a seated position. Based on the individual participant's responses, he/she experienced the best trunk stability and tolerable intensity, then the stimulation parameters were set for each participant. They were stimulated for 15-20 mins during this phase to develop their endurance and tolerance to the stimulation. During this period, 3-4 sessions of intervention were delivered to let the participants understand and learn the tasks taught. Participants were observed and examined to determine whether or not they were eligible for this research during the initial stage, which is also known as the preparatory phase. In addition, this allowed the researcher to plan ahead of time and identify potential dropouts. The second phase consisted of a 12-week primary intervention. It included the use of tsES and tsR in combination. Later, for another 12 weeks, only tsR training was delivered, and this period was referred to as the training phase. In the last phase, also known as the washout phase, no training or treatment was provided for a period of six weeks, after which a follow-up assessment was conducted. The four phases of the study was demonstrated in Fig. 2.

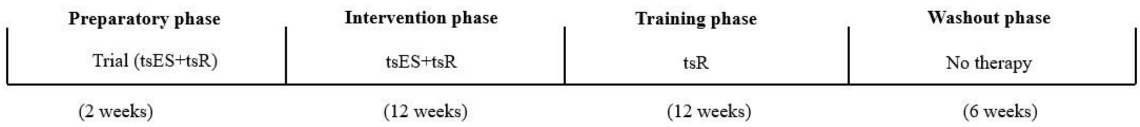


Figure 2: The study timeline was divided into four phases: Preparatory phase, Intervention phase, Training phase and Washout phase. (Trans-spinal electrical stimulation: tsES, Task-specific rehabilitation: tsR).

2.2.2 Intervention delivery

The frequency of intervention delivery was divided into three groups based on research participants' availability and schedules: (a) three sessions per week; (b) two sessions per week; and (c) one session per week. Each session lasted 45-60 minutes, divided into three 15-20-minute sub-sessions with a short break in between. The BP was measured repeatedly during the rest time. During the break, the stimulation was switched off. Once the training resumed after a rest, the intensity was gradually raised once again. SpO2 was also measured using a pulse oximeter on subjects with sudden changes in BP. Before starting the experiment, the individuals were instructed to empty their bladders or urine bags. In total, there were five participants, with three subjects attending three sessions per week and the other two subjects attending either two sessions or one session per week. Each week, participants P1, P2 and P4 attended three sessions, whereas P3 and P5 attended one session and two sessions, respectively. The subject was always accompanied by a physiotherapist to assure their safety.

2.2.3 tsES stimulation protocol

The 12th free rib was palpated and followed to identify the T11 and T12. Similarly, the iliac crest was palpated and followed till posterior superior iliac spine to reach L1 and L2. As illustrated in Fig. 3, the stimulation electrodes were positioned between T11-T12 and L1-L2 spinous processes in the middle, targeting the spinal cord (hereinafter called T11 and L1 electrodes), while referencing electrodes were put above the iliac crests on both sides. For the active electrodes, we utilized a pair of self-adhesive electrodes with a size of 3.2 centimeters (ValuTrode, Axelgaard Manufacturing Co. Ltd., USA) and another pair of internally linked 6.0 x 9.0 centimeter self-adhesive rectangle shape electrodes (Guangzhou Jetta Electronic Medical Device Manufacturing Co. Ltd., China) as ground electrodes. Before applying the electrodes, we used an alcohol swab to wipe the skin area where the stimulation would be applied. A cold cream was given to the same region following the stimulation in an effort to keep the skin from becoming too dry afterwards. The T11 and L1 region of the research participants were stimulated using two specifically designed constant current stimulators (DS8R, Digitimer, UK). In order to activate the stimulators, a function generator (AFG1022, manufactured by Tektronix, Inc.) was used that produced a burst of 10 kHz, which was transmitted at a frequency of 20–30 Hz. The burst configuration was raised to 10 biphasic pulses (1.06 msec. burst duration, henceforth referred to as 1 msec.) and the pulse lengths of each cycle were maintained constant at 50 µsec for both devices. The tsES was administered at an intensity of 95–115 milliamperes (mA), depending on the participant's response. The optimal stimulation paradigm maximizes intended motor performance while being pleasant for the person, which may be accomplished by carefully adjusting the electrical stimulus delivery parameters [187]. The previous study demonstrated that stimulation of the rostral portion of the lumbosacral enlargement (corresponding approximately to the T11-T12 vertebral level) at a frequency of 30 Hz is more specific for facilitating voluntary movements, whereas stimulation delivered over the caudal area of the lumbosacral enlargement (corresponding approximately to the L1-L2 vertebral level) at a frequency of 15 Hz results in facilitation of tonic extensor activity specific for postural control [10]. Therefore, the current study used the following protocol for placing electrodes. In the preparatory phase, stimulator settings were investigated and adjusted depending on the tolerability of the participants, who were able to perceive increased trunk stability with minimum assistance. The stimulation settings were also maintained constant during the training period. The physiotherapist was on hand to offer help needed at any time and the participants anytime were constantly watched to prevent falls

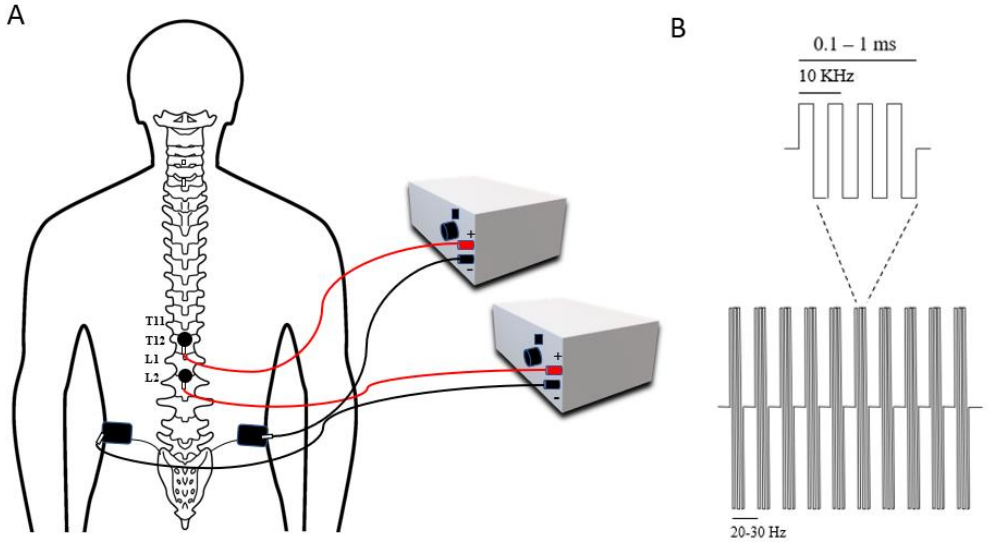


Figure 3: (A) Illustrates tsES active electrodes below T11 and L1 (real red) levels, with referencing electrodes typically positioned on both iliac crests. (B) Typical tsES signal generated at a frequency of 20–30 Hz with a pulse width of 0.1–1 ms modulated at a frequency of 10 kHz biphasic stimulation.

2.2.4 tsR training protocol

The tsR activities included spinal mobility exercises such as flexion, extension, lateral flexion, and rotation, as well as static and dynamic seated balancing exercises. The individuals were trained in a variety of experimental settings and positions, ranging from sitting in a wheel chair to lying in a bed to lying on a floor mat, with the help and supervision of a physiotherapist. They were assigned specific activities and were required to complete them ten to fifteen times, with three repetitions in each sub-session. The participants were first trained on their own wheelchairs. They were then moved to a floor mat to practise segmental and log rolling of the trunk. Later, after improving trunk control and static sitting balance, the participants were instructed to sit on the edge of the bed with or without their lower limbs supported on the floor.

Independent tsR training was conducted in a sitting position and included dynamic exercises. Additionally, the technique for transferring from a wheelchair to a bed and vice versa was shown using a transfer board. Every session includes a mirror to provide visual feedback and for proper training. An illustration of the tsR was given in Fig. 4.

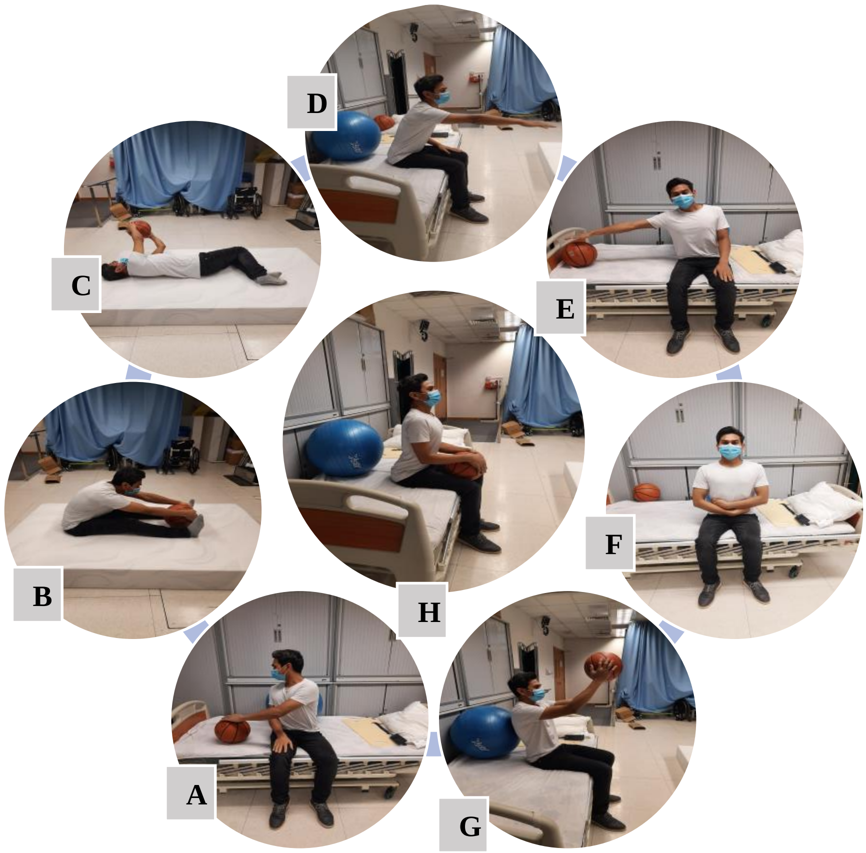


Figure 4: An illustration of task-specific rehabilitation training; (A) rotation to the right while sitting independently, with the left upper limb (U/L) supported over the thigh and the right U/L used for task completion; (B) trunk flexion with bilateral U/L support holding a medicine ball; (C) rolling to the left while holding a medicine ball with both U/L; (D) forward reaching with the right U/L and the left U/L supported over thigh; (E) lateral reaching to the right and left U/L supported over the thigh; (F) static siting practice with bilateral U/L placed over abdomen to avoid forward falls; (G) dynamic sitting practice with back supported by a swiss ball and both U/L lifting the medicine ball; and (H) trunk extension with medicine ball support placed over the thigh by bilateral U/L.

2.3 Outcome measures

The functional outcome measures were used to evaluate the strength and functional level of the participants who had difficulty with trunk and seated function. The 3-D ultrasound scan was used to assess changes in spinal curvature [188]. Additionally, movements in various planes were recorded using a kinematic motion capture system [100]. EMG was used to record the trunk muscles' motor evoked potentials [101]. The following is a list of the outcome measures used in this research:

2.3.1 Primary outcome measures

2.3.1.1 Modified Functional Reach Test (mFRT)

This test measures an individual's reaching ability by measuring the maximum distance reached with one upper limb in a specific direction while seated in a fixed position. The forward and lateral reach was measured through this functional tool. The ulnar styloid process was considered a landmark by study participants because tetraplegic individuals have trouble making a fist.

Experimental setup

The participant was seated in a wheel chair with his/her knees flexed at 90 degrees and feet placed together on a foot support. The side rails of the wheelchair were removed and the subject was instructed to maintain a neutral trunk posture without any back support. During the forward and lateral reaches, one hand was permitted to rest on the thigh while the other hand was stretched completely up to 90 degrees. The reading scale was attached to the wall, and the therapist stood nearby to ensure the participant's safety and provide guidance while they completed the task. Three successful trials were conducted, with the second and third repetitions being averaged for data analysis.

2.3.1.2 Trunk Control Test (TCT)

This test was used to assess trunk control and stability during a range of activities. It examines static and dynamic equilibrium, with the upper limbs involved in carrying out activities in dynamic equilibrium. Static sitting was tested by crossing the limbs over one another and in a neutral position. Similarly, rolling to both sides while performing dynamic activities with the upper limbs in the seated position indicated dynamic equilibrium. The overall score is 0–24, based on their performance, with the following scoring criteria: 0 = unable to accomplish the task, 1 = needs upper extremity's help to conduct the activity, 2 = able to finish the work without support. A higher score indicates improved performance.

Experimental setup

The subject was seated on the edge of the bed, with his/her feet resting on the floor. The participant was asked to sit independently and then instructed to do a series of dynamic tasks with their upper limb, with markers placed at specific distances with varied angles. Rest periods were scheduled at regular intervals to minimize fatigue.

2.3.1.3 Function in Sitting Test (FIST)

It measures the stability of a participant's equilibrium while sitting on the edge of the bed, considering sensory, motor, proactive, reactive, and steady state balance factors. It has a wide range of perturbation, reaching, and scooting-based activities that need dynamic control and balance in order to be accomplished. A score of 0–4 is assigned to each of the 14 items on the test. The lowest score indicates the need for total support, while the highest score reflects successful completion of the activity by oneself. The higher score indicates that there is a better dynamic sitting balance.

Experimental setup

The subject was sitting on the edge of the bed, feet flat on the floor. The participant was instructed to sit independently before being told to do a series of exercises showing static and dynamic sitting balance. The subjects were provided with objects that could be gripped with their hands, while those who lacked the correct grasp employed a tenodesis grasp to accomplish the tasks.

2.3.1.4 International standards for neurological classification of spinal cord injury (ISNCSCI)

The test consists of both motor and sensory examinations to assess sensory and motor levels on both the right and left sides, the neurological degree of damage, and the completeness of the injury.

Experimental setup

The subject was instructed to remain supine on the bed, wearing proper clothing. To test pin prick sensation, a sharp pin was utilized, whereas cotton was used for light touch. Similarly, the therapist examined the motor scores.

2.3.2 Secondary outcome measures

The electrophysiologic, kinesiologic, and radiologic assessments were carried out by these outcome measures:

2.3.2.1 Vicon motion capture system (VICON)

The motions performed during the assessment were recorded using an eight-camera three-dimensional (3D) motion capture system (Vicon Nexus 2.5.1, Vicon Nexus TM, Vicon Motion Systems Ltd., Yarnton, UK), maintaining a world error of between (maximum = 0.42, minimum = 0.23). A total of sixteen reflective markers were attached to the selected bony landmarks. Also, each motion was carried out on three successive trials. The placement of the VICON markers was shown in Fig. 5.

Markers placement

The following bony landmarks were designated using markers. Anteriorly, at the acromia, sternum, right and left anterior superior iliac spine (ASIS), and right and left patella; posteriorly, at the cervical spinous process (C7), thoracic spinous process (T3, T8, T12), lumbar spinous process (L2, L4), sacrum spinous process (S1), and right and left posterior superior iliac spine (PSIS) [10, 189].

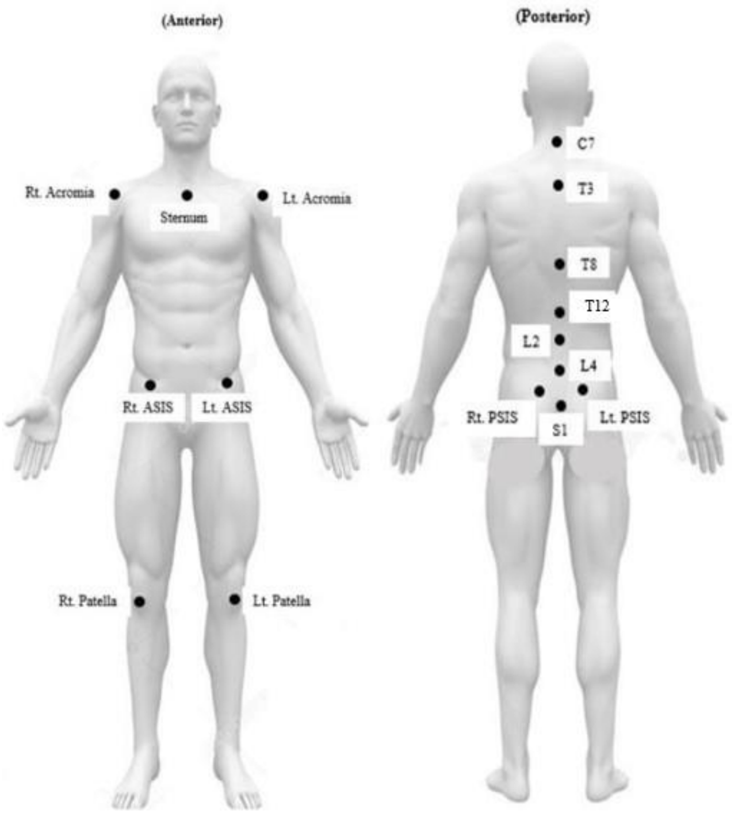
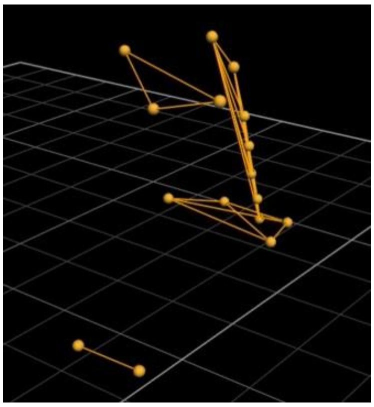


Figure 5: The placement of the VICON markers on anatomical landmarks in both anterior and posterior view to capture their motion during trunk movements. (Right: Rt, Left: Lt, Anterior superior iliac spine: ASIS, Posterior superior iliac spine: PSIS, Cervical spinous process: C7, Thoracic spinous process: T3, T8, T12, Sacrum spinous process: S1).

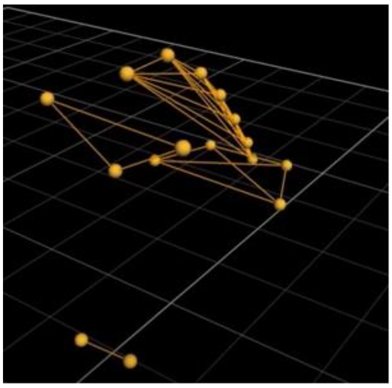
Procedure and movements performed

Prior to the assessment, the subject was positioned on the edge of the bed with both upper limbs resting on the thigh, hips, knees, and ankles flexed to 90 degrees, and feet flat on the floor. Then he/she subject was instructed to perform the guided movement and then return to the starting position. Moreover, the participant was required to complete the movement independently and with maximal voluntary contraction. The subject's upper limbs remained in their initial positions throughout the task and till its completion. Each activity was performed three times, and any change from the original position of the upper limbs was not counted. Likewise, a 30-second rest interval was allowed between two trials, followed by a 2-minute rest following each movement. The physiotherapist was there to prevent the subject from falling.

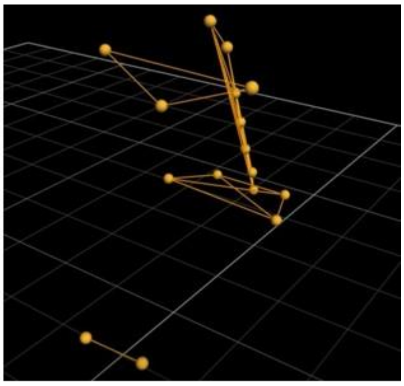
As demonstrated in Fig. 6, the trunk flexion (Fig. 6B) and extension (Fig. 6C) movements were performed to evaluate the participant's ability to reach and dynamic mobility, which plays an important role in preventing falls. Furthermore, the trunk lateral flexion to the right (Fig. 6D) and left (Fig. 6E) was conducted to measure their potential for transfer and scooting movement. Trunk rotations to the right (Fig. 6F) and left (Fig. 6G) were also performed to assess their ability to perform a variety of everyday activities with the assistance of their upper limbs.



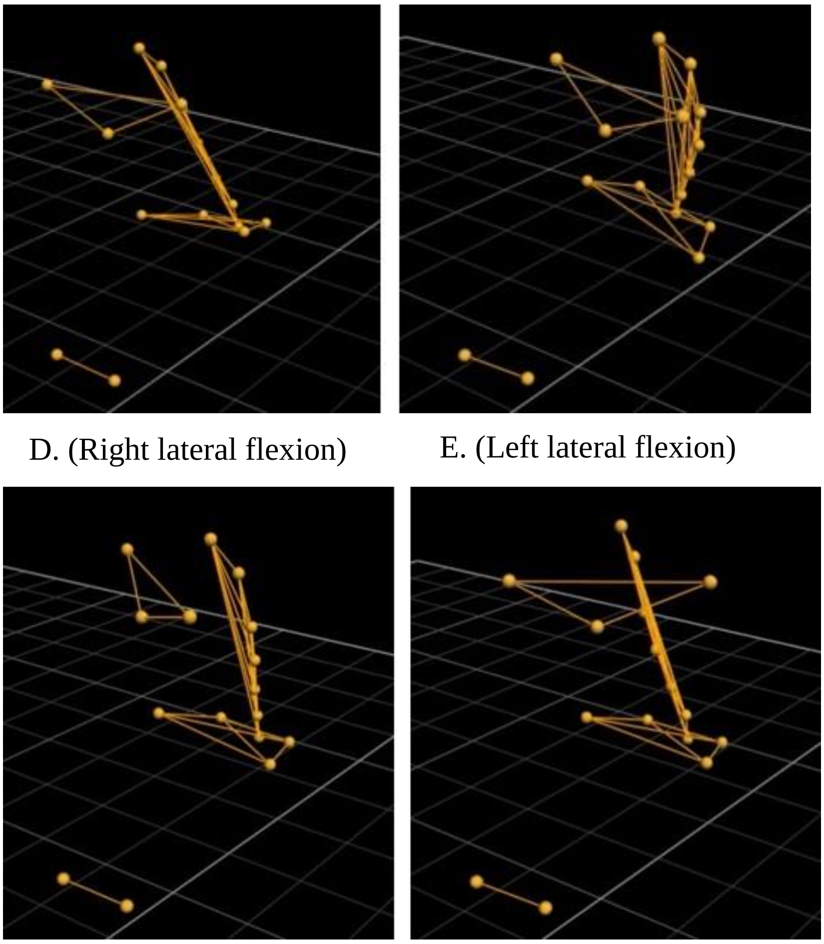
A. (Sitting in a normal erect posture with no movement)



B. (Flexion)



C. (Extension)



D. (Right lateral flexion) E. (Left lateral flexion)

F. (Right rotation) G. (Left rotation)

Figure 6: The trunk range of motions captured by the VICON motion capture system with the markers (yellow) placed at specified landmarks: (A) sitting in a normal erect posture with no movement; (B) flexion; (C) extension; (D) right lateral flexion; (E) left lateral flexion; (F) right rotation; and (G) left rotation.

