THE EFFECT OF HOME-BASED ARM TRAINING ON TRUNK CONTROL FOLLOWING SPINAL CORD INJURY: a pilot study

by

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MASTERS BY RESEARCH

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Abstract

Objective: This is a pilot and feasibility study to investigate the effects of a home-based arm cycling intervention on corticospinal excitability and neuromuscular control of trunk muscles in people with spinal cord injury (SCI).

Methods: Seven participants with chronic, incomplete cervical or thoracic SCI (mean age± SD: 57± 15 years; cervical SCI; 5) undertook 30 minutes of arm cycling exercise at home, 5 consecutive days a week for six weeks. Assessments were performed before, during and after the exercise intervention. Corticospinal excitability was assessed using transcranial magnetic stimulation (TMS) eliciting motor evoked potentials (MEPs) in the erector spinae (ES) muscle. Trunk function was evaluated using multidirectional reaching, rapid shoulder flexion and perturbation tasks. Movement trajectory of the upper limbs and the trunk and the centre of pressure (COP) were recorded using a 3-D motion capture system and a force platform. Neuromuscular function of the ES muscles during the tasks was assessed using high-density electromyography (HDEMG). Three participants took part in a virtual focus group after completion of the study.

Results: Participants improved lateral reaching distance and reaction times with increased muscle activity during the rapid shoulder flexion task after the exercise intervention. This indicates improvement of voluntary control of the trunk after the intervention. A trend for increased amplitudes of ES MEPs was observed after the exercise intervention, suggesting arm exercise-induced neuroplasticity in corticospinal pathways projecting to the ES muscle. Furthermore, focus group data revealed that the intervention had both physical and psychological benefits to the participants.

Conclusions: Six weeks of home-based arm cycling intervention improved dynamic sitting balance (i.e. increased reaching distance) and neuromuscular function of the ES muscles in people with SCI. Our findings suggest this exercise programme to be feasible for trunk rehabilitation in patients with chronic, incomplete SCI.

Acknowledgments

I would like to thank Dr Chloe Chiou for her continued support, encouragement and enthusiasm whilst supervising me throughout this project and over the past couple of years. An additional thank you to Dr Eduardo Martinez-Valdes and Dr Andy Sanderson for their support and guidance. I would also like to thank to all of the participants involved in the study for making this project possible. Lastly, thank you to my friends and family for your endless support during this project and throughout the COVID-19 global pandemic.

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1. Introduction

1.1 Spinal cord injury and quality of life

Spinal cord injury (SCI) is a serious, life-altering incident which significantly impacts on an individual's way of life (Lynch and Cahalan, 2017; WHO, 2013). SCI often leads to the loss or reduction of voluntary muscle activity and autonomic function (sia, 2009). SCI can have severe complications and consequences impacting on many bodily systems (Anderson et al., 2007; Klotz et al., 2002), with studies associating SCI to conditions such as; spasticity, neuropathic pain, neuromotor, sexual, bladder and bowel dysfunction (Hicken, Putzke and Richards, 2001; Akkoc, 2005; Lundqvist et al., 1991; Westgren and Levi, 1998). Worldwide, there are 40 million new cases every year (Nas et al., 2015) with SCI, and the associated complications, having a drastic impact on an individual's quality of life (QOL) (Lude et al., 2014; Tulsky and Kisala, 2015). In the United Kingdom (UK) survivors of neurological injuries have the lowest health-related QOL of any long-term disabilities (NHS England, 2019). Depression is closely linked to lower QOL (Hartoonian et al., 2014; Dijkers, 2005; Post and Noraeu, 2005) and is related to slower recovery, further health complications (Herrick, Elliott and Crow. 1994) and increased disability level (Hartoonian et al., 2014; Tate et al., 1994). Rehabilitation is critical for providing maximal functional recovery and QOL (Richard-Denis et al., 2020), with the overall aim of rehabilitation being to enable individuals to live productive and meaningful lives (Harvey, 2016). This therefore highlights the pivotal importance of rehabilitation on an individual's QOL and mental health.