2.3.2.2 Electromyography (EMG)

The responses of the relevant muscle groups were recorded using a 16-channel surface EMG (Model DE-2.1; Delsys USA, Inc., Boston, Massachusetts). Prior to the placement of the surface electrodes, the skin surface was cleansed using an alcohol sachet. VICON and EMG were used to capture trunk motions and muscle responses synchronously.

Electrodes placement

The responses of the superficial main muscles involved in trunk control and sitting function were recorded using the surface electrodes. The rectus abdominis (RA) and external oblique (EO) EMG responses were recorded anteriorly, while the erector spinae (ES) and latissimus dorsi (LD), EMG responses were obtained posteriorly. Signals were recorded from both the right and left sides. The RA electrodes were positioned five centimetres below the xiphoid process, while the EO electrodes were placed five centimetres superior to the ASIS and 10 cm lateral to the umbilicus. Similarly, the LD electrodes were attached 2 cm inferior and lateral to the scapula's inferior angle, while the ES electrodes were positioned 3 cm lateral to the L3 spinous process [190] (Fig. 7).

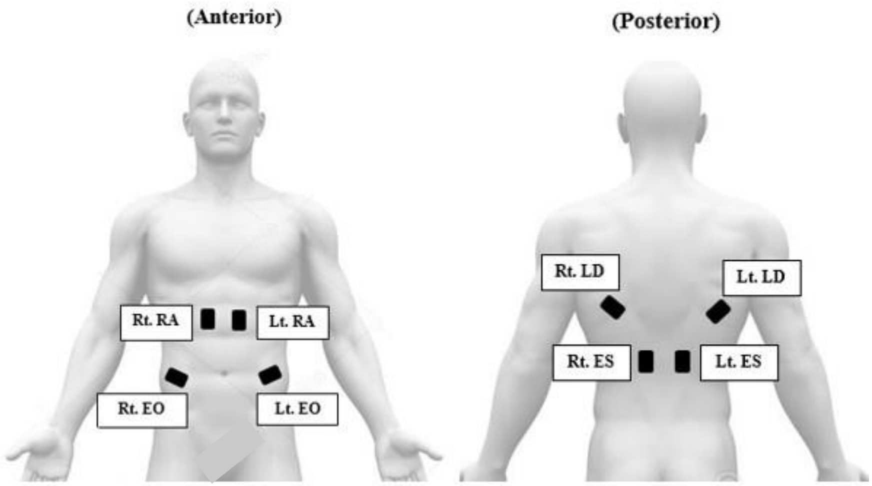


Figure 7: The EMG electrodes attached superficially over the targeted muscles to record their responses during trunk motions. (Right: Rt, Left: Lt, Rectus abdominis: RA, External oblique: EO, Latissimus dorsi: LD, Erector spinae: ES)

2.3.2.3 3D ultrasound scanning

3D ultrasound scanning was conducted to evaluate the changes in sagittal spinal curvature [188] before and after the end of the investigation. The duration between the two scanning was around 6 months. Moreover, the portable 3D (Scolioscan Air, SCN201, HKSAR) scanner was utilized to the scan participants. As the study participants were completely dependent on their wheel chairs and unable to sit in the specially designed scanning chair, they were scanned in the adjustable bed while they were seated on the edge and instructed to maintain an upright sitting posture with their best effort and upper limbs supported over their thighs. Their knees were positioned at 90 degrees, and their feet were placed flat on the floor in a neutral position. Each scan took around 50-60 seconds. Numerous scans were performed, and the best ones were selected for analysis. During the process, no external support was offered, and the physiotherapist stood near the subject to prevent him or her from falling and to observe the subject's fatigue status. The 3D ultrasound scanning setup was demonstrated in Fig. 8.

A B

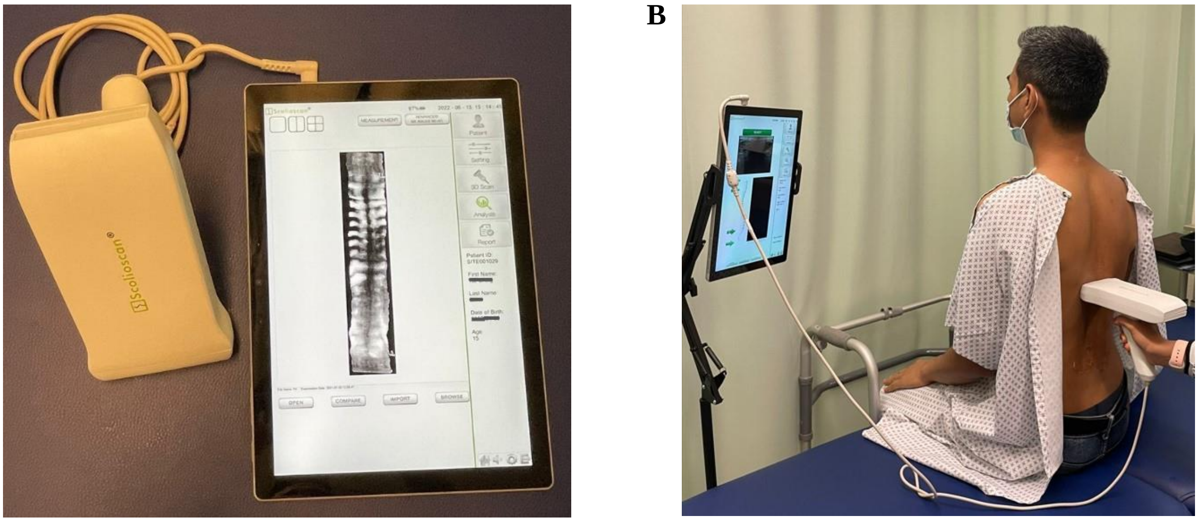


Figure 8: The 3D ultrasound scanning device and experimental setup. (A) Portable 3D ultrasound imaging used for scanning (B) scanning procedure with the subject seated on the edge of the bed, both feet on the floor, and upper limbs supported over the thigh while maintaining the best upright posture.

2.4 Data processing and analysis

The functional outcome scores were graphically and statistically analysed through GraphPad Prism version 9.0. Similarly, the kinesiologic and electrophysiologic data acquired from VICON and EMG were extracted, processed, and analysed through MATLAB (version 2016a, The MathWorks Inc., Natick, MA, USA). They were used to plot and analyse the trunk's angle, as well as to graph EMG activity recorded during each test. Fig. 9 (i-vi) illustrates the calculated trunk ROM for each individual motion connecting the selected landmarks. The angles were determined by connecting the body segments to the normal sitting position (Fig. 9-i), with erect sitting assumed to be a normal posture. The vertical line drawn relative to the truncal spine segment (Fig. 9, ii-b) shows the initial normal erect sitting position (Fig. 9, ii-a), with their best attempt by placing their upper limbs over their thighs.

Flexion (Fig. 9, ii-a,b,c) was defined as an axis connecting the cervical (C7), sacral (S1), and the mid-point between the two knees. Extension (Fig. 9, iii-a,b), on the other hand, was defined as an axis connecting the lumbar (L2), S1 and the mid-point between the both knees. Due to the C-shaped spinal curvature, maximum extension occurs at the lumbar region [165] and hence L2 was used to assess the extension. In addition, segments joining C7, L4 and the left posterior iliac spine (LPIS) were used to represent left lateral flexion (Fig. 9, iv-a,b), while segments linking C7, L4 and the right posterior iliac spine (RPIS) were adopted to represent right lateral flexion (Fig. 9, v-a,b). The axis joining the right acromia, also known as the right shoulder (RSHO), and the left acromia, also referred to as the left shoulder (LSHO), and its mid-point connecting the S1 segment with reference to the mid-line of both knees, defined the right and left trunk rotation (Fig. 9, vi-a,b,c). On the other hand, EMG responses were categorized according to the motions induced, and the primary muscles responsible for each movement were presented and their statistical values studied. The RA and LD muscles aid in trunk flexion, the EO and ES muscles assist in trunk lateral flexion, and the EO muscle helps in trunk rotation [61]. As a result, the responses of these specific muscles assisting specific trunk motions were analysed.

The normality and lognormality tests were performed to observe the normal and equal distribution of the data. Since, the sample size was smaller a non-parametric test was conducted. A Friedman one-way repeated measures of ANOVA was applied to compare the differences between the tsES+tsR, tsR, and follow-up. The root mean square (RMS) values of each muscle was calculated in micro-volt (μV) for EMG, and descriptive analysis was performed to calculate the average mean for each time period. In addition, a Spearman correlation analysis was performed to find out the correlation between the outcome measures. Again, the relative value analysis was conducted to show the percentage of improvement with reference to the corresponding baseline values, and the one-way repeated measures of ANOVA was used to determine the significant differences between the baseline, tsES+tsR, tsR, and follow-up. The VICON and EMG was assessed six weeks after tsES+tsR since the subjects were tetraplegic and lacked autonomous trunk control. Thus, after six weeks of intervention, the participant acquired some static control and was able to perform self-assisted movements, which served as baseline data. The VICON and EMG data was analysed at 6 weeks, 12 weeks, 24 weeks, and 30 weeks (referred to as baseline, tsES+tsR, tsR, and follow-up). Similarly, the scores of primary outcome measures were also analysed at 2 weeks, 12 weeks, 24 weeks, and 30 weeks (referred to as baseline, tsES+tsR, tsR, and follow-up). A *p* - value less than 0.05 was considered statistically significant.

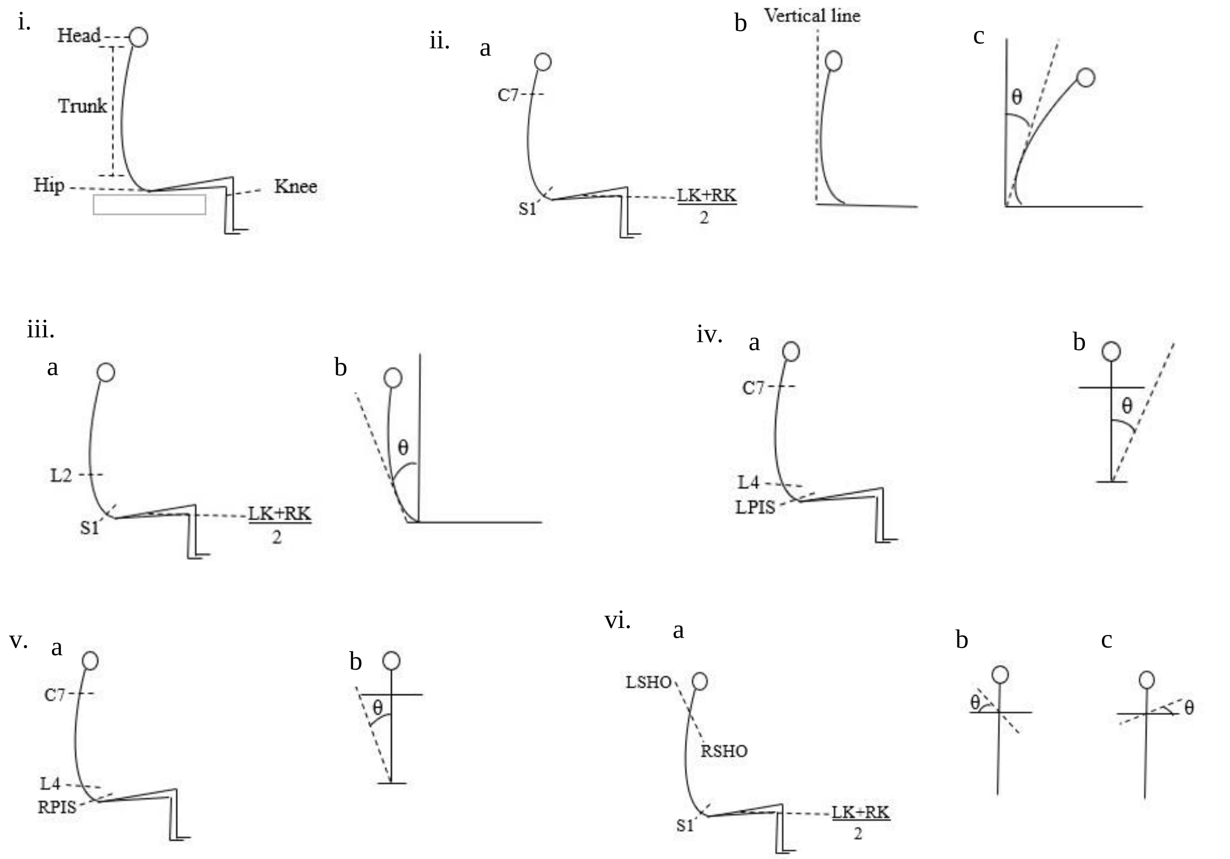
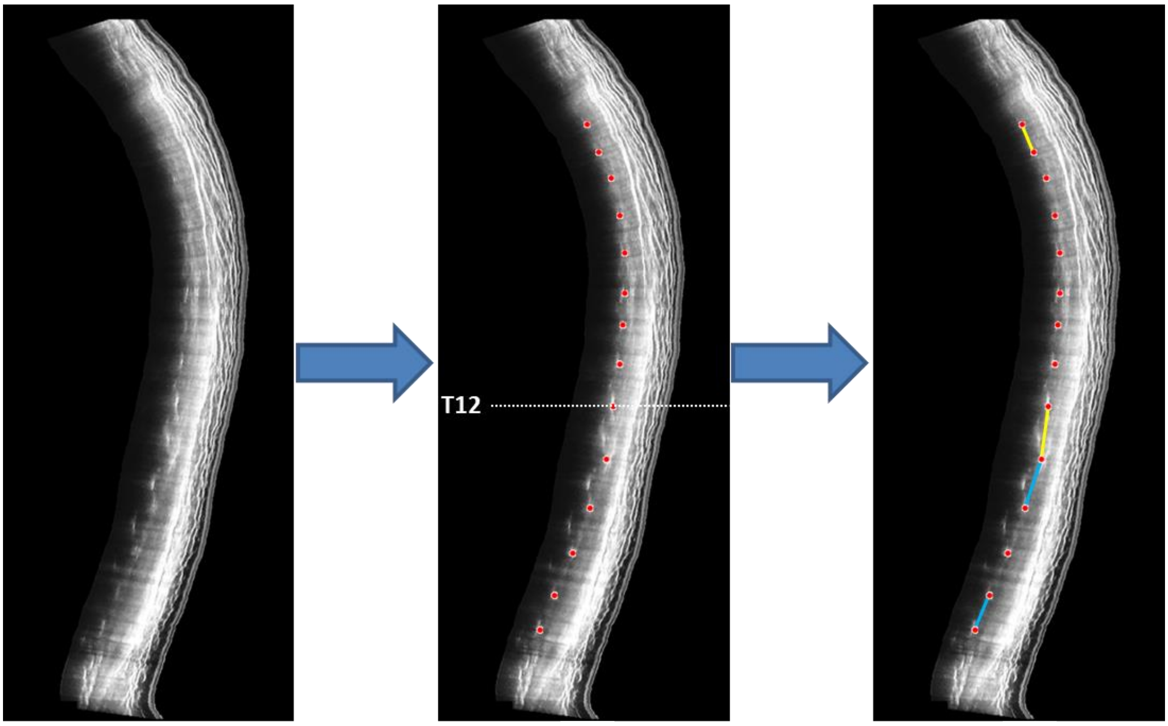


Figure 9: The detailed analysis process of VICON, by connecting selected markers at specific landmarks. (i) illustrates the erect sitting posture with knees 90 degrees flexed and feet flat on the floor (ii-a) segments C7, S1 and mid-line connecting left knee (LK) and right knee (RK), (ii-b) an axis connecting the C7, S1 segments with perpendicular line through the middle of the knees, (ii-c) flexion movement was performed, and angle measured in degrees (θ), (iii-a) segments L2, S1 and mid-line joining both knees (LK and RK), (iii-b) an axis connecting the L2, S1 segments with the perpendicular line through the middle of the knees, demonstrated the angle measured in degrees that was performed during extension of trunk, (iv-a) segments C7, L4 and left posterior iliac spine (LPIS) were used to measure left lateral flexion LLF, (iv-b) an axis joining the segments where LLF motion was performed and revealed through measured angle (θ), (v-a) segments C7, L4 and right posterior iliac spine (RPIS) were used to assess right lateral flexion (RLF), (v-b) an axis connecting the segments where RLF motion was performed and revealed through measured angle (θ), (vi-a) an axis joining the left shoulder (LSHO) and right shoulder (RSHO) with S1 segment meeting to a straight line drawn through the mid-point of bilateral knees, (vi-b) left rotation movement was performed and shown through measured angle (θ), (vi-c) right rotation motion was performed and revealed via measured angle (θ).

Moreover, each subject underwent 3D ultrasound scanning twice before and after intervention. After each scan, the 3D ultrasound volume file was transferred to the customized software for the manual generation of two sagittal images, which illustrated the left and right laminae of the spine, respectively (Fig. 10A). The Centre of laminae (CoL) from T4 to L5 level was identified from the bilateral sagittal images (Fig. 10B) and the corresponding coordinates were extracted using Image J (ver. 1.49, National Institutes of Health, USA). Thoracic kyphosis was acquired using the coordinates of T4, T5, T11 and T12 CoL, whereas lumbar lordosis was acquired using the coordinates of T4, T5, T11 and T12 CoL, from both left and right sagittal images, respectively. Thoracic kyphosis was defined as the angle formed between the line T4 and T5 coordinates and the line joining T11 and T12 laminae; whereas lumbar lordosis was defined as the angle formed between the line L1 and L2 coordinates and the line joining L4 and L5 laminae (Fig. 10C). The ultimate kyphosis and lordosis values reported were the averaged values obtained from the bilateral sagittal images. Generation of the sagittal ultrasound images and the evaluation of the sagittal angles were performed by an experienced researcher with more than 5 years of experience in studying the human spine using 3D ultrasound. The reliability and validity of the sagittal angle measurement had been demonstrated in a previous study [188].



A **B** **C**

Figure 10: (A) Ultrasound sagittal images of the spine; (B) Locations of the laminae were identified and the corresponding coordinates were extracted for computation of the sagittal curvatures (T12 level is indicated by the white dotted line); (C) Thoracic kyphosis was defined as the angle formed between the line T4 and T5 coordinates and the line joining T11 and T12 laminae (yellow); whereas lumbar lordosis was defined as the angle formed between the line L1 and L2 coordinates and the line joining L4 and L5 laminae (light blue) [179, 191].

Chapter 3 Results

3.1 Demographic and clinical characteristics of the participants

As shown in Table 2, the mean age of the participants was 42 years (SD = 13.72, range: 26-57), and the mean time since injury was 9.3 years (SD = 7.4, range: 1.5-19). Each participant had a traumatic complete cervical SCI with AIS-A category. The classification and level of injury varied among cervical injuries (C4-C7). There was a total of five participants, three of them were female and two of were male.

3.2 International standards for neurological classification of spinal cord injury (ISNCSCI)

According to Table 3, there were no significant changes in the Neurological Level of Injury (NLI), the American Spinal Injury Association impairment scale (AIS), or the motor level (right/left) during the administration of tsES+tsR. Moreover, after twelve weeks of tsES+tsR stimulation, the ISNCSCI sensory scores (Fig. 11) of P1 and P3 participants changed. The sensory scores from both the right and left sides were added together and presented as a total of 112 points. In addition, the sensory scores increased by 4 points to 18 points during the tsES+tsR phase and remained relatively stable during the tsR training and the follow-up. The P1 revealed an elevation of 8 points and 18 points in response to light touch and pin prick sensations (68/64 to 76/82), respectively, while the P3 showed a 4-point increase in response to pin prick sensation (64/64 to 64/68). Even after the tsR training and follow-up period, the increased motor and sensory scores remained unchanged. However, throughout the study period, there were no changes in ISNCSCI scores for P2, P4, or P5 (Fig. 11).

Table 2: The demographic and clinical characteristics of the participants.

Participants	Age	Gender	Time since injury (years)	Type of injury	NLI	AIS category
P1	57	F	1.5	Traumatic	C6	A
P2	55	F	19	Traumatic	C7	A
P3	26	F	12	Traumatic	C5	A
P4	40	M	12	Traumatic	C5	A
P5	32	M	2	Traumatic	C4	A

Table 3: The ISNCSCI classification of the participants.

Participants	P1	P2	P3	P4	P5
NLI, AIS					
Motor Level Right/Left					
Baseline	C6/A	C7/A	C5/A	C4/A	C5/A
	C6/C6	C8/C7	C6/C5	C5/C5	C6/C5
tsES+tsR	C6/A	C7/A	C5/A	C4/A	C5/A
	C6/C6	C8/C7	C6/C5	C5/C5	C6/C5
tsR	C6/A	C7/A	C5/A	C4/A	C5/A
	C6/C6	C8/C7	C6/C5	C5/C5	C6/C5
Follow-up	C6/A	C7/A	C5/A	C4/A	C5/A
	C6/C6	C8/C7	C6/C5	C5/C5	C6/C5
Light touch/Pin prick					
Baseline	68/64	40/34	64/64	28/30	22/21
tsES+tsR	**76**/**82**	40/34	64/**68**	28/30	22/21
tsR	**76**/**82**	40/34	64/**68**	28/30	22/21
Follow up	**76**/**82**	40/34	64/**68**	28/30	22/21

ISNCSCI: International standards for neurological classification of spinal cord injury; NLI: Neurological level of injury; AIS: American Spinal Injury Association impairment scale; Light touch and pin prick sensation (each 0 – 112 points). (Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U)

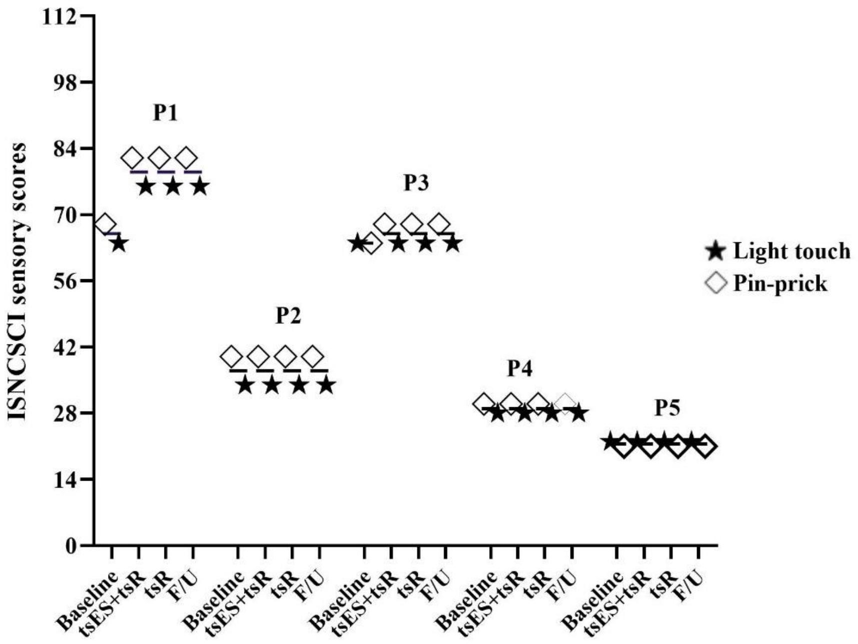


Figure 11: The ISNCSCI scores with light touch and pin-prick sensory sub-scores obtained in this study. (International standards for neurological classification of spinal cord injury: ISNCSCI, Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, Participant: P)

3.3 Modified Functional Reach Test (mFRT)

The mFRT scores have been described as a series of forward and lateral reaching movements with participants sitting in a wheel chair. As illustrated in Fig. 12A, when tsES+tsR was delivered from the baseline (3 cm), the maximum forward reach distance (FRD) increased by 16 cm during a 12-week period (19 cm) in P1, and further increased by 2.5 cm during the tsR (21.5 cm). Similarly, P2 demonstrated an increment of 13 cm throughout the intervention period (17 cm) compared to baseline (4 cm) and an additional 2 cm during the tsR (19 cm). Additionally, P3, P4, and P5 showed increases in FRD of 11.5 cm, 5 cm, and 6 cm, respectively, during the tsES+tsR, followed by 1.5 cm, 1 cm, and 0.5 cm increments during the tsR. At baseline, the FRD for P3, P4, and P5 was 2 cm, 1 cm, and 0 cm, respectively, indicating that they had very little static sitting control or were only able to maintain a neutral upright sitting posture. Again, for P2, P3, and P5 participants, very small decrements, i.e., by 0.5 cm, were observed over the follow-up period. As shown in Table 4, the overall mean ± SD for FRD was 2.0 ± 1.58 cm (range: 0.0-4.0) at baseline, but increased by 10.3 ± 4.54 cm after tsES+tsR (12.3

± 6.12 cm, range: 5.0-19.0). A 1.4 ± 0.72 cm increment in FRD was achieved during tsR (13.7 ± 6.84 cm, range: 6.0–21.5), which was maintained throughout the follow-up period in the absence of any intervention (13.4 ± 6.85 cm, range: 6.0–21.5). The FRD (Fig. 12B) revealed a significant relationship between baseline and tsES+tsR (p = 0.01), tsR (p = 0.01), and follow-up (p = 0.02), respectively.

On the other hand, the maximum right lateral reach distance (RLRD) increment in P1 (Fig. 12C) was 5.5 cm after 12 weeks of tsES+tsR administration (6.5 cm) compared to the baseline (1 cm), and increased further by 2 cm during the tsR delivery (8.5 cm). P2 also exhibited a 6 cm increase in RLRD during the intervention period (8 cm) compared to the baseline (2 cm), and an additional 1.5 cm increase during tsR (9.5 cm). Moreover, P3, P4, and P5 demonstrated 2 cm, 2 cm, and 3 cm increases in RLRD during the tsES+tsR phase, followed by 1.5 cm, 0.5 cm, and 0.5 cm increments during the tsR phase, respectively. At baseline, the RLRD for P3, P4, and P5 was 0.5 cm, 1 cm, and 0 cm, respectively, indicating that individuals could reach laterally with the greatest amount of difficulty. During the follow-up period, participant P2 had a reduction of 0.5 cm, participant P3 had a decrease of 1 cm, and participants P4 and P5 had a decline of 0.5 cm. The overall mean ± SD for RLRD (Table 4) was 0.9 ± 0.74 cm (range: 0.0-2.0) at baseline, which increased by 3.7 ± 1.84 cm after the introduction of tsES+tsR (4.6 ± 2.58 cm, range: 2.0-8.0). For the tsR training period (5.8 ± 3.03 cm, range: 2.5-9.5), RLRD increased by 1.2 ± 0.45 cm and then reduced to 5.7 ± 2.99 cm (range: 2.0-9.5), during the follow-up period. The RLRD (Fig. 12D) showed a significant relationship between baseline and tsES+tsR (p = 0.03), tsR (p = 0.03), and follow-up (p = 0.03), respectively.

The greatest increase in left lateral reach distance (LLRD) was found in P1 and P2 (Fig. 12E) after the introduction of tsES+tsR (5.5 cm and 6 cm, respectively), compared to the baseline (1.5 cm and 2 cm, respectively), which increased further by 1 cm and 0.5 cm throughout the tsR training period (6.5 cm and 6.5 cm, respectively). The LLRD for P3 was shown to be enhanced by 2.5 cm when tsES+tsR (3 cm) was delivered baseline (0.5 cm), and after the tsR period, another 1 cm increase was observed (4 cm). Similarly, P4 and P5 had a 2 cm and a 2.5 cm increment in LLRD during tsES+tsR (2 cm and 3.5 cm) administration, which remained unchanged during tsR (2 cm and 3.5 cm). For the LLRD of the follow-up period, P1 was decreased by 0.5 cm and P2 increased by 0.5 cm, while P3, P4, and P5 remained unchanged. The overall mean ± SD for LLRD (Table 4) was 1.0 ± 0.79 cm (range: 0.0-2.0) at baseline, which was increased by 3.0 ± 0.9 cm after the intervention period (4.0 ± 1.69 cm, range: 2.0-6.0), and increased by 1.5 ± 0.27 cm throughout the tsR training phase (4.5 ± 1.96 cm, range: 2.0-6.5), then remained constant during the follow-up period (4.5 ± 2.0 cm, range: 2.0-7.0). The LLRD (Fig. 12F) showed a significant relationship between baseline and tsES+tsR ($p < 0.01$), tsR ($p < 0.01$), and follow-up ($p < 0.01$), respectively.

Table 4: The Modified Functional Reach distances of participants.

Study timeline	**Forward reach (cm)** Mean ± SD	Min-Max	**Rt. Lat. reach (cm)** Mean ± SD	Min-Max	**Lt. Lat. reach (cm)** Mean ± SD	Min-Max
Baseline	2.0 ± 1.58	0.0-4.0	0.9 ± 0.74	0.0-2.0	1.0 ± 0.79	0.0-2.0
tsES+tsR	12.3 ± 6.12	5.0-19.0	4.6 ± 2.58	2.0-8.0	4.0 ± 1.69	2.0-6.0
tsR	13.7 ± 6.84	6.0-21.5	5.8 ± 3.03	2.5-9.5	4.5 ± 1.96	2.0-6.5
Follow-up	13.4 ± 6.85	6.0-21.5	5.7 ± 2.99	2.0-9.0	4.5 ± 2.0	2.0-7.0

(Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat)

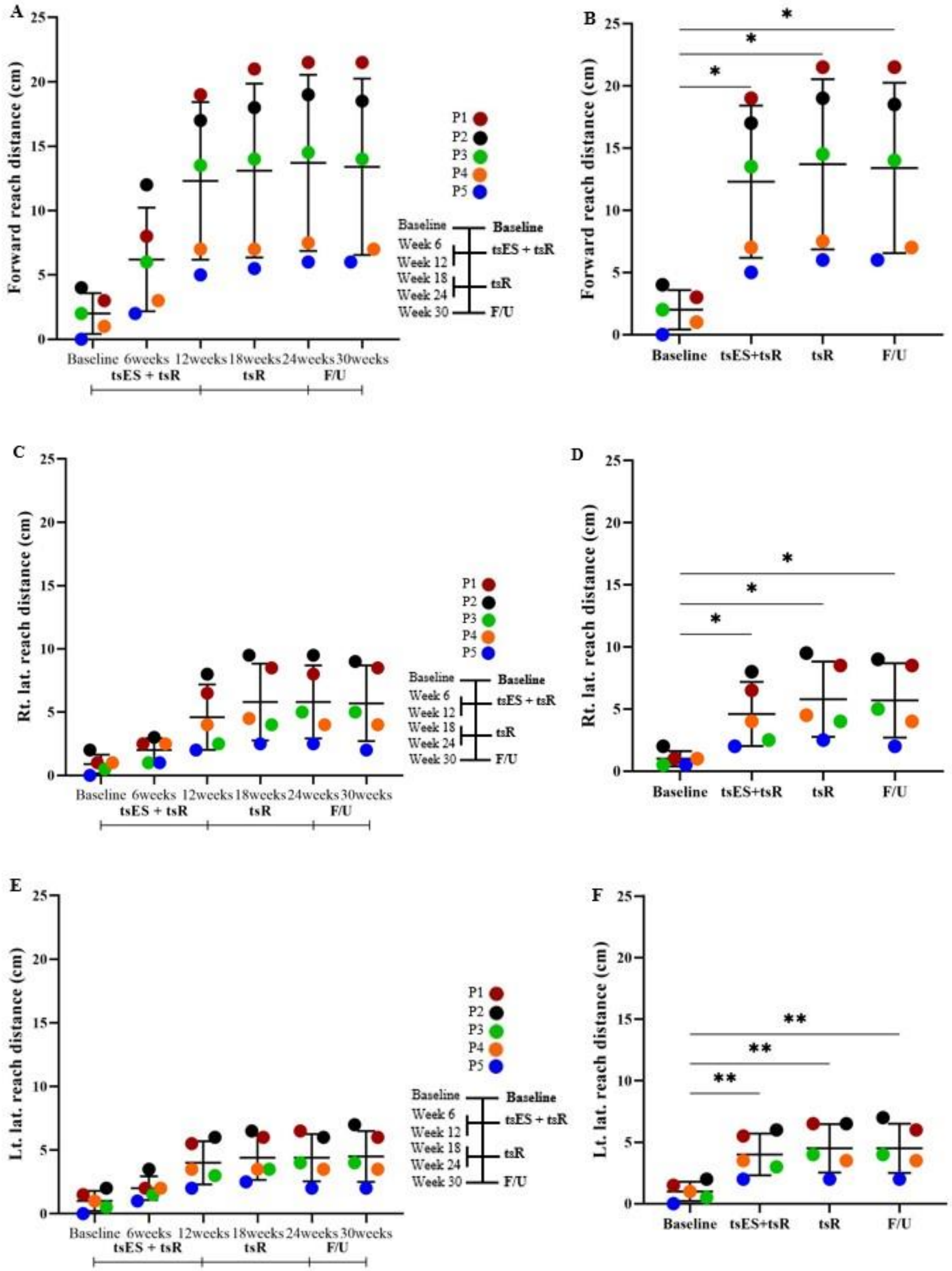


Figure 12: (A, C and E) Forward reach distance, right lateral reach distance and left lateral reach distance respectively, recorded for each participant during the study (B, D and F). Statistical significances were found between baseline and tsES+tsR*, tsR* and F/U*. (Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, ∗ $p < 0.05$, ∗∗ $p < 0.01$, ∗∗∗ $p < 0.001$).

3.4 Trunk Control Test (TCT)

As shown in Fig. 13A, P1, P3, and P5 all had baseline TCT scores of 3 points, whereas P2 had a score of 4 and P4 had the lowest score of 2 out of 24 points. This suggests that all individuals had only a very limited amount of trunk control and were hardly able to control their trunk independently. A significant increase in TCT scores was seen across all the subjects following the administration of tsES+tsR for 12 weeks. P1 demonstrated an increase of 10 points (3/24 to 13/24), whilst P2 showed an increment of up to 12 points (4/24 to 16/24) in the TCT score after the treatment. This indicates that the subjects obtained improvement in their trunk control abilities. Similarly, P3 (3/24 to 12/24), P4 (2/24 to 7/24), and P5 (3/24 to 10/24) showed an increase of 9 points, 5 points, and 7 points in their individual scores. After the intervention period, participants P1 and P2 were also able to do several of the activities with their upper extremities exhibiting dynamic trunk balance. In addition, during tsR, a 3-point increase in the TCT score was seen in P1 (16/24) and a 2-point increment in P2 (18/24) and P3 (14/24), respectively. P5 had an elevation in score of 1 point (11/24), but P4 showed no change in TCT score throughout the tsR period. On the other hand, the follow-up period revealed that participants P2, P3, and P4 sustained their TCT scores despite the absence of any intervention or training. P1 had a 2-point drop in TCT score, while P5 showed a 1-point increase after follow-up. As demonstrated in Fig. 13B, the overall mean ± SD for TCT scores was 3.0 ± 0.70 at baseline, which increased to 11.6 ± 3.36 after 12 weeks of tsES+tsR administration. It was raised again by 1.4 ± 1.11 during the tsR, 13.0 ± 4.47. Moreover, a slight reduction of 0.2 ± 0.39 was observed throughout the follow-up period (12.8 ± 4.08). TCT score analysis revealed a significant relationship between baseline and tsES+tsR ($p < 0.01$), tsR ($p = 0.01$), and follow-up ($p < 0.01$).

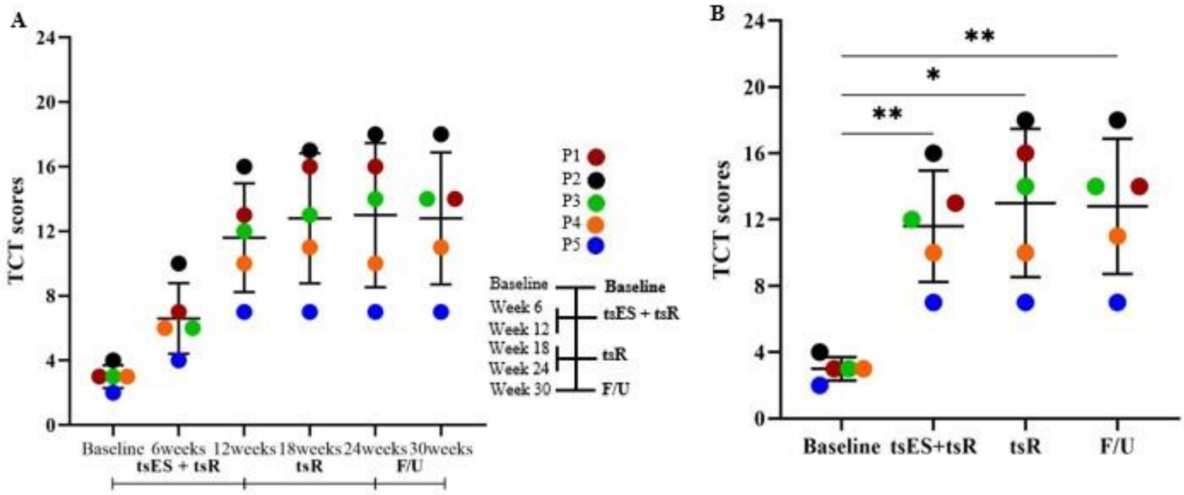


Figure 13: (A) Trunk Control Test score (each 0 - 24 points) measured for each participant during the study (B) Statistical analysis between baseline and tsES+tsR**, tsR*, and F/U** revealed a significant difference. (Trunk Control Test: TCT, trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

3.5 Function in Sitting Test (FIST)

As shown in Fig. 14A, participants P1 and P2 had FIST scores of 15 and 18 points respectively, at the baseline, while P4 had a score of 6 points. Both P3 and P5 scored 12 points out of 56 points. This suggests that the majority of participants were reliant on others and required help to complete the activities while seated. Again, all the subjects demonstrated an increase in their FIST scores after the tsES+tsR intervention. P1 (15/56 to 34/56) and P3 (12/56 to 31/56) showed a big increase of 19 points in FIST score throughout this 12-week period, while P2 (18/56 to 38/56) presented the greatest increase of 20 points. Additionally, P4 (6/56 to 15/56) and P5 (12/56 to 27/56) revealed a rise of 9-point and 15-point in FIST score respectively. This indicated that participants could do their activities while sitting with upper extremity assistance and were also able to execute several tasks independently. Furthermore, following two weeks of tsR training, obvious increases in FIST scores were also observed among most of the participants. P1 (38/56) and P3 (34/56) showed an additional increment of 4 points and 3 points respectively, while P2 (40/56) and P4 (16/56) reported an increase of 2 points and 1 point in FIST scores. However, P5's FIST score did not change over this period. Moreover, following a six-week washout period during which no training or assistance was provided, P1 and P5 maintained a steady score. P2 and P3 had a minor decrease in FIST score of 2 points each, although P4 had an increase of two points. The overall mean ± SD for FIST scores (Fig. 14B) was 12.6 ± 4.45. The greatest increase (16.4 ± 4.35) was observed after 12 weeks of tsES+tsR administration (29.0 ± 8.80). After, another 12 weeks of tsR training, an additional rise in FIST scores of 2.0 ± 0.94 was recorded. A minor decrease of 0.4 ± 1.33 was observed in the absence of any intervention or training after the follow-up period (30.6 ± 8.41). Statistical analysis revealed a significant relationship between baseline and tsES+tsR ($p < 0.01$), tsR ($p < 0.01$), and follow-up ($p < 0.01$), respectively.

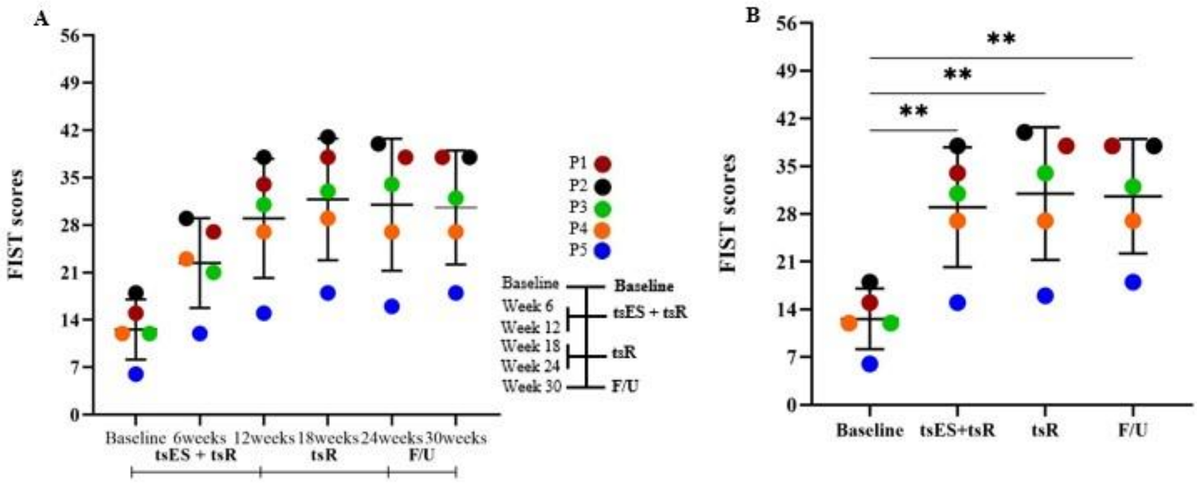


Figure 14: (A) Function in Sitting Test score (each 0 - 56 points) measured for each participant during the study (B) Statistical analysis between baseline, tsES+tsR**, tsR**, and F/U** revealed a significant difference. (Function in Sitting Test: FIST, trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

3.6 VICON motion capture system

The voluntary trunk range of motion (ROM) was shown to be increased throughout the tsES+tsR intervention delivery, including flexion, extension, right lateral flexion, left lateral flexion, right rotation, and left rotation. For the flexion (Fig.15A), the highest increase was 17.8° as demonstrated by P2, where the participant was able to perform the ROM of 36.35° after the delivery of tsES+tsR, compared to the baseline of 19.17°. P1 and P3 showed an increase in motion of 11.68° and 11.43° after the introduction of tsES+tsR with a maximum flexion of 25.82° and 23.51° respectively, in comparison to the baseline values of 14.14° and

12.08º. For P4 and P5, the corresponding values were 17.73º and 12.51º after the treatment of tsES+tsR, with increments of 10.23º and 4.12º, respectively. However, the tsR resulted in a modest decrease in ROM across all the subjects, which continued to fall over the follow-up period. Following completion of tsR training, P1 and P2 exhibited a 3.69º and 3.93º reduction respectively, which further dropped by 1.26º and 2.59º after the follow-up period. P3, P4, and P5 showed similar declines in motion of 2.45º, 1.26º, and 5.21º respectively, after 12 weeks of tsR followed by further decrease of 0.63º by P3 after the follow-up period. Interestingly, P4 and P5 showed elevations of 0.72º and 1.89º after 6 weeks of follow-up. As shown in Table 5A, the overall mean ± SD for flexion movement was 12.2 ± 4.71º (range: 7.5-19.1) at baseline, which increased to 23.1 ± 9.0º (range: 12.5-36.3) after the tsES+tsR administration. Then, a 3.7 ± 0.37º reduction in motion was seen after the tsR (19.4 ± 9.37º, range: 7.2-32.4), which was further reduced by 0.3 ± 1.69º after the follow-up period (19.1 ± 7.68º, range: 9.1–29.8) during which no intervention was administered. A significant relationship (Fig. 15B) was found between the results of the baseline and tsES+tsR (p = 0.01), and tsR (p = 0.03). However, no significant relationship between the baseline and follow-up was observed (p = 0.08).

According to Fig.15C, P2 achieved a maximum extension of 17.04º with an increase in motion of 8.17º after the tsES+tsR intervention, compared to the baseline of 8.87º, whilst P3 produced a greater increment of 10.19º and was able to extend the trunk to 16.79º in comparison to the baseline of 6.6º. Similarly, P1, P4, and P5 demonstrated an increase in ROM of 6.46º, 5.13º, and 3.19º after the tsES+tsR intervention with an extension of 11.81º, 9.77º, and 6.72º in comparison to the baseline 5.35º, 4.64º, and 3.53º, respectively. After the tsR, P1 and P2 (10.42º and 15.11º) exhibited a 0.49º and 1.93º reduction in extension, which was further lowered by 0.5º and 0.55º respectively, during the follow-up period (10.91º and 14.56º). Similarly, P3, P4, and P5 showed motion reductions of 1.15º, 0.95º, and 1.84º after 12 weeks of tsR, respectively, followed by a further reduction of 1.64º by P4, while P3 and P5 surprisingly experienced motion increments of 2.29º and 1.75º after 6 weeks of follow-up. It can be seen from Table 5A, that the overall mean ± SD for extension during the baseline was 5.7 ± 2.04º (range: 3.5-8.8), with an increase of 6.7 ± 2.44º after tsES+tsR delivery (12.4 ± 4.48º, range: 6.7-17.0). Furthermore, tsR (10.0 ± 4.03º, range: 4.1–15.1) demonstrated a 2.4 ± 0.45º decrease in extension, which was increased by 0.4 ± 0.13º on follow-up (10.4 ± 3.90º, range: 5.8–14.5). A significant relationship (Fig. 15D) was found between the baseline and tsES+tsR (p = 0.01), tsR (p = 0.02), and follow-up (p = 0.01), respectively.