1.2 Trunk Rehabilitation

Regaining adequate sitting balance is a key and important aim of rehabilitation for paraplegics (Chen et al., 2003). Despite the well-known physical and mental health benefits of physical activity (Nightingale et al., 2018; Kroll et al., 2012; Froehlich-Grobe et al., 2014; Sweet, Martin Ginis and Tomasone, 2013; Tomasone et al., 2013), research suggests SCI patients perform little to no physical activity (Martin Ginis et al., 2010; Tanhoffer et al., 2014; Tanhoffer et al., 2015). The rehabilitation process for SCI is timely and expensive highlighting biophysical, psychosocial and economic implications (Nas et al., 2015; Pickett et al., 2006). SCI rehabilitation is an ongoing process extending into life-long treatment (Nas et al., 2015), requiring long-term therapist input. However, patients requiring NHS physiotherapy can wait to up 6 months and receive fewer sessions due to NHS cuts and staff shortages (Campbell, 2011), demonstrating financial and economic barriers to rehabilitation. A lack of equipment (Nightingale et al., 2018; Fekete and Rauch, 2012; Stephens, Neil and Smith, 2012) and reduced motivation (Williams, Smith and Papathomas, 2014) are also identified as key barriers for exercise in SCI patients. During SCI rehabilitation physiotherapists are often guided by other specialities due to the lack of high-quality trials involving SCI patients and specifically trunk rehabilitation (Harvey, 2016; Munn et al., 2005). The importance of trunk control in SCI is well known, but despite this there are currently no standardised, valid clinical outcome measures to evaluate trunk control in SCI (Quinzaños et al., 2014). Although different functional training methods have been assessed in SCI, there are no definitive conclusions regarding the most effective or standardised methods (Kakade and Kanase, 2020). Current interventions often use exercise directly or indirectly involving trunk muscles, with exercises specifically focusing on core

stability or alternatively utilising whole body or upper-body exercises to target the trunk. For example, a study conducted by Kakade and Kanase, (2020) found that a six week programme of core and lower limb muscle strengthening improved strength and functional capacity of the core and lower limbs. However a study by Galea et al., (2018) found that a full body exercise programme over 12 weeks did not improve ASIA motor scores compared with upper body training in chronic SCI. The full-body exercise programme involved locomotor training, FES-assisted cycling and trunk and lower limb extremity exercises including motor imagery, resistive exercises and practicing functional tasks. It is possible that this study did not find significant improvements due to the clinical outcome used; ASIA testing is not as sensitive to detecting improvements than that of manual muscle testing as utilised in the study by Kakde and Kanase (2020). Other types of rehabilitation for SCI include; wheelchair tai chi (Qi et al. 2018), virtual reality balance exercises (Sengupta et al. 2020) and hippotherapy (Choi et al. 2013). Qi et al., (2018) conducted a wheelchair tai chi study involving an intensive programme with 16-wheelchair tai chi movements, utilising the upper limb and challenging core strength. They found it to be effective in improving static sitting balance, left handgrip strength and psychological domain of QOL when compared to a control group. A further SCI rehabilitation method is community based circuit training classes. A study by Sliwinski et al., (2020) found that a weekly community exercise programme, for eight weeks, including a four station training circuit of resistance exercises, aerobic conditioning, trunk stability and health education improved forward functional reach and QOL reported by participants. These studies demonstrate the additional importance of exercise programmes on improving QOL following SCI. Although trunk training exercises following other neurological injuries, such as stroke, are also not well documented, there is some

existing evidence into different modalities utilised (Cabanas-Valdés, Cuchi and Bagur-Calafat, 2013) which include; an exercise programme involving unstable supporting surfaces (Karthikbabu et al., 2011) and reaching tasks in a seated position (Dean and Shepherd, 1997). In stroke populations, 30 minutes of trunk rehabilitation in addition to conventional rehabilitation is recommended, with intensive rehabilitation programmes involving at least thrice weekly sessions (Cabanas-Valdés, Cuchi and Bagur-Calafat, 2013). The optimal duration is unclear but it is suggested the best results in trunk performance and dynamic sitting balance are observed following an eight week intervention (Saeys et al., 2012). This therefore identifies the need to establish a patient-driven, cost-effective and timely rehabilitation protocol for improvements in trunk control in SCI patients.

1.3 Postural control and movement kinematics

Maintaining upright trunk stability is essential for activities of daily living (ADLs) (Gabison et al., 2014; Chen et al., 2003; Sprigle, Maurer and Holowka, 2007). Dynamic postural control is a complex process involving coordinated actions from the sensorimotor and biomechanical components of the central nervous system (CNS) (Chen et al., 2003). These processes are often impaired following SCI as a result of altered neuromuscular control and sensory information being transmitted along the spinal cord (Shin and Sosnoff, 2013; Seelen et al., 1997; Seelen et al., 2001). The ability to simultaneously maintain an upright sitting position whilst utilising the upper limbs is also challenging for SCI patients (Hastings, Ntsiea and Olorunju, 2015; Scivoletto et al., 2003). This again poses a huge problem for paraplegics as many ADLs, such as eating, washing and dressing, are performed from a seated position (Chen et al., 2003).

In order to maintain postural stability, an individual must keep or return the centre of mass (COM) over the base of support (BOS) in a static or dynamic scenario (Chen et al., 2003). Prior to upper limb initiation, in a seated position, activation of a number of trunk muscles, such as erector spinae (ES) and rectus abdominis, occurs to stabilise the body, keeping the COM over the BOS (Gabison et al., 2014; Tyler and Hasan, 1995).

Anticipatory and compensatory postural adjustments occur in preparation and in response to perturbations respectively to maintain balance (Alexandrov et al., 2005; Hall et al., 2010). During anticipatory postural adjustments (APA), corticospinal output is modulated in preparation for movement at the supraspinal level (Federico and Perez, 2017; Chen et al., 1998; Leocani et al., 2000). Whereas, compensatory postural adjustments (CPA) are controlled by feedback control mechanisms (Kanekar and Aruin, 2014) to restore balance following movement (Park et al., 2004; Alexandrov et al., 2005). It is unknown to what extent these mechanisms are persevered following SCI (Federico and Perez, 2017; Chen et al., 1998; Leocani et al., 2000).

It is, however, well documented that postural control is impaired after SCI, with altered APAs and CPAs being a contributing factor. Many studies have reported increased postural sway, during seated positions, in SCI patients compared to their healthy counterparts, indicating reduced postural stability and compromised sitting balance (Milosevic et al., 2015; Shirado et al., 2004; Grangeon et al., 2012). Milosevic et al., (2015) found that in an upright seated position, without back support, the magnitudes of overall COP postural sway were at least twice as large in the SCI participants compared with healthy participants. Grangeon et al., (2012) found in neutral sitting or with the dominant or non-dominant arm extended, SCI participants

demonstrated larger mean COP displacements. Impaired sitting balance is also known to consequently cause an altered sitting strategy (Milosevic et al., 2015), resulting in an increased posterior pelvic tilt and increased thoracolumbar kyphosis to increase the BOS (Gabison et al., 2014; Triolo et al., 2013; Hobson and Tooms, 1992) and therefore hinders functional reach (Gabison et al., 2014; Sprigle et al., 2003).

1.4 Altered neuromuscular function of the trunk muscles after SCI

Individuals with SCI often adopt altered postural strategies (Do, Bouisset and Moynot. 1985), with tendencies to recruit innervated, non-postural muscles, such as their pectoralis major and trapezius muscle to regulate sitting balance as compensatory strategies (Seelen et al., 1998; Seelen et al., 1997; Seelen and Vuurman, 1991). This can occur by fixating the upper limbs and upper thoracic muscles to compensate for a posteriorly rotated pelvis to maintain balance. For example, research using bipolar surface electromyography (EMG) has shown increased activity in latissimus dorsi and the ascending part of the trapezius muscle during a bimanual, seated, forward-reaching task in individuals with SCI compared with able-bodied participants (Potten et al., 1999). Although conventional bipolar surface EMG is the standard way to measure muscle activity, high-density EMG (HDEMG) allows for a more detailed insight to activity across the muscle (Drost et al., 2006). HDEMG can record inputs from multiple electrodes placed over one muscle (Drost et al., 2006) which increases sensitivity in detecting changes in muscle activation and allows for more reliable recordings (Martinez-Valdes et al., 2019; Martinez-Valdes et al., 2017; Gallina et al., 2016; Martinez-Valdes et al., 2018).