For the right lateral flexion (RLF), P4 and P5 had a larger increase in ROM (Fig. 15E) of 5.78º and 4.9º after tsES+tsR administration (9.95º and 5.17º) respectively, compared to the baseline (4.17º and 0.27º). P1, P2, and P3 also demonstrated an increase in motion by 1.93º, 2.93º, and 0.82º after the intervention period (6.28º, 18.28º, and 5.99º), in comparison to the baseline (4.35º, 15.35º, and 5.17º), respectively. Similarly, RLF motion was shown to decrease in all the participants after the tsR training. In P1 and P2, the ROM was decreased to 6.09º and 17.62º after the tsR and further to 5.72º and 17.54º after the follow-up period. P3, P4, and P5 also showed a decrease in motion by 5.14º, 8.50º, and 5.03º, respectively after the tsR, but demonstrated an increase of motion by 1.58º, 0.11º, and 0.34º after the follow-up (6.72º, 8.61º, and 5.37º). According to Table 5B, the overall mean ± SD for RLF was 5.8 ± 5.63º (range: 0.2–15.3) at baseline, which increased to 9.1 ± 5.43º (range: 5.1–18.2) after the tsES+tsR delivery, while a 0.7 ± 0.14º reduction in motion was observed during tsR (8.4 ± 5.29º, range: 5.0-17.6), followed by an increase of 0.3 ± 0.24º after the follow-up period (8.7 ± 5.05º, range: 5.3-17.5) during which no intervention was administered. Statistical analysis revealed (Fig. 15F) a significant relationship between the RLF of baseline and tsES+tsR (p = 0.03). There was, however, no relationship in the RLF between baseline and tsR (p = 0.06), and follow-up (p = 0.08).

As shown in Fig. 15G, all the participants improved their left lateral flexion (LLF) after the tsES+tsR. For baseline, the LLF values for P1, P2, P3, P4 and P5 were 3.52º, 9.10º, 7.89º, 6.98º, and 2.60º which elevated to 7.18º, 12.92º, 11.02º, 11.72º, and 6.21º respectively after the tsES+tsR. P1 and P2 exhibited some degrees of motion reduction after the tsR (6.89º and 11.45º), which was further reduced by 1.02º in P1 and raised by 0.20º in P2 during the follow-up (5.87º and 11.65º). The LLF values of P3, P4, and P5 dropped to 10.10º, 9.60º, and 5.97º, respectively after tsR training, which further decreased to 9.95º, 8.13º, and 5.69º after 6-weeks of no intervention or training. The overall mean ± SD for LLF was 6.0 ± 2.82º (range: 2.6–9.1) at baseline and was raised to 9.8 ± 2.94º (range: 6.2–12.9) after the tsES+tsR (Table 5B). Then, it decreased to 8.8 ± 2.29º (range: 5.9–11.4) after the tsR delivery, and further dropped by 0.6 ± 0.29º on follow-up (8.2 ± 2.58º, range: 5.6-11.6). A significant relationship was found between the LLF of the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.01$), and follow-up ($p < 0.01$).

For the right rotation (RR), P1 and P2 increased their ROM (Fig. 15I) by 2.34º and 3.83º respectively, after the delivery of tsES+tsR (7.33º and 7.16º) compared to the baseline (4.99º and 3.33º). P3, P4, and P5 also exhibited an increase in RR by 2.65º, 1.27º, and 3.68º after the same treatment (2.74º, 1.31º, and 3.98º) compared to the baseline (0.09º, 0.04º, and 0.13º). The RR values of P1, P2, P3, P4, and P5 reduced to 5.10º, 5.36º,1.70º, 0.37º, and 2.57º after the tsR training, followed by a further reduction to 1.70º, 0.37º, and 2.57º in P3, P4, and P5, while P1 and P2 surprisingly showed increment to 6.03º and 6.21º respectively. The overall mean ± SD (Table 5C) for RR was 1.7 ± 2.30º (range: 0.04-4.9) at baseline, and increased by 2.8 ± 0.37º after the tsES+tsR intervention (4.5 ± 2.67º, range: 1.3-7.3). Similarly, a 1.51 ± 0.51º drop in RR was seen during tsR (3.0 ± 2.16º, range: 0.3-5.3), followed by an increase of 1.1 ± 0.27º on follow-up (4.1 ± 1.89º, range: 2.2-6.2). A significant relationship (Fig. 15J) was observed between baseline and tsES+tsR ($p = 0.01$), and tsR ($p < 0.01$), but not between the baseline and follow-up ($p = 0.10$).

It can be seen from Fig. 15K, that the greatest increase in left rotation (LR) was 28.46º in P4 and 25.29º in P2 after the administration of tsES+tsR (33.11º and 55.93º), respectively, in comparison to baseline (4.65º and 30.64º). P1, P3, and P5 also demonstrated an increase in ROM to 37.31º, 49.70º, and 22.13º, respectively, compared to the baseline (21.14º, 31.0º, and 4.74º). P3 had the greatest reduction in motion by 8.9º after the tsR training (40.80º), which was further reduced by 3.17º after follow-up (37.63º). Moreover, P1 and P2 experienced a slight decrease in motion by 2.06º and 1.86º after the tsR phase (35.25º and 54.07º respectively), which further showed decrease in motion after follow-up (35.22º and 38.18º). Similarly, P4 and P5 showed reductions of 5.7º and 2.7º, respectively, after the tsR, whereas P4 demonstrated an increase of 2.45º and P5 showed a decrement of 1.01º during the follow-up (29.86º and 18.42º). As shown in Table 5C, the overall mean ± SD for LR was 18.4 ± 13.15º (range: 4.6-31.0) at baseline, which increased by 21.2 ± 0.28º after the tsES+tsR intervention (39.6 ± 13.43º, range: 22.1-55.9), followed by a decrease of 4.3 ± 0.23º after the tsR (35.3 ± 13.20º, range: 19.4–54.1), and a reduction of 3.5 ± 5.0º during the follow up (31.8 ± 8.20º, range: 18.4–38.1). A significant relationship (Fig. 15L) was revealed between the LR of the baseline and tsES+tsR ($p < 0.01$), tsR ($p < 0.01$), and follow-up ($p = 0.03$).

Table 5: The trunk range of motion of the subjects measured through Vicon.

A

Study timeline	**Flexion (degrees)** Mean ± SD	Min-Max	**Extension (degrees)** Mean ± SD	Min-Max
Baseline	12.2 ± 4.71	7.5-19.1	5.7 ± 2.04	3.5-8.8
tsES+tsR	23.1 ± 9.0	12.5-36.3	12.4 ± 4.48	6.7-17.0
tsR	19.4 ± 9.37	7.2-32.4	10.0 ± 4.03	4.1-15.1
Follow-up	19.1 ± 7.68	9.1-29.8	10.4 ± 3.90	5.8-14.5

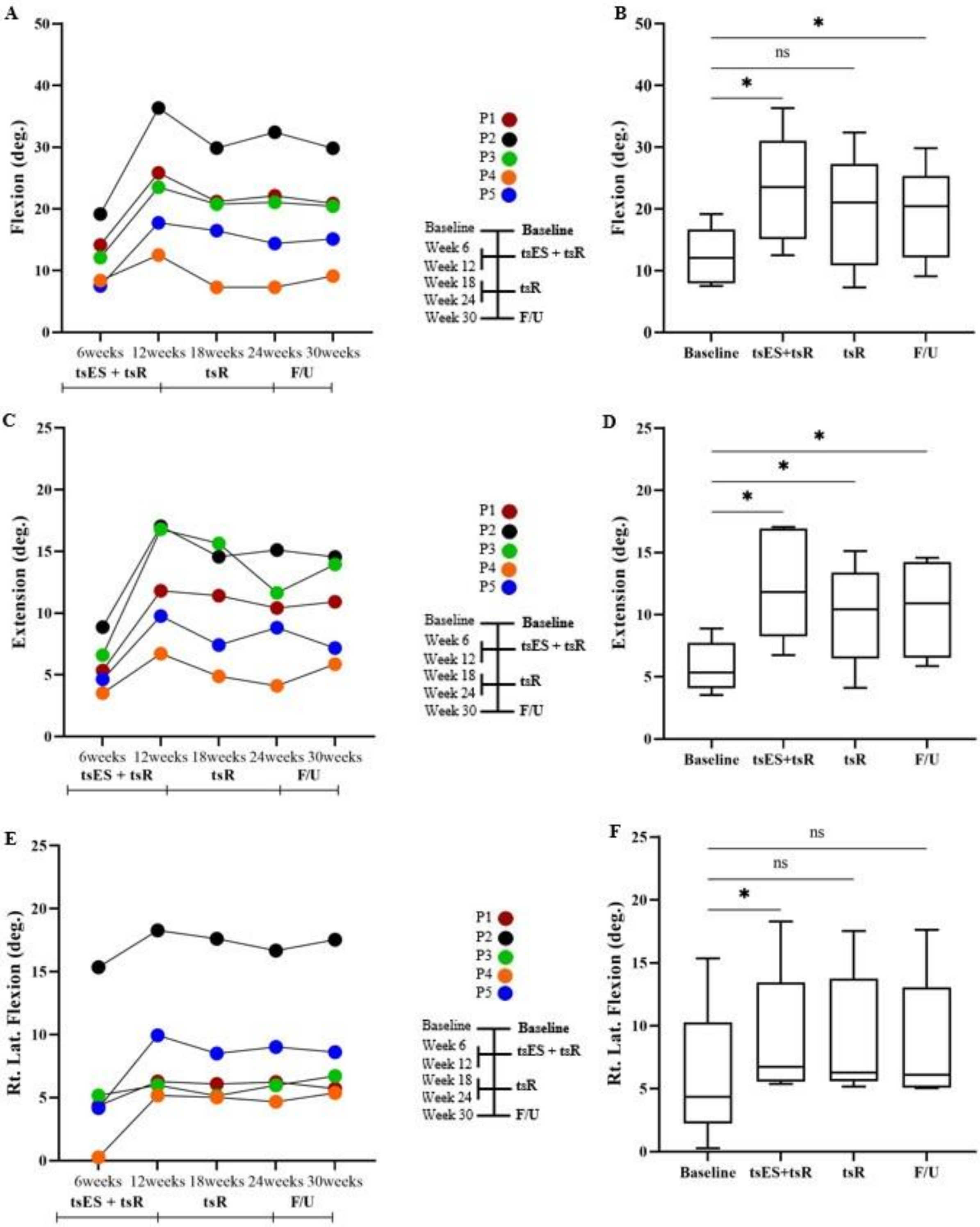
B

Study timeline	**Rt. Lat. Flexion (degrees)** Mean ± SD	Min-Max	**Lt. Lat. Flexion (degrees)** Mean ± SD	Min-Max
Baseline	5.8 ± 5.63	0.2-15.3	6.0 ± 2.82	2.6-9.1
tsES+tsR	9.1 ± 5.43	5.1-18.2	9.8 ± 2.94	6.2-12.9
tsR	8.4 ± 5.29	5.0-17.6	8.8 ± 2.29	5.9-11.4
Follow-up	8.7 ± 5.05	5.3-17.5	8.2 ± 2.58	5.6-11.6

C

Study timeline	**Rt. Rotation (degrees)** Mean ± SD	Min-Max	**Lt. Rotation (degrees)** Mean ± SD	Min-Max
Baseline	1.7 ± 2.30	0.04-4.9	18.4 ± 13.15	4.6-31.0
tsES+tsR	4.5 ± 2.67	1.3-7.3	39.6 ± 13.43	22.1-55.9
tsR	3.0 ± 2.16	0.3-5.3	35.3 ± 13.20	19.4-54.1
Follow-up	4.1 ± 1.89	2.2-6.2	31.8 ± 8.20	18.4-38.1

(Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, standard deviation: SD, minimum: min, maximum: max)


A
B
C
D
E
F
Flexion (deg.)
Extension (deg.)
Rt. Lat. Flexion (deg.)
P1
P2
P3
P4
P5
Baseline
Week 6
Week 12
Week 18
Week 24
Week 30
tsES + tsR
tsR
F/U
6weeks 12weeks 18weeks 24weeks 30weeks
Baseline tsES+tsR tsR F/U
ns
*

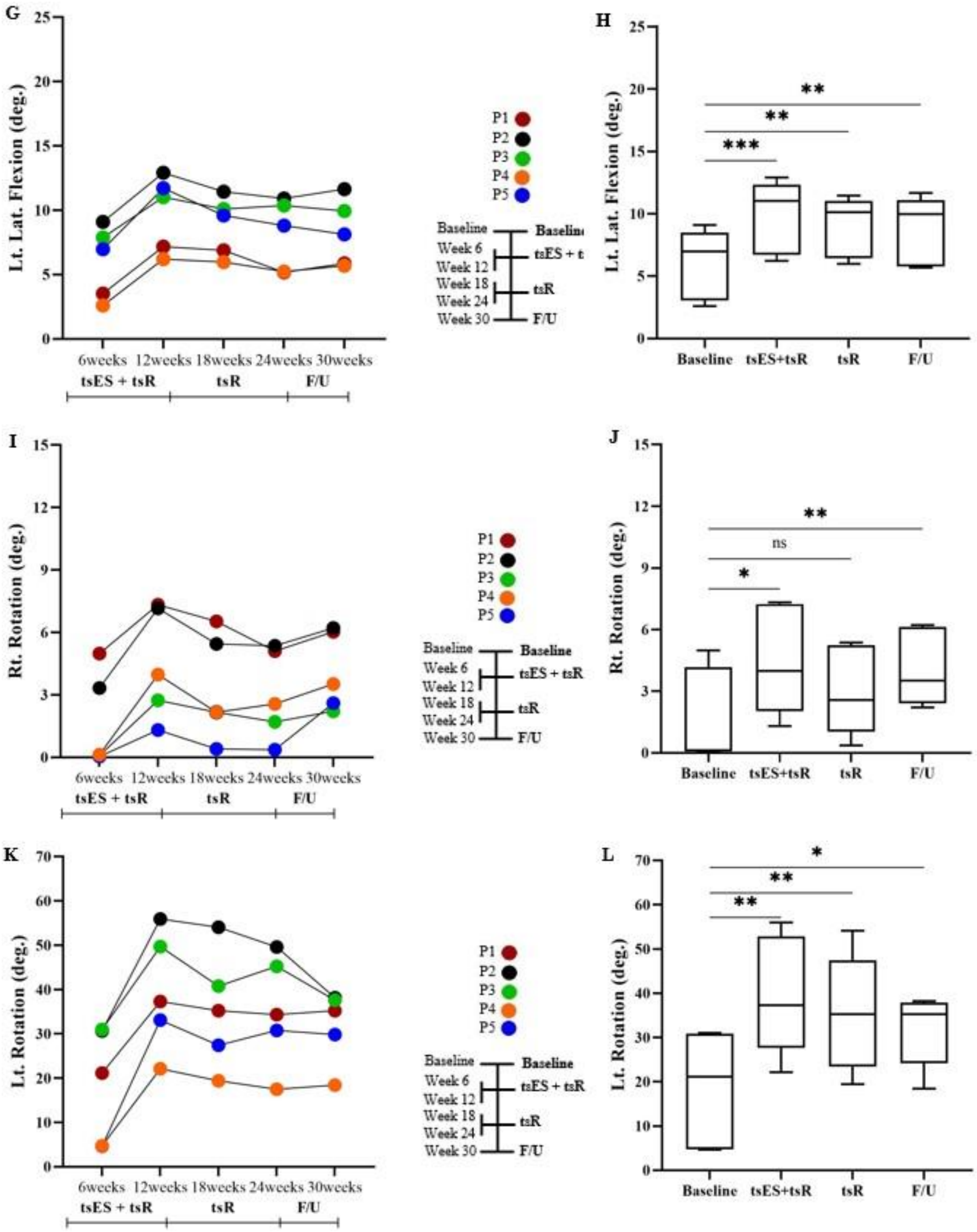


Figure 15: (A, C, E, G, I and K) Flexion, extension, right lateral flexion and left lateral flexion, right rotation and left rotation respectively, measured through Vicon motion capture system for each participant during the study; (B, D, F, H, J and L) Statistical significances were found between baseline and tsES+tsR*, tsR**, and F/U*. (Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, $*$ $p < 0.05$, $**$ $p < 0.01$, $***$ $p < 0.001$, ns: no significant difference)

3.7 Electromyography (EMG)

The EMG activity was shown to be increased after the tsES+tsR during all the trunk movements, i.e. flexion, extension, right lateral flexion, left lateral flexion, right rotation, and left rotation, respectively. For the flexion (Fig. 16A; Table 6A), the EMG responses was 2.65 ± 1.82 μV for Rt LD and 2.90 ± 1.85 μV for Lt LD at baseline, which increased to 6.54 ± 4.26 μV and 7.14 ± 4.49 μV after the tsES+tsR, respectively. However, it was slightly reduced to 4.82 ± 2.94 μV and 5.11 ± 2.76 μV after the tsR and remained almost unchanged at follow-up period (4.97 ± 2.90 μV and 5.15 ± 2.55 μV, respectively). It indicated that both (Rt LD and Lt LD) showed muscle activation during the flexion movement. A significant relationship was found for Rt LD between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). Similarly, the values of EMG for Lt LD also showed significant relationship between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). In addition, from the baseline, the Rt RA (0.66 ± 0.27 μV) and Lt RA (1.23 ± 0.56 μV) showed a little increment to 1.30 ± 0.60 μV and 2.27 ± 0.16 μV after the tsES+tsR. Interestingly, the EMG response was further increased to 1.39 ± 0.26 μV and 1.57 ± 0.32 μV after the tsR and stayed consistent at follow-up (1.39 ± 0.24 μV and 1.50 ± 0.30 μV, respectively). Statistical analysis revealed a significant relationship for Rt RA between baseline and tsES+tsR ($p < 0.01$), and tsR ($p < 0.001$). There was, however, no significant relationship between baseline and follow-up ($p = 0.08$). Similarly, a significant relationship was also found for Lt RA between the baseline and tsES+tsR ($p = 0.01$), tsR ($p < 0.001$), and follow-up ($p < 0.001$).

As demonstrated in Fig. 16B and Table 6B, during the trunk extension, the EMG responses increased significantly in both muscle groups (erector spinae and latissimus dorsi) after the tsES+tsR intervention. The EMG values of Rt ES (1.62 ± 0.95 μV) and Lt ES (1.79 ± 1.25 μV) from baseline was increased to 6.93 ± 6.32 μV and 7.53 ± 5.47 μV, respectively, after the tsES+tsR, followed by a decrement to 4.11 ± 2.68 μV and 4.57 ± 3.02 μV after the tsR, and remained unchanged at follow up (4.19 ± 2.58 μV and 4.69 ± 2.97 μV, respectively). A significant relationship was found for Rt ES between the baseline and tsES+tsR ($p = 0.03$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). Similarly, the values of EMG for Lt ES also showed a significant relationship between the baseline and tsES+tsR ($p = 0.02$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). In addition, the EMG response was 2.20 ± 1.60 μV for Rt LD and 2.57 ± 1.81 μV for Lt LD at baseline, then increased to 8.86 ± 6.04 μV and 9.94 ± 6.70 μV, respectively, after the tsES+tsR, which was further reduced to 5.01 ± 3.71 μV and 5.70 ± 4.86 μV after the tsR and remained almost unchanged at follow-up (5.02 ± 3.03 μV and 6.07 ± 4.45 μV, respectively). The EMG signals of both muscle groups indicated activation during the extension movement. Statistical significance showed a significant relationship for Rt LD between the baseline and tsES+tsR ($p < 0.001$), and tsR ($p < 0.001$). There was, however, no significant relationship between baseline and follow-up ($p = 0.10$). Similarly, a significant relationship was also found for Lt LD between the baseline and tsES+tsR ($p = 0.03$), tsR ($p = 0.04$), and follow-up ($p < 0.001$).

For the right lateral flexion (RLF) (Fig. 16C; Table 6C), the EMG responses was 2.0 ± 1.98 μV for Rt ES and 1.53 ± 1.64 μV for Lt ES at baseline, which increased to 6.89 ± 4.57 μV and 5.19 ± 2.76 μV after the tsES+tsR, respectively. However, it was slightly reduced to 6.33 ± 4.63 μV and 5.02 ± 3.07 μV after the tsR and remained consistent at follow-up period (6.43 ± 4.70 μV and 5.12 ± 2.86 μV, respectively). This indicated the activation of Rt ES and Lt ES during the RLF. Statistical analysis revealed a significant relationship for Rt ES between baseline and tsES+tsR ($p = 0.04$). There was, however, no significant relationship between baseline and tsR ($p = 0.06$) or follow-up ($p = 0.06$). Similarly, a significant relationship was also found for Lt ES between the baseline and tsES+tsR ($p = 0.01$), tsR ($p = 0.01$), and follow-up ($p = 0.01$). In addition, from the baseline, the Rt EO (1.96 ± 1.0 μV) and Lt EO (3.22 ± 2.09 μV) showed an increment to 3.24 ± 2.54 μV and 9.15 ± 6.71 μV after the tsES+tsR. Then, the

EMG response was further decreased to 3.11 ± 1.95 μV and 7.76 ± 5.37 μV and remained almost unchanged at follow-up (3.0 ± 1.84 μV and 7.77 ± 5.11 μV, respectively). A significant relationship was found for Rt EO between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). Similarly, the values of EMG for Lt EO also showed significant relationship between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). This indicated that Lt EO showed greater muscle activation than Rt EO during RLF.

As shown in Fig. 16D and Table 6D, both Rt ES and Lt ES had a significant increase in EMG response during left lateral flexion (LLF). The EMG values of Rt ES (1.40 ± 1.17 μV) and Lt ES (2.02 ± 1.70 μV) from baseline was increased to 5.32 ± 3.34 μV and 6.46 ± 4.38 μV after the tsES+tsR which was further increased to 5.69 ± 4.65 μV and 5.92 ± 4.68 μV after the tsR and was remained almost unchanged at follow up (5.53 ± 4.22 μV and 6.01 ± 4.62 μV, respectively). Statistical significance showed a significant relationship for Rt ES between the baseline and tsES+tsR ($p = 0.03$). There was, however, no significant relationship between baseline and tsR ($p = 0.11$) or follow-up ($p = 0.11$). Similarly, a significant relationship was also found for Lt ES between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). In addition, the EMG response was 1.10 ± 0.79 μV for Rt EO and 2.81 ± 2.60 μV for Lt EO at baseline, then increased to 2.06 ± 1.55 μV and 7.80 ± 5.64 μV, respectively, after the tsES+tsR, followed by a further increment to 2.36 ± 1.39 μV and a decrement to 7.11 ± 4.65 μV after the tsR and remained consistent at follow-up (2.34 ± 1.30 μV and 6.94 ± 4.61 μV, respectively). A significant relationship was found for Rt EO between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). Similarly, the values of EMG for Lt EO also showed a significant relationship between the baseline and tsES+tsR ($p = 0.02$), and tsR ($p = 0.02$), but not between the baseline and follow-up ($p = 0.05$).

As demonstrated in Fig. 16E and Table 6E, during the right rotation (RR), the EMG values of Rt EO (1.75 ± 1.31μV) and Lt EO (2.42 ± 1.69 μV) from baseline was increased to 6.15 ± 4.83 μV and 9.97 ± 6.08 μV, respectively, after the tsES+tsR, followed by a decrement to 5.62 ± 4.34 μV and 9.41 ± 4.96 μV after the tsR and was remained unchanged at follow up (5.51 ± 4.15 μV and 9.08 ± 4.82 μV, respectively). A significant relationship was found for Rt EO between the baseline and tsES+tsR ($p = 0.04$). However, there was no significant relationship between baseline and tsR ($p = 0.10$), or follow-up ($p = 0.09$). Similarly, the values of EMG for Lt EO also showed significant relationship between the baseline and tsES+tsR ($p = 0.04$), tsR ($p = 0.02$), and follow-up ($p = 0.02$). For the left rotation (LR) (Fig. 16F; Table 6F), the EMG responses was 1.55 ± 0.93 μV for Rt EO and 2.07 ± 1.17 μV for Lt EO at baseline, which increased to 6.86 ± 3.94 μV and 13.47 ± 7.49 μV after the tsES+tsR, respectively. However, it was slightly reduced to 6.06 ± 3.38 μV and 12.06 ± 6.73 μV after the tsR and remained consistent at follow-up period (5.84 ± 3.40 μV and 11.19 ± 6.23 μV, respectively). This indicated the activation of Rt EO and Lt EO during the LR. Statistical analysis revealed a significant relationship for Rt EO between baseline and tsES+tsR ($p = 0.04$), tsR ($p = 0.03$), and follow-up ($p = 0.04$). Similarly, a significant relationship was also found for Lt EO between the baseline and tsES+tsR ($p = 0.03$), tsR ($p = 0.03$), and follow-up ($p = 0.03$).

Table 6: The responses recorded from trunk muscles measured through EMG.

A

Study timeline	**Flexion**							
	Rt. RA (μV)		**Lt. RA** (μV)		**Rt. LD** (μV)		**Lt. LD** (μV)	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Baseline	0.66 ± 0.27	-	1.23 ± 0.56	-	2.65 ± 1.82	-	2.90 ± 1.85	-
tsES+tsR	1.30 ± 0.60	**	2.27 ± 0.16	*	6.54 ± 4.26	***	7.14 ± 4.49	***
tsR	1.39 ± 0.26	***	1.57 ± 0.32	***	4.82 ± 2.94	***	5.11 ± 2.76	***
Follow-up	1.39 ± 0.24	ns	1.50 ± 0.30	***	4.97 ± 2.90	***	5.15 ± 2.55	***

B

Study timeline	**Extension**							
	Rt. ES (μV)		**Lt. ES** (μV)		**Rt. LD** (μV)		**Lt. LD** (μV)	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Baseline	1.62 ± 0.95	-	1.79 ± 1.25	-	2.20 ± 1.60	-	2.57 ± 1.81	-
tsES+tsR	6.93 ± 6.32	*	7.53 ± 5.47	*	8.86 ± 6.04	***	9.94 ± 6.70	*
tsR	4.11 ± 2.68	***	4.57 ± 3.02	***	5.01 ± 3.71	***	5.70 ± 4.86	*
Follow-up	4.19 ± 2.58	***	4.69 ± 2.97	***	5.02 ± 3.03	ns	6.07 ± 4.45	***

C

Study timeline	**Right lateral flexion**							
	Rt. EO (μV)		**Lt. EO** (μV)		**Rt. ES** (μV)		**Lt. ES** (μV)	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Baseline	1.96 ± 1.0	-	3.22 ± 2.09	-	2.0 ± 1.98	-	1.53 ± 1.64	-
tsES+tsR	3.24 ± 2.54	***	9.15 ± 6.71	***	6.89 ± 4.57	*	5.19 ± 2.76	*
tsR	3.11 ± 1.95	***	7.76 ± 5.37	***	6.33 ± 4.63	ns	5.02 ± 3.07	*
Follow-up	3.0 ± 1.84	***	7.77 ± 5.11	***	6.43 ± 4.70	ns	5.12 ± 2.86	*

(Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, standard deviation: SD, electromyography: EMG, rectus abdominis: RA, latissimus dorsi: LD, erector spinae: ES, external oblique: EO, right: Rt, left: Lt, lateral: lat, $*$ $p < 0.05$, $**$ $p < 0.01$, $***$ $p < 0.001$, ns: no significant difference).

D

Study timeline	Left lateral flexion							
	Rt. EO (μV)		**Lt. EO** (μV)		**Rt. ES** (μV)		**Lt. ES** (μV)	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Baseline	1.10 ± 0.79	-	2.81 ± 2.60	-	1.40 ± 1.17	-	2.02 ± 1.70	-
tsES+tsR	2.06 ± 1.55	***	7.80 ± 5.64	*	5.32 ± 3.34	*	6.46 ± 4.38	***
tsR	2.36 ± 1.39	***	7.11 ± 4.65	*	5.69 ± 4.65	ns	5.92 ± 4.68	***
Follow-up	2.34 ± 1.30	***	6.94 ± 4.61	ns	5.53 ± 4.22	ns	6.01 ± 4.62	***

E

Study timeline	Right rotation			
	Rt. EO (μV)		**Lt. EO** (μV)	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Baseline	1.75 ± 1.31	-	2.42 ± 1.69	-
tsES+tsR	6.15 ± 4.83	*	9.97 ± 6.08	*
tsR	5.62 ± 4.34	ns	9.41 ± 4.96	*
Follow-up	5.51 ± 4.15	ns	9.08 ± 4.82	*

F

Study timeline	Left rotation			
	Rt. EO (μV)		**Lt. EO** (μV)	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Baseline	1.55 ± 0.93	-	2.07 ± 1.17	-
tsES+tsR	6.86 ± 3.94	*	13.47 ± 7.49	*
tsR	6.06 ± 3.38	*	12.06 ± 6.73	*
Follow-up	5.84 ± 3.40	*	11.19 ± 6.23	*

(Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, standard deviation: SD, electromyography: EMG, rectus abdominis: RA, latissimus dorsi: LD, erector spinae: ES, external oblique: EO, right: Rt, left: Lt, lateral: lat, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns: no significant difference).

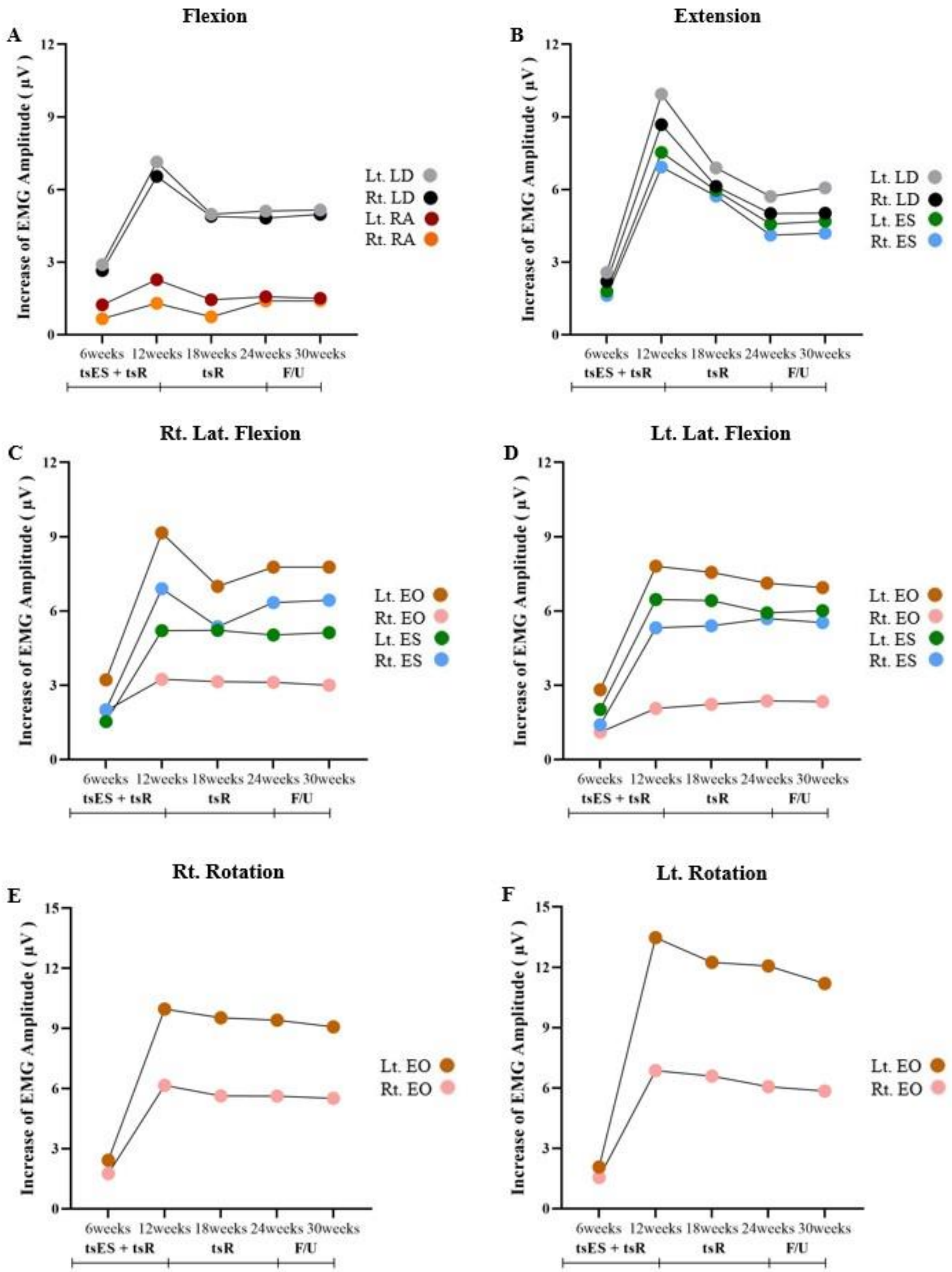


Figure 16: (A, B, C, D, E, and F) Electromyographic responses recorded from the trunk muscles during the specific trunk movements (flexion, extension, right lateral flexion and left lateral flexion, right rotation and left rotation respectively), measured through electromyography for each participant during the study. (Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, electromyography: EMG, rectus abdominis: RA, latissimus dorsi: LD, erector spinae: ES, external oblique: EO, right: Rt, left: Lt, lateral: lat).

3.8 Spinal sagittal curvature

The spinal sagittal curvature demonstrated a decreased mean angle of thoracic kyphosis and an increased mean angle of lumbar lordosis (Table 7). As shown in Fig. 17, P1 had a reduction in thoracic kyphosis by 5.7º (Pre: 23.8º; Post: 18.1º) and an increase in lumbar lordosis by 5.6º (Pre: -2.0º; Post: 3.6º). P2 demonstrated a relatively smaller decrease in thoracic kyphosis (Pre: 21.2º; Post: 20.1º) and a bigger increase in lumbar lordosis (Pre: 5.1º; Post: 11.2º). P3 had the highest reductions in sagittal angles, where thoracic kyphosis (Pre: 34.9º; Post: 10.6º) and lumbar lordosis (Pre: 24.8º; Post: 20.2º) both decreased. Due to the rapid outbreak of COVID-19, however, the post-evaluation for P4 and P5 could not be performed on time. Consequently, they were excluded from the analysis. The average mean ± SD of the thoracic kyphosis decreased by 5.7 ± 5.6º (Pre: 26.6 ± 7.3º; Post: 16.3 ± 5.0º) and that of the lumbar lordosis increased by 2.4 ± 5.6º (Pre: 9.3 ± 13.9º; Post: 11.7 ± 8.3º).

Table 7: Sagittal curvature pre and post intervention (positive values stands for kyphotic and negative for lordotic).

	P1 (Mean in degree)		**P2** (Mean in degree)		**P3** (Mean in degree)		**Average** (Mean ± SD)	
	Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
(T4-T12)	23.8	18.1	21.2	20.1	34.9	10.6	26.6 ± 7.3	16.3 ± 5.0
(L1-L5)	-2.0	3.6	5.1	11.2	24.8	20.2	9.3 ± 13.9	11.7 ± 8.3

(Thoracic kyphosis: T4-T12; lumbar lordosis: L1-L5; SD: standard deviation; **+**: kyphotic; **-**: lordotic)

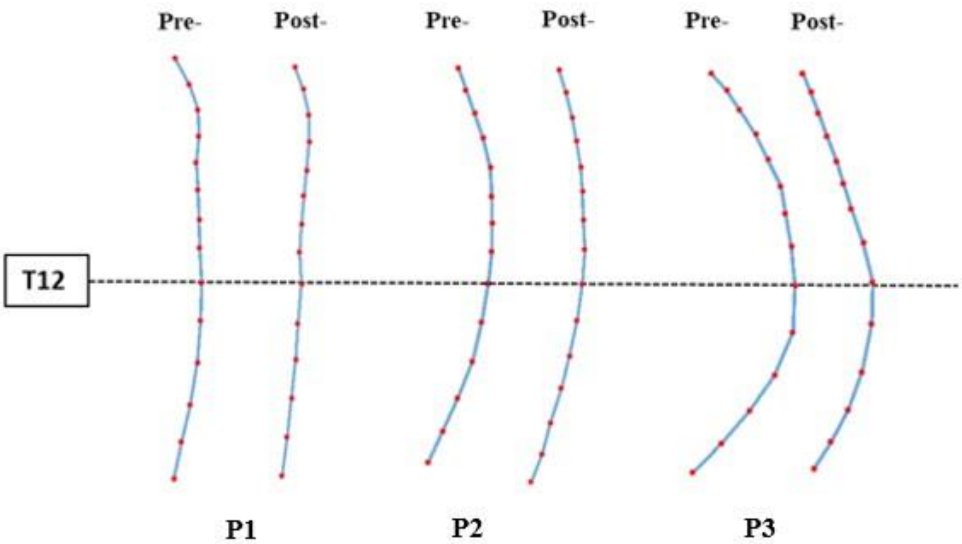
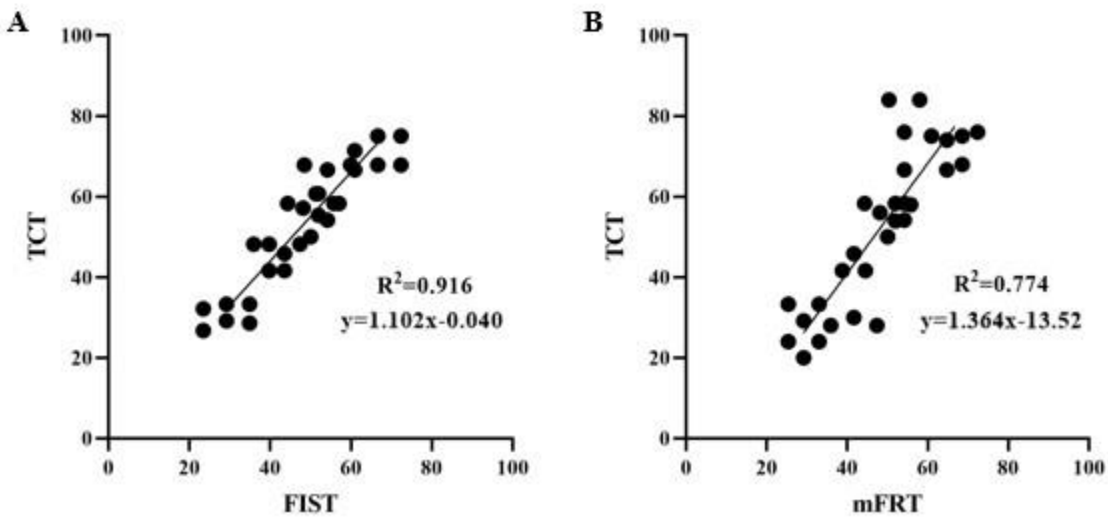


Figure 17: The sagittal profile of the spine based on the coordinates obtained from the sagittal ultrasound images using the laminae landmarks.

3.9 Correlation between the improvements of different assessment parameters

As shown in Fig. 18, a strong positive correlation was found between the TCT and FIST (R^2 = 0.916, $p < 0.01$) after the tsES+tsR (Fig. 18A). The TCT and mFRT (R^2 = 0.774, p = 0.01), TCT and EMG (R^2 = 0.743, $p < 0.01$), EMG and VICON (R^2 = 0.626, $p < 0.01$), FIST and EMG (R^2 = 0.746, p = 0.01), respectively, revealed a mild positive correlation between baseline and the tsES+tsR. Similarly, FIST and mFRT (R^2 = 0.305, $p < 0.01$), EMG and mFRT (R^2 = 0.233, p = 0.04), tsR and tsES+tsR (R^2 = 0.217, p = ns) had a weak correlation between baseline and the tsES+tsR. However, no correlation existed between other assessment parameters.



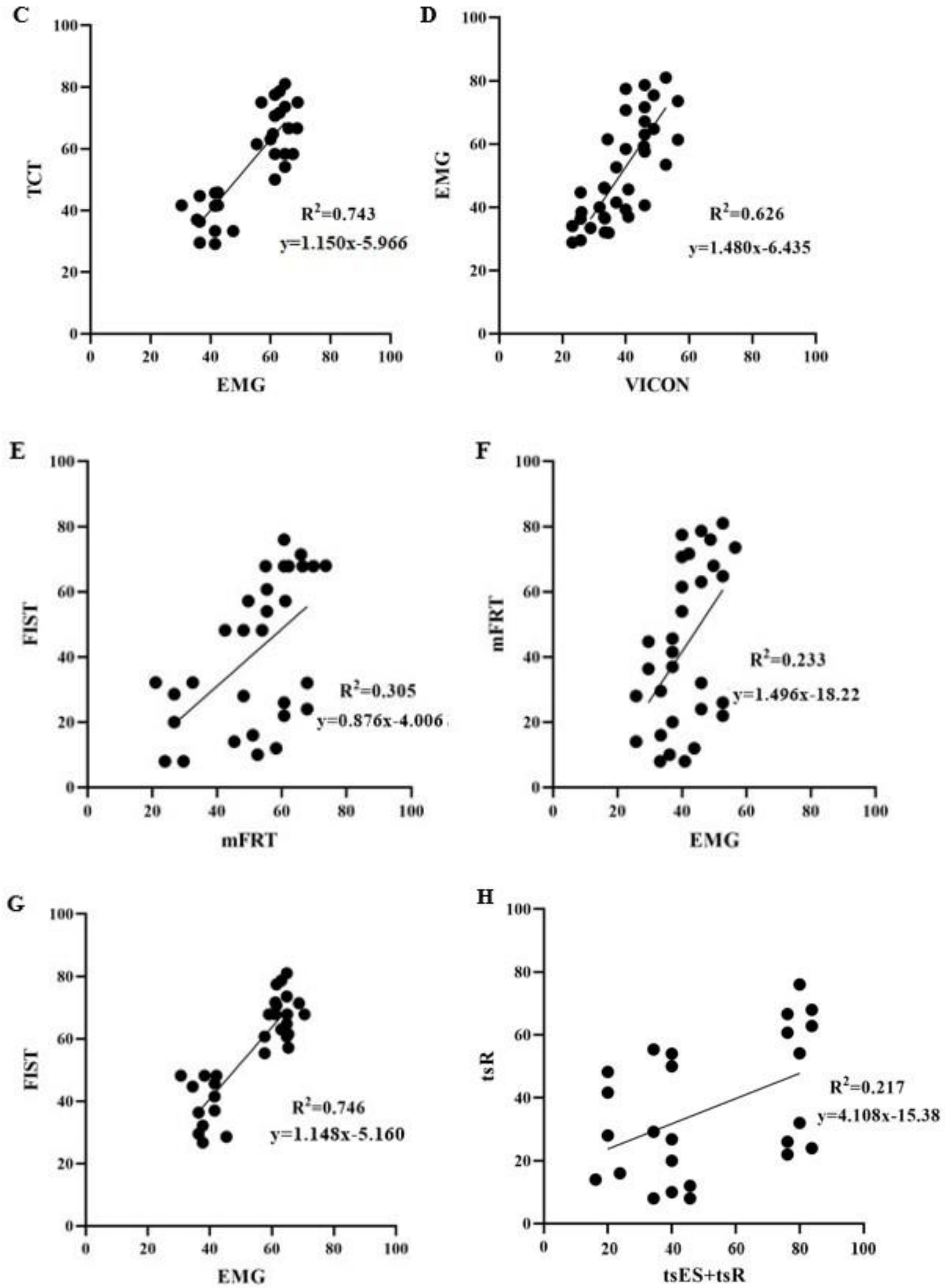


Figure 18: The correlation between the assessment parameters (A) TCT and FIST (B) TCT and mFRT (C) TCT and EMG (D) EMG and VICON (E) FIST and mFRT (F) EMG and mFRT (G) FIST and EMG, and (H) tsR and tsES+tsR, respectively.

3.10 Relative value analysis of improvements in percentage

The scores attained from the functional assessment parameters, VICON and EMG, were converted into percentages with reference to the corresponding baseline values and the relative improvement in percentage were described in the following sections.