HDEMG can also provide insight into the spatial distribution of muscle activity, in which conventional bipolar EMG is unable to provide (Sanderson et al., 2019). Following neurological injury, some muscle groups have no or reduced innervation, which can lead to altered motor control causing reduced strength, altered coordination and spasticity. Rehabilitation can contribute to improved motor control and could allow improved functionality of affected muscles or compensatory muscles to improve function (Jordanic et al., 2016). Therefore assessing spatial distribution and muscle activation in detail using HDEMG across a wider area is of paramount interest following rehabilitation. To the best of my knowledge this is the first study to investigate HDEMG in trunk muscles following SCI. However, research in low back pain (LBP) populations have found alterations in the spatial distribution of muscle activity in symptomatic patients compared with asymptomatic patients (Sanderson et al., 2020; Sanderson et al., 2019). A recent study found that the centroid of erector spinae EMG amplitude is activated in a more caudal direction in LBP patients during a repetitive mono-planar lifting task, indicating altered muscle distribution (Falla et al., 2014). It is unknown whether SCI patients demonstrate altered muscle activations during movement as well, however Sung et al., (2015) found LBP patients had decreased trunk motor control, during unstable sitting, which could suggest impaired central processing, proprioception and motor output, similarly to SCI patients. Further research is needed utilising HDEMG to investigate alterations in volitional recruitment of trunk muscles in people with SCI using HDEMG.

1.5 Pathological changes and corticospinal reorganisation after SCI

The corticospinal pathway significantly contributes to motor control and movement (Lemon, 2008) and has therefore become a target for investigating motor

recovery following SCI in recent decades. Predominantly, the corticospinal tract is a crossed pathway, interacting with both hemispheres (Bunday and Perez, 2012; Brus-Ramer et al., 2009; Ferbert et al., 1992; Lemon, 2008). Approximately 10% of the corticospinal pathway is uncrossed and accounts mainly for the projection to the upper limbs and trunk (Carson et al., 2004). In humans the corticospinal pathways can be assessed non-invasively by stimulating the primary motor cortex via transcranial magnetic stimulation (TMS) (Barker, Jalinous and Freeston, 1985; Amassian, Quirk and Stewart, 1990; Ellaway et al., 2007). TMS elicits motor evoked potentials (MEPs) in paravertebral muscles which can be recorded by surface EMG for offline analysis (Ellaway et al., 2007).

MEPs elicited by TMS, in acute and chronic SCI, provide information on corticospinal functional integrity (Oudega and Perez, 2012). Following SCI, research has shown decreased corticospinal synaptic drive to musculature (Bunday and Perez, 2012; Hansen et al., 2005; Norton and Gorassini. 2006), due to neuropathophysiological changes occurring as a result of the injury. For example, there is atrophy of corticospinal neurones (McBride et al., 1989; Tang et al., 2004; Carter et al., 2008) with progressive fragmentation and Wallerain degeneration occurring soon after the injury has occurred (Hill, Beattie and Bresnahan, 2001). Degeneration and demyelination of corticospinal axons contributes to delayed latencies and reduced amplitudes (Bronson et al., 1978; Fishman, 1987; Yamamoto et al., 1989; Bunday and Perez, 2012; Barthélemy et al., 2010; Ellaway et al., 2007; Thomas and Gorassini. 2005). These pathological changes following SCI result in impaired neuromuscular control, leading to un-coordinated muscle movement, spasticity and reduced muscle activity (Jordanic et al., 2016). This in turn results in

reduced function and SCI patients' ability to carry out activities of daily living (ADLs) (Chen et al., 2003).

As a result of damage after a SCI, the corticospinal tract undergoes extensive reorganisation (Oudega and Perez, 2012), with extensive injury-induced sprouting, close to and away from the lesion site, being reported (Fouad et al., 2001; Fouad et al., 2011; Ghosh et al., 2009: Onifer, Smith and Fouad, 2011). It has also been demonstrated that corticospinal neurones acquire a modifiable and immature pattern of connectivity (Kim et al., 2006). A review by Oudega and Perez (2012) concluded these anatomical and electrophysiological changes within the corticospinal tract, that occur following injury, demonstrate the potential for neuroplasticity and functional recovery.