3.10.1 Modified Functional Reach Test

As shown in Fig. 19A, there was a great improvement in the forward reach test, including right lateral reach and left lateral reach, among all the participants. For the forward reach, P1, P2, and P3 had the larger increases in reaching distance by 76.66%, 68.75%, and 54.39%, respectively, while P4 and P5's forward reach improved relatively smaller by 20.66% and 28.58% after the tsES+tsR, which further slightly increased after the tsR and follow-up. Since we found that P1, P2 and P3 improved more in most of parameters in comparison with P4 and P5, in the subsequent analysis, they were separted into these two groups for such situations. Statistical analysis showed a significant improvement between the baseline and tsES+tsR (p = 0.02), baseline and tsR (p = 0.02), as well as baseline and follow-up (p = 0.02). The right lateral reach (Fig. 19B) of P1, P2, P3, P4, and P5 was improved by 26.18%, 32.33%, 10.0%, 8.66%, and 16.57%, repsectively, after the tsES+tsR, followed by a sustainable improvement after the tsR and follow-up. A significant improvement was found between the baseline and tsES+tsR (p = 0.03), the baseline and tsR (p = 0.02), as well as the baseline and follow-up (p = 0.02). Similarly, the left lateral reach (Fig. 19C) was increased by 22.50%, 24.44%, 12.44%, 8.66%, and 14.28% after the tsES+tsR for P1 to P5, respectively. In addition, the improved percentage remained almost unchanged after the tsR and follow-up period. A significant improvement was found between the results of the baseline and tsES+tsR (p = 0.01), baseline and tsR (p = 0.01), as well as baseline and follow-up (p = 0.01).

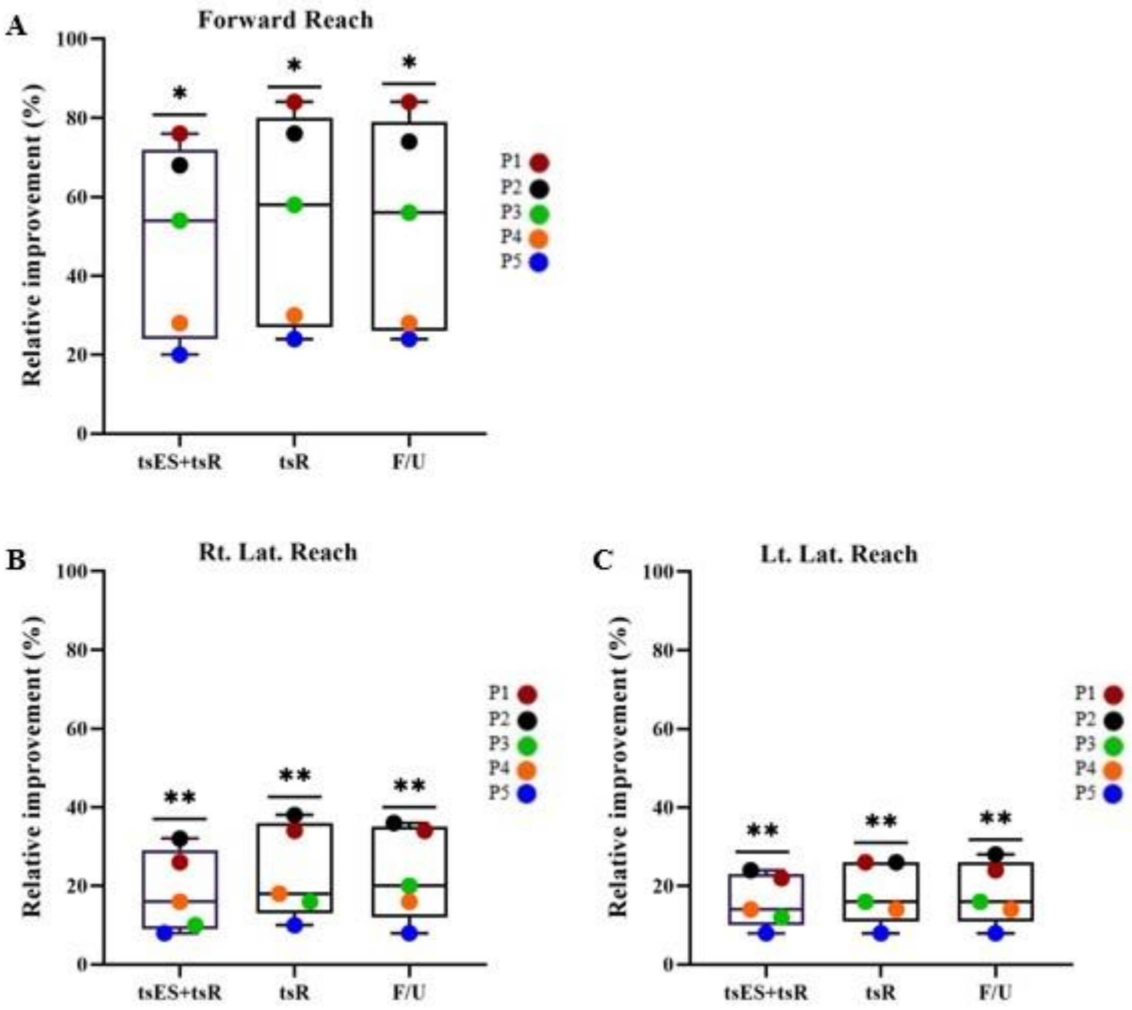


Figure 19: The relative improvement of mFRT in percentage (A) Forward Reach (B) Rt. Lat. Reach (C) Lt. Lat. Reach. (Modified Functional Reach Test: mFRT, Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, ∗ $p < 0.05$, ∗∗ $p < 0.01$, ∗∗∗ $p < 0.001$).

3.10.2 Trunk Control Test

The trunk function (Fig. 20) was shown to be increased among all the subjects after the tsES+tsR intervention. P1, P2, and P3 showed the greatest improvement in trunk control (54.16%, 66.66%, and 50.05%, respectively). The results showed that that P4 and P5 increased the trunk function by 29.16% and 41.66%, respectively after the tsES+tsR. In addition, the improvement was consistently maintained after the tsR and follow-up. However, P1 had a slight reduction in trunk ability after the follow-up. Statistical analysis revealed a significant improvement between the baseline and tsES+tsR ($p < 0.01$), baseline and tsR ($p < 0.01$), as well as baseline and follow-up ($p < 0.01$).

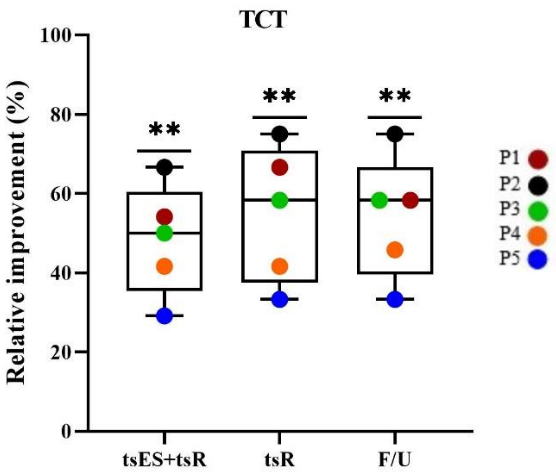


Figure 20: The relative improvement of TCT in percentage. (Trunk Control Test: TCT, Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, $*$ $p < 0.05$, $**$ $p < 0.01$, $***$ $p < 0.001$).

3.10.3 Function in Sitting Test

As shown in Fig. 21, the sitting function was improved in all the participants. Interestingly, P1 and P2 achieved a dynamic sitting balance improvement and were able to perform the transfer task from wheel chair to bed and vice-versa after the training. P1, P2, and P3 had improved the sitting function by 60.71%, 67.85%, and 55.35%, respectively after the tsES+tsR. Similarly, the sitting ability was increased by 26.78% for P4 and 48.21% for P5. In addition, the values obtained remained consistent after the tsR and follow-up. A significant improvement was found between the baseline and tsES+tsR ($p < 0.01$), baseline and tsR ($p < 0.01$), as well as baseline and follow-up ($p < 0.01$).

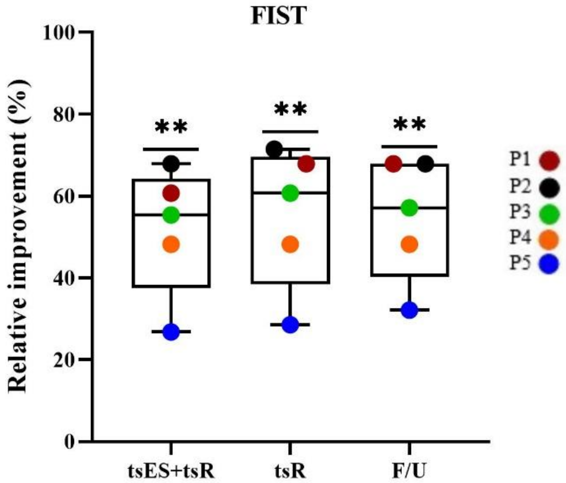


Figure 21: The relative improvement of FIST in percentage. (Function in Sitting Test: FIST, Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, $*$ $p < 0.05$, $**$ $p < 0.01$, $***$ $p < 0.001$).

3.10.4 Vicon motion capture System

The trunk range of motion was significantly improved after the intervention, which increased the functional ability of the participants. For the flexion (Fig. 22A), the improved range of motion (ROM) was 56.97% for P1, 47.26% for P2, and 48.61% for P3, respectively, after the tsES+tsR. P4 and P5 showed improvements of 45.23% and 32.93%, which was further decreased after the tsR and follow-up. Since we found that the obtained values were slighly reduced for P1 to P4 participants, while P5 showed consistent large decrement throughout the tsR and follow-up period. Statistical analysis showed a significant improvement between the baseline and tsES+tsR ($p = 0.02$), tsR ($p < 0.01$), and follow-up ($p < 0.001$). According to Fig. 22B, P1, P2, and P3 had the highest increase in extension by 54.69%, 47.94%, and 60.69%, respectively, while the P4 and P5 ranges improved by 52.50% and 47.47% after the tsES+tsR, which further reduced after the tsR and follow-up. A significant improvement was found between the results of the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.001$), and follow-up ($p < 0.001$). Similarly, for the right lateral flexion (RLF) (Fig. 22C), P1, P2, and P3 had improved the range by 58.09%, 56.09%, and 23.06%, respectively, after the tsES+tsR. Similarly, the RLF was increased by 30.73% for P4 and 16.02% for P5. In addition, the values obtained remained almost unchanged after the tsR and follow-up. A significant improvement was found between the baseline and tsES+tsR ($p = 0.01$), tsR ($p < 0.01$), and follow-up ($p < 0.01$).

As shown in Fig. 22D, P1, P2, and P3 revealed the maximum improvement of the left lateral flexion (LLF) by 50.97%, 58.13%, and 40.44%, respectively, after the tsES+tsR. It was also shown that P4 and P5 increased the LLF range by 29.56% and 28.40%, which further slightly decreased after the tsR and follow-up. Statistical analysis showed a significant improvement between the baseline and tsES+tsR ($p = 0.01$), tsR ($p = 0.01$), and follow-up ($p < 0.01$). For the right rotation (RR) (Fig. 22E), P1, P2, and P3 had improved the range by 62.08%, 53.49%, and 60.21%, respectively after the tsES+tsR. Similarly, the RR was increased by 20.61% for P4 and 31.92% for P5. In addition, the values obtained remained consistent after the tsR and follow-up. A significant relation was found between the baseline and tsES+tsR ($p = 0.01$), tsR ($p < 0.01$), and follow-up ($p < 0.01$). It can be seen from Fig. 22F, that the maximum increment in left rotation (LR) was 43.33% for P1, 45.21% for P2, and 37.62% for P3, respectively after the tsES+tsR. P4 and P5 had the improvements in LR by 25.55% and 33.39%. Significant improvement was found between the results of the baseline and tsES+tsR ($p = 0.01$), tsR ($p = 0.01$), and follow-up ($p < 0.01$).

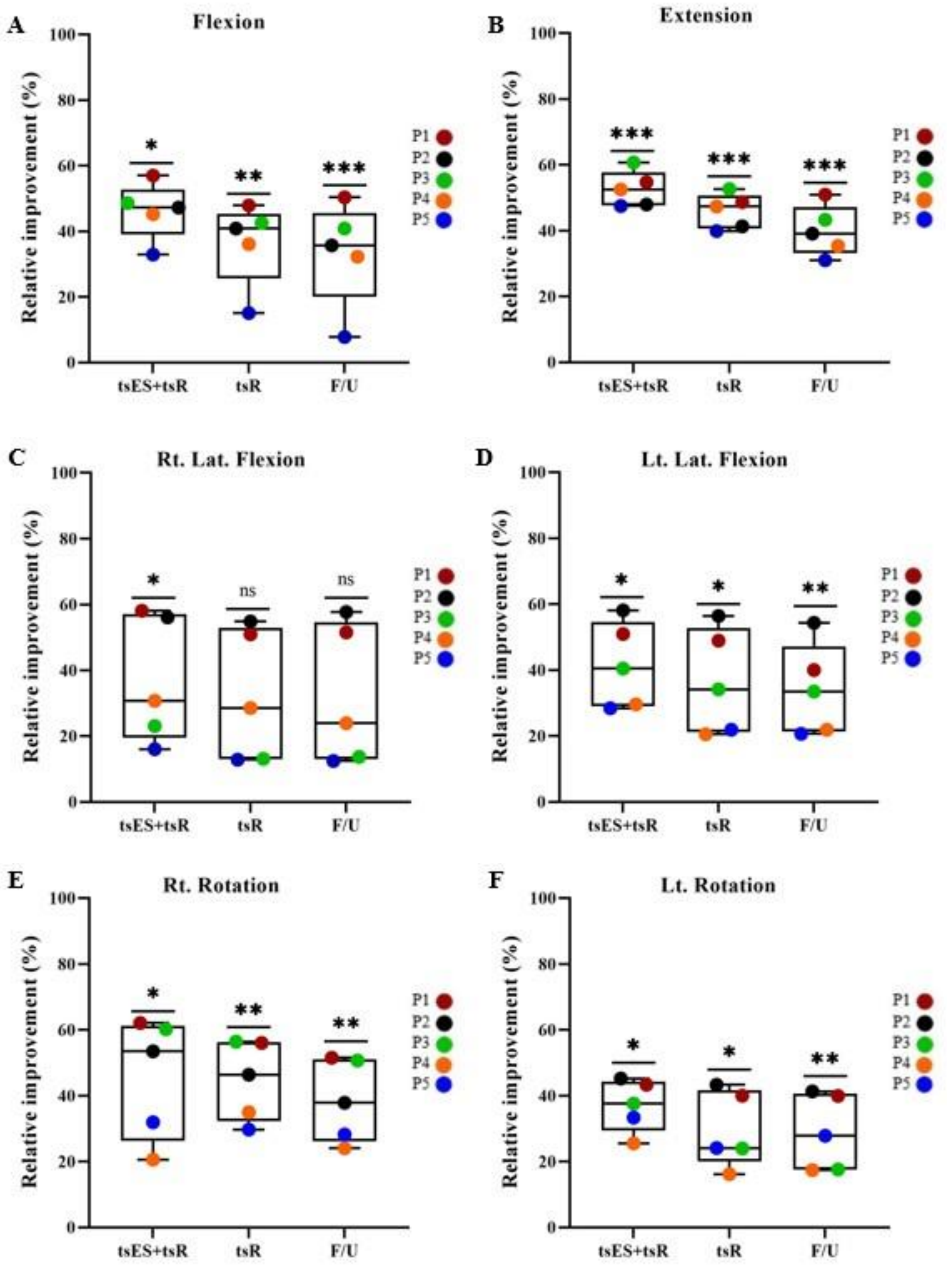


Figure 22: The relative improvement of range of motion measured through Vicon motion capture system in percentage. (Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, $*$ $p < 0.05$, $**$ $p < 0.01$, $***$ $p < 0.001$, ns: no significant difference).

3.10.5 Electromyography

The electromyography (EMG) activity of the muscles (rectus abdominis, latissimus dorsi, erector spinae, and external oblique) showed increased amplitude after the tsES+tsR intervention. As shown in Fig. 23A, for the flexion, the higher EMG response was revealed by Rt LD (59.48%) and Lt LD (59.38%) after the tsES+tsR. Similarly, the increase in EMG response was improved by 45.81% for Rt RA and by 49.23% for Lt RA. In addition, the EMG values obtained was slightly reduced after the tsR and follow-up period. Statistical analysis showed a significant improvement between the baseline and tsES+tsR (p = 0.01), tsR (p = 0.02), and follow-up ($p < 0.01$). For the extension (Fig. 23B), Rt LD (76.62%) and Lt LD (76.22%) showed the maximum increase in EMG amplitude, while Rt ES showed an improvement of 74.65% and Lt ES of 74.14% after the tsES+tsR intervention. Similarly, the EMG response revealed some decrement after the tsR and follow-up. A significant improvement was found between the baseline and tsES+tsR ($p < 0.001$), tsR ($p < 0.01$), and follow-up ($p < 0.001$).

According to Fig. 23C, the right lateral flexion showed EMG acitivity increment by 39.19% for Rt EO and by 70.86% for Lt EO after the tsES+tsR. Rt ES was improved by 70.57% and Lt ES by 64.80%, which remained almost unchanged after the tsR and follow-up. A significant improvement was found between the results of the baseline and tsES+tsR (p = 0.01), tsR ($p < 0.01$), and follow-up ($p < 0.01$). The left lateral flexion (Fig. 23D), revealed the increase of EMG amplituide for Rt EO by 52.90% and for Lt EO by 73.68%, respectively after the tsES+tsR. In addition, the improvement for Rt ES was 63.89% and Lt ES was 66.38%. The values remained consistent after the tsR and follow-up period. Statistical analysis showed significant improvement between the baseline and tsES+tsR ($p < 0.01$), tsR ($p < 0.01$), and follow-up ($p < 0.01$). As shown in Fig. 23E, the right rotation showed the greater improvement in Rt EO (71.42%) and Lt EO (75.72%) after the tsES+tsR treatment which remained almost unchanged after the tsR and follow-up. A significant improvement was found between the baseline and tsES+tsR ($p = 0.02$), tsR ($p = 0.04$), and follow-up ($p = 0.03$). For the left rotation (Fig. 24F), the Rt EO had improved by 77.40% and Lt EO by 84.63% after the the tsES+tsR. Similarly, the EMG values obtained remained consistent after the tsR and follow-up period. Significant improvement was found between the results of the baseline and tsES+tsR ($p = 0.04$), but not between the baseline and tsR ($p = 0.05$), and follow-up ($p = 0.05$).

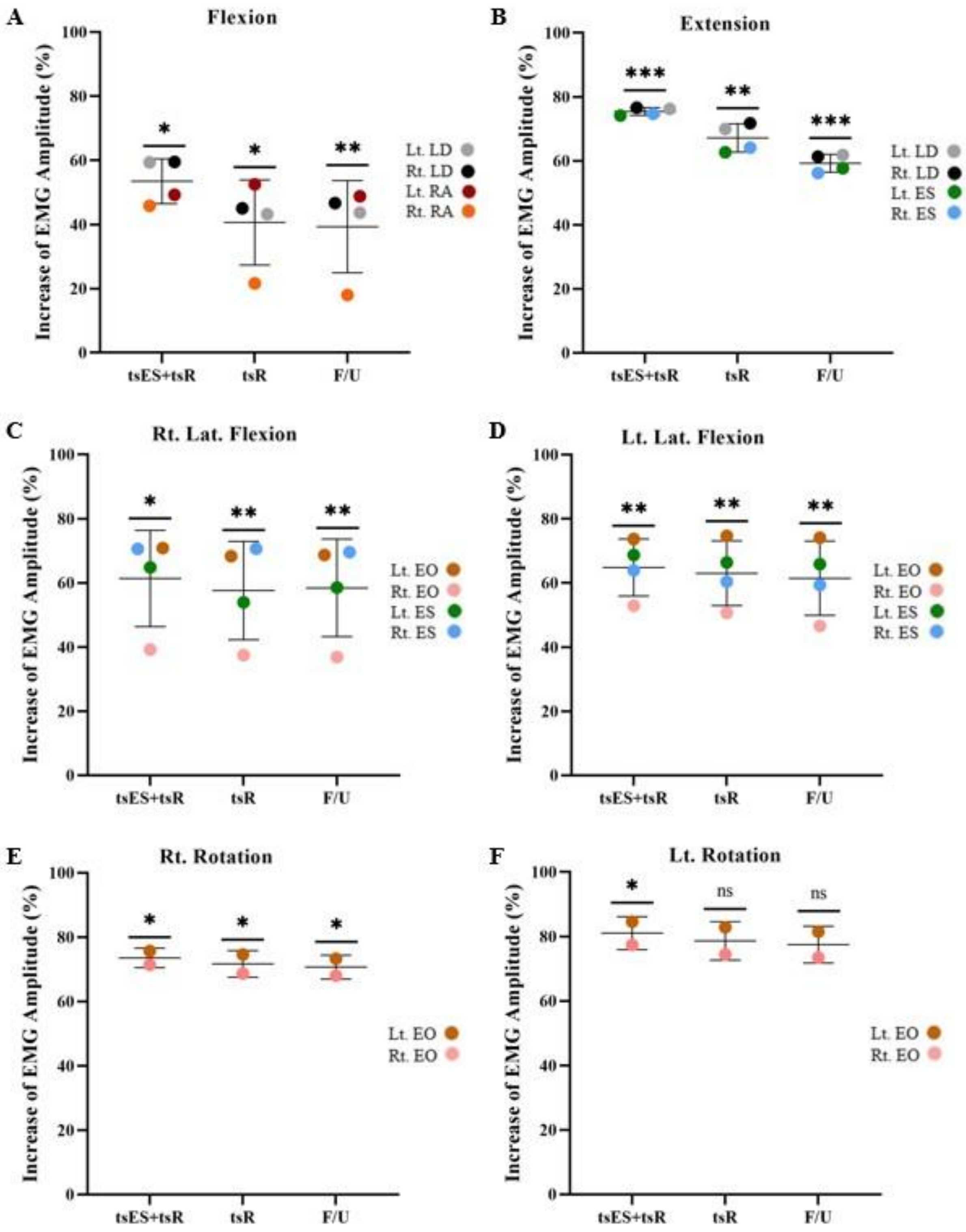


Figure 23: The increase of muscle electromyography amplitude in percentage. (Trans-spinal electrical stimulation: tsES, task-specific rehabilitation: tsR, follow-up: F/U, right: Rt, left: Lt, lateral: lat, rectus abdominis: RA, latissimus dorsi: LD, erector spinae: ES, external oblique: EO, $*$ $p < 0.05$, $**$ $p < 0.01$, $***$ $p < 0.001$, ns: no significant difference).

3.11 The impact of treatment frequency on functional outcome

The impact of treatment frequency on functional outcome has been analysed to observe the effects on outcome. The participants P1, P2, and P4 received the intervention three times per week and had an injury level of C6, C7, and C5, respectively. Similarly, P3, who attended just one session per week, had a SCI level of C5. In addition, P5, who participated twice per week, had an injury level of C4. As shown in Fig. 24, the scores of mFRT (forward reach), TCT, and FIST showed that P1 and P2 demonstrated the greatest improvement in their function. In addition, P4, who attended the same sessions as P1 and P2, had lower outcomes than them. This could be due to the different levels of SCI. Interestingly, P3, who received one session every week, demonstrated higher scores than P5, who attended two sessions per week. However, their levels of injury were different. Moreover, P3 receiving less intervention had better improvement than P4 and had the same level of injury. This may be due to the presence of grasp ability that assisted in the effective training. The results showed that SCI subjects with C5, C6 and C7 level injury received equal frequency of treatment. The subject with C7 had maximal improvement followed by C6 and C5. Similarly, subject with C4 and C5 level injury, the C5 attending less session than C4, while C5 had more improvement. Therefore, it could be assumed that subjects with higher level cervical cord injury (severe tetraplegia) had less improvement compared to lower tetraplegia instead of attending equal frequency of treatment. Therefore, it could be assumed that the improvement depends on the severity of SCI rather than the frequency of therapy. The training did, however, improve all the participants' functional abilities. However, it is suggested that continual training and intervention sessions are advantageous for motor recovery [113]. Nonetheless, further research is required to confirm this concept.

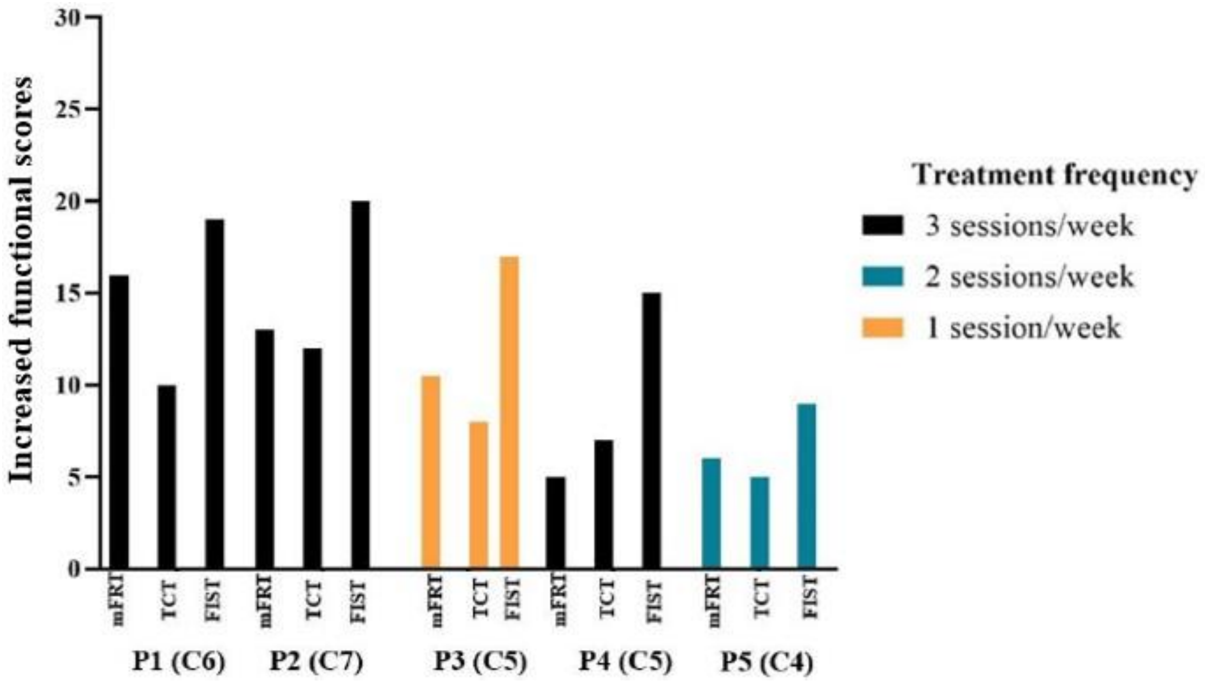


Figure 24: The increased functional scores based on treatment frequency after tsES+tsR, with the maximum scores obtained after subtracting from baseline by the participants during the functional assessment of mFRT (forward reach), TCT, and FIST, where an increase in score indicates an improvement in function (Modified Functional Reach Test: mFRT; Trunk Control Test: TCT; Function in Sitting Test: FIST, Cervical vertebrae injury level: C4, C5, C6, C7. etc.).

Chapter 4 Discussion

The present investigation examined the effects of tsES on trunk control and sitting function when used in combination with tsR in individuals with complete cervical SCI. This was performed over a 24-week period, with 12 weeks of tsES+tsR followed by another 12 weeks of tsR alone, in five participants with chronic complete tetraplegia and an age ranging from 26–57 years. We demonstrated that the combined intervention of tsES+tsR, improved the trunk stability, static and dynamic sitting balance, compared to tsR alone. The results showed that all participants' trunk control and sitting function progressively improved during the tsES+tsR. In addition, functional improvements were strengthened during the tsR alone and sustained during the follow-up period, showing long-term effects. This indicates that trunk recovery is possible even in complete chronic cervical SCI, and functional gains could be preserved.

4.1 Functional reaching ability in sitting

Reaching ability is essential for individuals who rely on a wheelchair to accomplish everyday tasks. The capacity to reach forward may assist people with SCI and preserve energy during daily duties, allowing them to participate in exercising to a greater extent [192]. In the present study, all the participants showed an increase in reaching distances. The forward reaching distance was increased, enabling the participants to reach objects in front of them. In addition, there was some increment in the lateral distances, which assisted in trunk balance maintenance. Previous research demonstrated that stimulation of trunk muscles in SCI individuals with thoracic level injuries led to a rise in mean reach distance by 5.5 ± 6.6cm while sitting [23]. And, when the paralyzed trunk muscles were stimulated with FES implanted intramuscular electrodes, the forward trunk lean was recorded to increase by 19% to 26% ($p < 0.001$) [193]. Similarly, the present investigation showed an increase in mean forward reach distance by 10.3 ± 4.54 cm ($p = 0.02$) after the tsES+tsR. Moreover, the stimulation of the trunk muscles with eSCS following total paralysis showed an increase in forward reach of greater than 7 cm [183].

There is evidence that in people with thoracic SCI, forward reach lengths rose while lateral reach lengths stayed constant [24]. The results of this study were mostly consistent with this statement, only the lateral reach distances were also found to rise somewhat. It has been previously revealed that people with increased reaching forward distance, as measured by the mFRT, also exhibited greater sitting control and postural stability [192]. Besides, the current investigation revealed comparable results, where the participants with a greater forward reach had better trunk and sitting function. The improved mFRT may assist health practitioners in planning exercise training programs based on an individual's potential to improve daily task performance while seated in a wheelchair [184]. Researchers examined forward reaching after SCI where they did not show a mean FRD, they reported a range of forward reach between 2.5 cm and 29.1 cm [194]. Hence, focusing on individuals with a higher level of SCI, our results supported this research presenting a mean FRD of 12.3 ± 6.12 cm as well as forward reach distance between 0 cm to 21.5 cm. Grangeon et al. found that people with severe SCI performed poorer across both forward-backward and sideways movements while sitting unassisted [195]. Therefore, the dominant hand was used more often for reaching while supporting themselves with the non-dominant hand, thus acquiring greater sitting balance [195]. Furthermore, it was reported that the stimulation "off and on" conditions had an influence on reach lengths. When the stimulator was on, the forward reaching lengths increased, while, during turned off period, the subjects' reaching abilities returned to normal [24]. Nevertheless, in the current investigation, the increased reach distances were preserved even after the washout phase. In the previous study, with stimulation on, forward reaching distances were much larger than lateral reach distances [24], however, in the current study comparable results were obtained without stimulation. As a result, in the present investigation, achieved distances were always recorded in the absence of stimulation to avoid this impact. When it comes to physical functioning, it was claimed that those with lower degrees of paraplegia were more capable than those with tetraplegia [184]. The present results supported this notion, as subjects with a greater degree of SCI displayed decreased forward reaching ability followed by reduced lateral reaching compared to participants with lower level of injury. The current investigation demonstrated that the forward reach distance increased to a greater extent with the introduction of the tsES+tsR, although the lateral reach distance increased slightly. Thereafter, the functional gains were maintained during the tsR alone and after the follow up period. Consequently, the findings of this study revealed the potential of employing tsES to improve functional reaching ability during sitting in people with tetraplegia.

4.2 Trunk control stability during tsES

In the presence of the tsES+tsR, static trunk control was improved in all the participants, allowing them to sit independently with or without support, while dynamic trunk control was shown in some participants. Hence, it could help to reduce the risk of fall from wheel chair. Moreover, it was found that FES therapy could improve sitting posture and bimanual reach for those with lower cervical and thoracic SCI [196]. Falls have been found to occur at a rate of up to 75% in people with SCI, with lack of control being the predominant reason [197]. However, the exact causes of falls in SCI are unknown. As, trunk stability is a significant contributor to falls, rehabilitation aimed at increasing balance is essential. To reduce the risk of falling from a wheelchair, individuals with paraplegia were fitted with a chest strap. It was shown to be beneficial for trunk stability in wheel chair sitting, however, it was only temporary external assistance [198]. On the other hand, the present investigation demonstrated improved independent sitting and trunk control with increased functional reach after paralysis that were preserved even after the end of intervention. In light of its success in enhancing trunk control and sitting balance, the tsES+tsR may complement or even replace traditional techniques like chest straps, seating adjustments, and other forms of personal support. The results also suggested that this intervention might be used to enhance the ability of people with tetraplegia who are completely reliant on carers to turn in bed, which is critical in preventing the development of pressure ulcers. As trunk stability increased, so did functional reach, which had the potential to promote the independence of people with SCI in daily life activities [192]. It was previously reported that the severity of the injury had a direct impact on the rehabilitation success [199]. This echoes with the findings from the current study, where the participants with lower levels of SCI had greater improvements. The use of assistive equipment during locomotor training required some hand function, so people with lesions above the C5 vertebra presented substantial obstacles during walking [199]. In the current study, the participant with a C4 AIS-A injury had more difficulties and needed more assistance than the other participants, which was similar to the findings in that study. Additionally, activating paralysed trunk muscles may restore skeletal alignment and provide adequate sitting control to eliminate the need for chest harnesses. Thus, trunk stability may facilitate the use of the shoulder muscles more efficiently [193]. When it came to trunk control, both upper extremities support was the preferred choice for those with SCI. It is reasonable to conclude that despite the greater control effort, the stability function with one limb support was similar, indicating that the capacity to hold this posture for an extended period of time was restricted due to increased tiredness [195]. The present study showed similar characteristics among the study participants during the reaching task. Regaining one's trunk control after SCI might be severely hindered by one's ability to extend forward or laterally in an upright sitting position. As a consequence of a reduced capacity to reach, a person's level of dependence and chance of falling greatly increase. Therefore, the tsES may be a potential treatment for re-establishing trunk control in individuals who have an impaired trunk or only slightly improved after longer rehabilitation intensive training programs [192]. The present results showed that the participants were able to maintain an upright sitting posture with increased static and dynamic balance. They were also able to sit independently with or without assistance from the upper limbs, roll from supine to prone and side-line, and conduct functional activities while maintaining dynamic balance in sitting. Additionally, improved sitting function aided participants in performing daily living tasks such as reaching and picking up objects, scooting for pressure relief and transfer, etc. The findings from this study showed an important move towards the recovery of trunk control utilizing tsES to improve sitting in people with SCI.

4.3 Seated postural stability

For those who are unable to stand, sitting stability is essential to their ability to function. The inability to appropriately transfer could restrict wheelchair independence and everyday tasks [200]. A previous study explored the sitting balance and functional outcomes of individuals with lower and higher thoracic SCI, and found that those with a lower level of SCI had more dynamic stability. The assumption that a decrease or gain in trunk strength predicts sitting balance in SCI, on the other hand, remained inconclusive [136]. The comparable outcomes were found in the present research regarding injury severity, where people with a lower SCI had more improvement in seated function, and those with enhanced trunk strength had improved trunk control and sitting stability. However, the ability to sit with good balance after SCI depends on a variety of variables, including the degree of neurological damage and the extent of sensorimotor impairments [195]. In our study, it was probable that age, sensorimotor dysfunction, level of severity, and duration of the lesion had an impact on the sitting stability of people with severe SCI. In addition, the tsES stimulation has been shown to increase the ability of SCI people to maintain an upright sitting position more than two years after a complete or incomplete injury [10]. It was also found that activating the trunk musculature following neurologic impairments such as SCI may help to achieve trunk control and sitting stability in individuals with SCI [183, 196]. In the current study, despite not being assessed, three participants reported gains in propelling ability after they were switched from their motorized wheel chair to a manual wheel chair. It was also found that two of them were able to independently transfer from their wheelchairs to their beds and vice versa, using a sliding board while being observed by their caregivers. Interestingly, participants claimed to have a better sense of security and less anxiety about falling. Prior studies have reported that voluntary effort by the individual during training was vital. They claimed that there was no continuous recovery in tasks where only stimulation was delivered [201]. During locomotion training for paraplegia, with full passive support by the trainers showed a lesser outcome than active participation, which means that mobility was generated from the individual's attempts [201, 202]. Therefore, the participants of this study were encouraged to carry out every task on their own with the assistance of their own upper limbs. Besides, people with SCI utilized their upper limbs for support while performing activities [127, 150]. The, participants in the current investigation relied on their upper limbs to support themselves to sit erect and maintain dynamic balance while doing physical activities.

4.4 Trunk EMG responses and range of motion (ROM) after tsES

The trunk flexors (RA and EO) and lateral flexors or extensors (LD and ES), have been identified to have a vital function in the stability of the trunk [203]. The RA, OE, LD, and ES muscles are located on the trunk either anteriorly, laterally, or posteriorly [34]. Individuals with SCI above L1 level injury experience trunk instability as a result of impairment in trunk musculature, including the RA, ES, EO, and LD, among others [34]. Therefore, in order to achieve proper trunk control, it is essential to activate trunk muscles [204]. It has been previously demonstrated that in children with SCI, the EMG revealed that the RA and EO muscles were much more activated than other trunk muscles and contributed significantly more to trunk stability [205]. Similarly, in the present study we observed elevated EMG activity in the trunk muscles, particularly in LD, ES, and EO, across all trunk movements during tsES+tsR.

A previous study examined the performance of the functional electrical stimulation (FES) in combination with therapeutic exercise (TE) in chronic SCI people with AIS-B or C, where ES and RA were stimulated with FES+TE for six weeks, followed by only TE. The FES+TE raised ES muscle activity by 6% and RA muscle activity by 6%, while improving flexion movement by 30.1 %. And after a six-month follow-up, ES was reduced by 0.8%, RA by 1.4%, and flexion by 31.9%. It was observed that FES+TE improved trunk muscle tone and dynamic sitting stability more than TE alone, but reverted ROM effects to the initial phase [130]. This supports the notion that, in the current study, the participants with chronic SCI AIS-A demonstrated an increase in EMG responses of ES, EO, LD, and trunk ROM (maximum during flexion and rotation) with the treatment of tsES+tsR and a slight decrease with tsR, whereas functional improvements were maintained even after the follow-up period with preservation of functional outcomes. Previous research has shown that stimulating trunk muscles in thoracic level injuries in SCI resulted in increased mean trunk extension of 9.2 ± 9.5 Nm while sitting [23] compared to the mean extension of 12.4 ± 4.48º in the current study. This was particularly noticeable since the engaged muscles were trunk flexors and extensors (i.e. RA and LD), which are primarily responsible for forward and backward trunk stability [206]. Moreover, the lateral reach and lateral flexion demonstrated the lowest measurement values compared to other variables among all the participants. The findings are consistent with other research, which showed instability in the medial-lateral direction was most common in those with SCI [129]. Additionally, a recent study found that stimulation with tsES resulted in an increased EMG response of the ES, RA, and EO muscles, which enhanced trunk stability, spinal curvature, and sitting balance [10]. When assessing any therapeutic treatment, it was possible that the effects might not immediately appear at a functional level but may be reflected at the neuromuscular level, which would be evaluated using EMG [90]. Similarly, the participant with C4 level injury in this study had a greater EMG response in comparison to the limited functional benefits. In addition to previously conducted studies, utilizing tsES across the lumbar spinal connections established it as a potential therapy for SCI by demonstrating increased activity in the trunk muscles in a comparable way to FES [10, 36, 68].

4.5 Sagittal spinal curvature alignment in sitting

A more upright sitting position may be attained by stimulation of the trunk extensor muscles, which could improve spinal alignment and restore a more normal curvature of the low back [23]. This result supports the finding from the current study, that the participants' sagittal spinal curvature angle decreased, i.e., reduced thoracic kyphosis and lumbar lordosis, providing a more proper erect sitting posture. Moreover, a case study demonstrated that a FES implanted in an individual with C4 (AIS-A) presented a decrease in the lateral spinal convexity from 38º to 12º and kyphosis from 55º to 34º after the application of eSCS stimulation. However, the values returned to baseline on removal of stimulation [183]. Rath et al. reported that with the application of tsES, the overall trunk curvature angle was decreased by 6º resulting in improved upright sitting posture [10]. In the present study, the sagittal spinal curvature was improved in all the participants, who developed a more erect and upright posture during sitting. The thoracic kyphosis decreased from 26.6 ± 7.3 º to 16.3 ± 5.0 º and lumbar lordosis increased from 9.3 ± 13.9 º to 11.7 ± 8.3 º respectively. Although lordosis is associated with increased thoracic-kyphosis, some research has shown that lordosis was actually associated with a reduction in kyphosis [207, 208]. In current study tsES+tsR treatment showed that it could be effective in reducing thoracic kyphosis that could improve sagittal spinal alignment. But the mean angle of lumbar lordosis was increased. This could be due to a posteriorly tilted pelvis measured till 15º in people with SCI during sitting [167]. However, the underlying mechanism is still not yet clear. The post evaluation was carried out after the tsR period, where there was no stimulation delivered for a period of 12 weeks. This indicated that sagittal curvature changes were maintained even in the absence of stimulation when compared to the study using invasive stimulation.

4.6 tsES and tsR for motor improvement

In recent days, tsES has become increasingly popular as a treatment option for people who have SCI and are left paralyzed. In particular, during locomotion training, recent trials combining tsES with activity-based therapy have demonstrated exceptional gains in motor performance previously believed unattainable in people with chronic SCI, which remained even when stimulation was not used [199]. Edgerton et al. have also shown that tsES, when used in conjunction with a specific motor activity, could facilitate the repair of supraspinal-spinal connections and reactivate spinal circuits even in chronic severe SCI [209]. In addition, researchers have revealed that tsES alone could improve posture and promote upright sitting in people with complete and incomplete SCI [10, 63]. The present research demonstrated that the tsES when combined with tsR, resulted in improved trunk control and sitting function with functional outcomes preserved for a longer term in individuals with complete cervical tetraplegia. Non-invasive tsES had been invented to stimulate the same neural areas as epidural spinal cord stimulation (eSCS) via the same methods [68, 210, 211]. Although, the invasive methods have been shown to be beneficial, non-invasive tsES reduced the risk of surgical complications [193] while increasing participants' confidence and interest in participating in research. Therefore, this technique is still in its emerging phase as a treatment option for SCI, there is still more to understand about its application and therapeutic potential [90].

Furthermore, people classified as AIS B or C have reportedly recovered movement in their previously paralysed extremities even in the absence of stimulation. This did not apply to those who had suffered a total SCI of the sensorimotor systems (AIS A) [199]. Longer rehabilitation using tsES in conjunction with activity-based therapy has been shown to enhance standing and balancing and promote functional improvement in individuals with SCI [105, 212]. The importance of combining the tsES technique with tsR was highlighted in order to achieve continual improvements in locomotion [213, 214], standing [55], upper extremity function [215], and sitting posture [10, 63] in individuals with SCI. Correspondingly, tsES has been shown to enhance functional ability when combined with various forms of activity-based therapy, ranging from locomotion to upper extremity performance [58-60, 215]. However, it has not been utilized in cervical SCI individuals with AIS-A to improve trunk control and sitting function. Also, only a few studies have investigated the impact of tsES stimulation on trunk function after SCI [10, 63], and none of them had coupled tsR training with tsES stimulation. The present study contributed to the prior research by demonstrating that combining tsES with tsR was effective in improving trunk function even in complete tetraplegia.

Previously published study suggested that people in different status of SCI should be tested on physiological measurements (e.g. motion capture system, electromyography, etc.) to get a greater understanding of interrelations during the tsES [24]. The current research filled the gap with the help of recommended instruments. Moreover, stimulation responses have been proven to be extremely diverse amongst the subjects based on the extent of the damage [23], as seen in the current research, where the participants' functional improvements varied with the severity of the injury. According to a review paper, tsR in the acute phases of SCI did not seem to enhance seated performance much beyond traditional therapy. And, there is limited evidence to suggest that this training may be useful in more chronic periods of injury [124]. Nevertheless, the current study has demonstrated that tsR when combined with tsES was found to be effective in restoring motor trunk control in chronic tetraplegia. In addition, the combination approach might be performed in an outpatient department. The tsES was well-tolerated by participants, with no notable adverse health effects or other concerns reported over the course of the experiment [96]. Although stimulation restored motor movement and activated spinal motoneurons, hence overcoming muscular paralysis, it had a temporary impact, with its effects quickly disappearing when the stimulator was switched off [216, 217].

Previously, it had been shown that the tsES was therapeutically viable and successful in terms of effectiveness and practicality [96]. Therefore, it was advised that further research should be done on the use of tsES in conjunction with tsR to observe long-term functional outcome in people with chronic SCI [96]. Some previous studies claimed that individuals with both acute and chronic SCI did not benefit from a six-week motor training program aimed at enhancing their capacity to sit unassisted [119, 218], while an 8-week training program on trunk muscles followed by eSCS exhibited immediate and reversible benefits in improving posture, reaching distance, and seated balance after a complete cervical SCI [183]. In this study, an intervention over a twelve-week period using tsES+tsR was administered, which produced long term and sustained functional improvement. The results of Rath et al. and Keller et al. about the effects of tsES on trunk stability during sitting showed an immediate effect on maintaining an upright posture [10, 63]. In another study, a preliminary evidence was provided in favor of intensive tsR for enhancing the ability of people with chronic SCI to sit independently, however the practical effects of the intervention effects used remained unknown [119]. In the current study, we demonstrated the efficacy of the combined treatment of tsES+ tsR in improving functional ability. The improvement was sustained even when tsR was delivered alone, which supported their findings [119]. Although prior investigations had shown that the tsES showed an immediate effect to maintain an upright sitting position in both adults and children with SCI [10, 63], and tsES had the potential to be an important additional therapy for people with tetraplegia to enhance trunk control and sitting function. One of the contributions of the present study is that we have demonstrated the long-term benefits of motor improvement.

4.7 Correlation between improvement of assessment parameters

There was a high correlation found between the TCT and FIST. The question arises as to why such a strong correlation was only seen between TCT and FIST. In the TCT and FIST assessments, there are several static and dynamic balancing activities involving the trunk. These activities provide a more stable sitting position [185, 219]. Consequently, when the trunk control was enhanced, the sitting function was also improved. This may explain why their correlation was stronger. The other assessment parameters showed weak or no correlation between them. The mFRT did not reveal a strong correlation with other outcome measures. A possible explanation for this may be that everyday life requires a wide range of motions, and the forward or lateral body movements alone may not be enough to accurately reflect the functional ability [155]. In addition, a previous study reported no correlation between mFRT and the mobility of the functional assessment of spinal cord independence measure-III in chronic SCI [155]. Similarly, the VICON results had no correlation with other functional assessment parameters. The possible reason could be that SCI individuals' capacity to flex or extend their trunks had no effect on sitting stability [136]. A moderate correlation was reported between FIST and mFRT in a previous study [219], while in the present study, a weak correlation existed between FIST and mFRT. The EMG showed a mild correlation with VICON, i.e., EMG activity was found to be increased during the trunk ROM. Yang et al. demonstrated that following trunk flexion in paraplegia, EMG measurements of the abdominal muscle group (RA, EO) showed an increased response [220]. Additionally, the EMG activity was substantially increased during the sitting pivot transfer task [221]. Interestingly, the present study revealed that there was a positive correlation between the EMG and FIST, but the other assessment parameters had weak or no correlation between them. This could be explained by the fact that the previous study [218], focused on assessing specific trunk motion, which might not reflect the trunk control and stability.

Chapter 5 Conclusion

5.1 Summary

The purpose of this research was to investigate if the combined administration of the tsES+tsR could sustainably improve trunk control and sitting function in people with complete tetraplegia. The findings showed that, in individuals with chronic complete cervical SCI, the tsES+tsR intervention improved independent trunk control with increased static and dynamic sitting balance, as well as the ability to perform upper-limb activities and perform functional tasks in sitting. This was demonstrated by an increase in trunk stability and sitting balance. In addition, our results found that forward and lateral reaching distances were increased, lowering the chance of falling from the wheel chair. Every technique that helps people with SCI improve or recover their sitting and postural stability is thought to be a significant improvement in their daily activities [198]. The increased trunk range of motion enhanced trunk mobility, facilitating daily tasks and decreasing reliance on the caregiver. Therefore, it was found in this study that, the tsES+tsR treatment elevated EMG responses of key trunk muscles (ES, EO, and LD). The sagittal spinal curvature was reduced, and the participants demonstrated an increased ability to maintain an erect posture with self-regulating control of upright sitting. The functional gains were sustained throughout tsR alone and follow-up, suggesting that the effects were long-lasting. Sensorimotor scores, on the other hand, did not alter much. Finally, the major improvements enabled people to transfer independently or with assistance from wheelchair to bed and vice versa, relieving the carers' physical stress. These findings have relevance for people with all types of SCI who seek functional rehabilitation after SCI. In contrast to previous research [10] that demonstrated the short-term effects of tsES, our results suggest that tsES+tsR may be used to produce the desired long-term effects. The present study demonstrated the effectiveness of tsES with tsR, showing functional recovery for people with complete chronic tetraplegia. However, the mechanism of combined treatment is still unknown. The possible mechanism could be that supraspinal adaptations contribute significantly to improve balance performance even following externally challenged balance training and facilitated by feed-forward mechanism [10]. Furthermore, the present results indicate the potential of developing a rehabilitation program for individuals with SCI who have impaired trunk control and seated instability in order to improve their stability and balance.

The major contributions of this study can be summarized as follows:

1. All the participants showed improved trunk and sitting function after the tsES+tsR.
2. The participants with C6 and C7 levels of injury demonstrated greater trunk stability compared to C4 and C5.
3. The increased reaching ability decreased the risk of falling from the wheelchair and enhanced the upper limb tasks.
4. The participants P1, P2, and P3 revealed a dynamic sitting balance, while P4 and P5 could maintain a static balance. Interestingly, P1 and P2 could perform the transfer task from bed to wheel chair and vice versa after the training.
5. The participants P1 and P2 started to use manual wheelchair with increased trunk ability and confidence after the training.
6. The 3D ultrasound scan showed correction of the sagittal spinal alignment and improved the participants' ability to maintain upright erect posture.
7. The improvement depends on the severity of SCI rather than frequency of treatment.
8. The functional improvements were preserved throughout the tsR and follow-up period demonstrating long-term effects of tsES.

5.2 Limitations of the study

The research described herein includes several limitations to this study. Firstly, it restricts the generalisation of its results, such as being unable to collect electrophysiological and kinesiological data at the beginning of the intervention. Secondly, the variability of SCI characteristics, i.e., individuals having different levels of tetraplegia that would affect their ability to perform the motor tasks. The severity of the injury has a direct impact on the rehabilitation success [199]. Thirdly, the difference in the sessions during intervention delivery and a smaller number of participants. Fourthly, although motor improvements were observed in all the participants irrespective of the unequal training sessions, greater functional gain was obtained in those with lower levels of tetraplegia, despite the fact that the sample was too small to make conclusive statements concerning these interactions. Fifthly, selection bias is a concern in this research since the individuals were not randomized and recruited via convenience sampling. Sixthly, electrophysiological and kinesiological assessments of subjects were conducted after 6 weeks of tsES+tsR. At the moment, it is uncertain if any gains made by participants will be maintained or improved over the intervention period. Seventhly, due to the cohort nature of this study, randomization of individuals into control and experimental groups was impractical, restricting the study's ability to detect cause and effect. The absence of proper instruments for evaluating seated trunk control could hamper its evaluation [205]. Eighthly, due to a sudden change in the individual's BP with a C4 level of injury, training was hampered due to the requirement for frequent pauses to prevent AD. Lastly, one participant suffered from skin rashes after the tsES, which took some days to resolve, necessitating the suspension of training.

5.3 Indications for future research

The present research demonstrated the effectiveness of tsES in improving the functional ability of chronic SCI individuals, 1.5 to 19 years following injury. Therefore, identifying the ideal time frame to initiate therapy is another critical objective in order to avoid the learned non-use and adaptations that occur after SCI. To confirm the present results, a larger population of subjects across a wider geographic region are necessary. In addition, further research using randomised controlled trials is recommended to confirm the findings of this investigation. And, more studies are recommended to determine whether other factors such as equal sessions of intervention delivery, body mass index (BMI), duration of injury, preserved upper limb function, and grasp function have an effect on the results. Future studies using a bigger sample size are also necessary to determine the impact of variables such as individuals' body composition, training, or practice in a variety of settings such as supine, sitting with support or unsupported, and so on. Moreover, future work should focus on investigating the evidence of improved quality of life and spinal cord independence measures after the effectiveness of tsES for trunk and sitting function is revealed. Further studies can also explore the effectiveness of tsES+tsR for traumatic brain injury paralysis to see if it has similar improvements in rolling movements during the mat activities, which are very essential for individuals with trunk impairments, especially tetraplegics. Furthermore, one major recommendation provided by this study is to recruit participants with stable vital parameters and preserved grip function to ensure smoother training.

5.4 Recommendations of tsES and tsR protocols for individuals with SCI

Our recommendation of the tsES protocol for SCI individuals has been described as follows: as each person has a different level of sensory impairment after SCI, the intensity shall be lower when starting, e.g., 60-80 mA for the trunk muscles (even if the subject reports no stimulus or effect). The pain assessment shall be conducted, and the best stimulation parameter shall be determined based on the individual's response. The skin sensitivity shall be examined as stimulation interrupts the delivery. The change in blood pressure was observed; therefore, continuous monitoring is required throughout the session. People with complete tetraplegia experience sudden episodes of postural hypotension, autonomic dysreflexia, etc., which may arise due to fatigue or a change in posture during training. Therefore, we recommend that the tsR protocol should divide a single session into many sub-sessions depending on the participant's capacity and keep continuous monitoring of heart rate and blood pressure.

APPENDICES

Appendix I: Consent form

THE HONG KONG
POLYTECHNIC UNIVERSITY
香港理工大學

CONSENT TO PARTICIPATE IN RESEARCH

Trans-spinal electrical stimulation for improving trunk and sitting function in tetraplegics with cervical cord injury

I ________________________ hereby consent to participate in the captioned research supervised by Prof. Yong-Ping Zheng.

I understand that information obtained from this research may be used in future research and publication(s). However, my right to privacy will be retained, i.e. my personal details will not be revealed.

The procedure as set out in the attached information sheet has been fully explained. I understand the benefit and potential risks involved. My participation in the project is voluntary.

I acknowledge that I have the right to question any part of the procedure and can withdraw at any time without penalty of any kind.

Name of participant: ____

Signature of participant: ____

Name of researcher: ____

Signature of researcher: ____

Date: ____

Hung Hom Kowloon Hong Kong 香港 九龍 紅磡

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Appendix II: International standards for neurological classification of spinal cord injury (ISNCSCI)

ASIA AMERICAN SPINAL INJURY ASSOCIATION — INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY (ISNCSCI) — ISCOS INTERNATIONAL SPINAL CORD SOCIETY

Patient Name ______ Date/Time of Exam ______

Examiner Name ______ Signature ______

RIGHT — MOTOR KEY MUSCLES — SENSORY KEY SENSORY POINTS: Light Touch (LTR), Pin Prick (PPR)

LEFT — SENSORY KEY SENSORY POINTS: Light Touch (LTL), Pin Prick (PPL) — MOTOR KEY MUSCLES

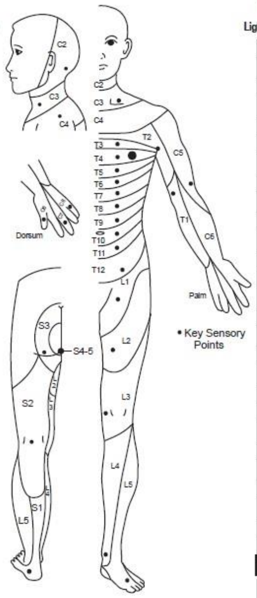
C2, C3, C4

UER (Upper Extremity Right) / **UEL** (Upper Extremity Left):

- C5 Elbow flexors
- C6 Wrist extensors
- C7 Elbow extensors
- C8 Finger flexors
- T1 Finger abductors (little finger)

Comments (Non-key Muscle? Reason for NT? Pain? Non-SCI condition?):

T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12, L1



MOTOR (SCORING ON REVERSE SIDE)

0 = Total paralysis
1 = Palpable or visible contraction
2 = Active movement, gravity eliminated
3 = Active movement, against gravity
4 = Active movement, against some resistance
5 = Active movement, against full resistance
NT = Not testable
0*, 1*, 2*, 3*, 4*, NT* = Non-SCI condition present

SENSORY (SCORING ON REVERSE SIDE)

0 = Absent
1 = Altered
2 = Normal
NT = Not testable
0*, 1*, NT* = Non-SCI condition present

LER (Lower Extremity Right) / **LEL** (Lower Extremity Left):

- L2 Hip flexors
- L3 Knee extensors
- L4 Ankle dorsiflexors
- L5 Long toe extensors
- S1 Ankle plantar flexors

S2, S3, S4-5

(VAC) Voluntary Anal Contraction (Yes/No)

(DAP) Deep Anal Pressure (Yes/No)

RIGHT TOTALS (MAXIMUM) (50) (56) (56)

LEFT TOTALS (MAXIMUM) (56) (56) (50)

MOTOR SUBSCORES

UER ___ + UEL ___ = UEMS TOTAL ___ — MAX (25) (25) (50)

LER ___ + LEL ___ = LEMS TOTAL ___ — MAX (25) (25) (50)

SENSORY SUBSCORES

LTR ___ + LTL ___ = LT TOTAL ___ — MAX (56) (56) (112)

PPR ___ + PPL ___ = PP TOTAL ___ — MAX (56) (56) (112)

NEUROLOGICAL LEVELS (Steps 1-6 for classification as on reverse) — R L — 1. SENSORY — 2. MOTOR

3. NEUROLOGICAL LEVEL OF INJURY (NLI)

4. COMPLETE OR INCOMPLETE? Incomplete = Any sensory or motor function in S4-5

5. ASIA IMPAIRMENT SCALE (AIS)

(In injuries with absent motor OR sensory function in S4-5 only) 6. ZONE OF PARTIAL PRESERVATION — Most caudal levels with any innervation — R L — SENSORY — MOTOR

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REV 04/19

Muscle Function Grading

0 = Total paralysis

1 = Palpable or visible contraction

2 = Active movement, full range of motion (ROM) with gravity eliminated

3 = Active movement, full ROM against gravity

4 = Active movement, full ROM against gravity and moderate resistance in a muscle specific position

5 = (Normal) active movement, full ROM against gravity and full resistance in a functional muscle position expected from an otherwise unimpaired person

NT = Not testable (i.e. due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of > 50% of the normal ROM)

0*, 1*, 2*, 3*, 4*, NT* = Non-SCI condition present *

Sensory Grading

0 = Absent 1 = Altered, either decreased/impaired sensation or hypersensitivity

2 = Normal NT = Not testable

0*, 1*, NT* = Non-SCI condition present *

* Note: Abnormal motor and sensory scores should be tagged with a '*' to indicate an impairment due to a non-SCI condition. The non-SCI condition should be explained in the comments box together with information about how the score is rated for classification purposes (at least normal / not normal for classification).

When to Test Non-Key Muscles:

In a patient with an apparent AIS B classification, non-key muscle functions more than 3 levels below the motor level on each side should be tested to most accurately classify the injury (differentiate between AIS B and C).

Movement	Root level
Shoulder: Flexion, extension, adbuction, adduction, internal and external rotation **Elbow**: Supination	C5
Elbow: Pronation **Wrist**: Flexion	C6
Finger: Flexion at proximal joint, extension **Thumb**: Flexion, extension and abduction in plane of thumb	C7
Finger: Flexion at MCP joint **Thumb**: Opposition, adduction and abduction perpendicular to palm	C8
Finger: Abduction of the index finger	T1
Hip: Adduction	L2
Hip: External rotation	L3
Hip: Extension, abduction, internal rotation **Knee**: Flexion **Ankle**: Inversion and eversion **Toe**: MP and IP extension	L4
Hallux and Toe: DIP and PIP flexion and abduction	L5
Hallux: Adduction	S1

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 at the most caudal sacral segments for voluntary anal contraction (VAC) OR the patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segments S4-5 by LT, PP or DAP), and has some sparing of motor function more than three levels below the ipsilateral motor level on either side of the body. (This includes key or non-key muscle functions to determine motor incomplete status.) For AIS C – less than half of key muscle functions below the single NLI have a muscle grade ≥ 3.

D = Motor Incomplete. Motor incomplete status as defined above, with at least half (half or more) of key muscle functions below the single NLI having a muscle grade ≥ 3.

E = Normal. 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.

Using ND: To document the sensory, motor and NLI levels, the ASIA Impairment Scale grade, and/or the zone of partial preservation (ZPP) when they are unable to be determined based on the examination results.

ASIA AMERICAN SPINAL INJURY ASSOCIATION

INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

ISCOS INTERNATIONAL SPINAL CORD SOCIETY

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Steps in Classification

The following order is recommended for determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
The sensory level is the most caudal, intact dermatome for both pin prick and light touch sensation.

2. Determine motor levels for right and left sides.
Defined by the lowest key muscle function that has a grade of at least 3 (on supine testing), providing the key muscle functions represented by segments above that level are judged to be intact (graded as a 5).
Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level, if testable motor function above that level is also normal.

3. Determine the neurological level of injury (NLI).
This refers to the most caudal segment of the cord with intact sensation and antigravity (3 or more) muscle function strength, provided that there is normal (intact) sensory and motor function rostrally respectively.
The NLI is the most cephalad of the sensory and motor levels determined in steps 1 and 2.

4. Determine whether the injury is Complete or Incomplete.
(i.e. absence or presence of sacral sparing)
*If voluntary anal contraction = **No** AND all S4-5 sensory scores = **0** AND deep anal pressure = **No**, then injury is **Complete**.*
*Otherwise, injury is **Incomplete**.*

5. Determine ASIA Impairment Scale (AIS) Grade.

Is injury Complete? If YES, AIS=A

NO ↓

Is injury Motor Complete? If YES, AIS=B

NO ↓ (No=voluntary anal contraction OR motor function more than three levels below the motor level on a given side, if the patient has sensory incomplete classification)

Are at least half (half or more) of the key muscles below the neurological level of injury graded 3 or better?

NO ↓ **AIS=C** — **YES** ↓ **AIS=D**

If sensation and motor function is normal in all segments, AIS=E
Note: AIS E is used in follow-up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact and the ASIA Impairment Scale does not apply.

6. Determine the zone of partial preservation (ZPP).
The ZPP is used only in injuries with absent motor (no VAC) OR sensory function (no DAP, no LT and no PP sensation) in the lowest sacral segments S4-5, and refers to those dermatomes and myotomes caudal to the sensory and motor levels that remain partially innervated. With sacral sparing of sensory function, the sensory ZPP is not applicable and therefore "NA" is recorded in the block of the worksheet. Accordingly, if VAC is present, the motor ZPP is not applicable and is noted as "NA".

Appendix III: Modified Functional Reach Test

Instructions:

- Instruct the patient to “Reach as far as you can forward without taking a step”

Consists of three conditions over three trials:

o Sitting with the unaffected side near the wall and leaning forward

o Sitting with the back to the wall and leaning right

o Sitting with the back to the wall leaning left.

Score sheet:

Date	Direction	Trial one (Practice)	Trial Two	Trial Three	Total (average of trial 2 and 3 only)

Appendix IV: Trunk Control Test for SCI

Item	Description of the task	Description of the scoring	Score
Static equilibrium			
1	Maintain initial position during 10 sec	Falls Need support of upper limbs Maintains position for 10 sec	0 1 2
2	Crosses one pelvic limb over the other	Falls Needs support of upper limbs to maintain position Maintains position for 10 sec	0 1 2
3	Same test as 2, but with other pelvic limb	Falls Needs support of upper limbs Maintains position for 10 sec	0 1 2
Dynamic equilibrium			
1	Touch the feet	Not done Requires support of upper limbs Touches feet with both hands	0 1 2
2	Lie down in supine decubitus position and return to initial position	Not done Requires aid of upper limbs Does this without aid	0 1 2
3	Roll onto right side	Not done Done	0 1
4	Roll onto left side	Not done Done	0 1
Dynamic equilibrium to carryout activities with upper limbs			
1	Place the dartboard mid-line at the height of glenohumeral joint 10 cm from point of the fingers and ask the individual to touch this with right hand	Not done Requires support of contralateral limb Done without support	0 1 2
2	Same as 1 with left hand	Not done Requires support of contralateral limb Done without support	0 1 2
3	Place dartboard 45° to the right of position 1 and ask individual to touch it with right hand	Not done Requires support of contralateral limb Done without support	0 1 2
4	Same as 3 but the dartboard moves 45° to the left	Not done Requires support of contralateral limb Done without support	0 1 2
5	Same as 3 with left hand	Not done Requires support of contralateral limb Done without support	0 1 2
6	Same as 4 with left hand	Not done Requires support of contralateral limb Done without support	0 1 2

Appendix V: Function in Sitting Test

FIST Test Item ½ femur on surface; hips & knees flexed to 90° = Used step/stool for positioning & foot support	**Date:**	**Date:**	**Date:**
Anterior Nudge: superior sternum			
Posterior Nudge: between scapular spines			
Lateral Nudge: to dominant side at acromion			
Static sitting: 30 seconds			
Sitting, shake 'no': left and right			
Sitting, eyes closed: 30 seconds			
Sitting, lift foot: dominant side, lift foot 1 inch twice			
Pick up object from behind: object at midline, hands breadth posterior			
Forward reach: use dominant arm, must complete full motion			
Lateral reach: use dominant arm, clear opposite ischial tuberosity			
Pick up object from floor: from between feet			
Posterior scooting: move backwards 2 inches			
Anterior scooting: move forward 2 inches			
Lateral scooting: move to dominant side 2 inches			
TOTAL	/ 56	/ 56	/ 56
Administered by:			
Notes/comments:			

Scoring Key:
- 4 = **Independent** (completes task independently & successfully)
- 3 = **Verbal cues/increased time** (completes task independently & successfully and only needs more time/cues)
- 2 = **Upper extremity support** (must use UE for support or assistance to complete successfully)
- 1 = **Needs assistance** (unable to complete w/o physical assist; **document level: min, mod, max**)
- 0 = **Dependent** (requires complete physical assist; unable to complete successfully even w/physical assist)

Appendix VI: Ethical Approval

THE HONG KONG POLYTECHNIC UNIVERSITY
香港理工大學

To	Zheng Yongping (Department of Biomedical Engineering)		
From	Yang Mo, Chair, Departmental Research Committee		
Email	mo.yang@	Date	09-Jan-2020

Application for Ethical Review for Teaching/Research Involving Human Subjects

I write to inform you that approval has been given to your application for human subjects ethics review of the following project for a period from 01-Mar-2019 to 28-Feb-2022:

Project Title:	Trans-spinal electrical stimulation along with body-weight-support training to restore walking in paraplegic patients
Department:	Department of Biomedical Engineering
Principal Investigator:	Zheng Yongping
Project Start Date:	01-Mar-2019
Reference Number:	HSEARS20190201002-01

You will be held responsible for the ethical approval granted for the project and the ethical conduct of the personnel involved in the project. In case the Co-PI, if any, has also obtained ethical approval for the project, the Co-PI will also assume the responsibility in respect of the ethical approval (in relation to the areas of expertise of respective Co-PI in accordance with the stipulations given by the approving authority).

You are responsible for informing the Human Subjects Ethics Sub-committee in advance of any changes in the proposal or procedures which may affect the validity of this ethical approval.

Yang Mo

Chair

Departmental Research Committee (on behalf of Human Subjects Ethics Sub-Committee)

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