1.6 Neural interaction between upper limbs and the trunk in SCI

It has been well established that the amplitude of MEPs in a resting arm muscle can be increased by voluntary contractions of the contralateral arm muscle, in a phenomenon known as crossed facilitation (Bunday and Perez, 2012; Hortobagyi et al., 2003; Muellbacher et al., 2000; Perez and Cohen, 2008; Perez and Cohen, 2009; Stedman et al, 1998). This phenomenon involves transmission changes at cortical and spinal cord levels (Bunday and Perez, 2012; Meyer et al, 1995; Muellbacher et al., 2000; Perez and Cohen, 2008). Studies report that crossed facilitation is impaired after SCI and the severity of the impairment is associated with the level of injury (Bunday, Oudega and Perez, 2013). A study involving participants practicing a right index finger ballistic task, found improved function and corticospinal excitability bilaterally; suggesting that unilateral tasks have the potential to generate bilateral cortical activity for crossed hemispherical improvement (Lee et al., 2010).

Another study found that during left wrist flexion, MEPs were evoked in the right arm muscles via TMS over the left motor cortex (M1). Cathodal direct-current (DC) over the M1 was then found to counteract crossed-facilitatory effects to the right wrist muscles; demonstrating corticospinal excitability can be altered by DC stimulation ipsilateral to simulation hemisphere (Carson et al., 2008). Crossed facilitation may also contribute to enhanced motor performance after repeated training (Lee et al., 2010; Perez et al., 2007). Previous research has demonstrated that unilateral training of one limb facilitated the MEP amplitude of the contralateral homologous muscles (Carroll et al., 2008; Carson et al., 2004), highlighting the potential of utilising crossed facilitation to improve motor skills.

Several lines of evidence have shown the association between corticospinal excitability and motor function with TMS and coherence analysis studies demonstrating the importance of the corticospinal pathway in the functional recovery following SCI (Oudega and Perez, 2012). Rehabilitative techniques have been shown to promote corticospinal reorganisation following SCI and have the potential to elicit corticospinal sprouting, contributing to neuroplasticity (Fouad et al., 2000; Girgis et al., 2007; Krajacic et al., 2010). For individuals with incomplete SCI, daily locomotor training for 3-5 months increased the MEPs of the leg muscles. These changes in MEP were also significantly correlated to locomotor recovery, indicating increased corticospinal drive resulted in increased function (Thomas and Goarassini, 2005).

Studies have demonstrated that arm movements concurrently cause increased trunk muscle activity (Chiou, Strutton and Perez, 2018; Aruin and Latash, 1995; Benvenuti et al., 1997; Bouisset and Zattara, 1987; Hodges and Richardson 1997b). The direction and selection of upper limb muscles have been shown to

influence ES EMG (Chiou, Strutton and Perez, 2018; Marcolin et al., 2015; Hodges and Richardson, 1997b). Furthermore, studies have demonstrated the interaction between physiological pathways controlling the arms and trunk with corticospinal excitability of trunk muscles increasing with voluntary muscle activation of arm muscles in healthy adults (Davey et al., 2002; Chiou et al., 2018). Moreover, research has shown in some SCI patients, crossed facilitation was preserved in the trunk muscles, which was also related to trunk control of those patients (Chiou and Strutton, 2020), suggesting functional relevance of the crossed facilitation between the arms and the trunk. Recent evidence suggests that the crossed facilitation between the upper limbs and trunk may have clinical applications. Corticospinal excitability of the trunk has been found to be increased after rhythmic arm cycling in healthy adults (Chiou et al., 2020) which is in line with investigations of crossed facilitation in upper limbs, highlighting the potential of inducing neuroplasticity in the corticospinal pathways projecting to the trunk muscles via the use of upper-limb exercise.

There is increasing evidence that regular exercise induces cortical plasticity in humans (Cirillo et al., 2009). Neuroplasticity has also been demonstrated following SCI, with sprouting of axonal connections influencing brain-spinal cord connectivity (Loy and Bareyre, 2019). Following cervical SCI, intense, repetitive training can enhance cortical plasticity (Beekhuizen and Field-Fote, 2005; Hoffman and Field-Fote, 2007; Winchester et al., 2005). This indicates the importance of regular training to induce plasticity and improve function following SCI.

1.7 Rationale for inducing neuroplasticity in corticospinal projections to the trunk muscles via the use of upper limbs

Upper limb exercise has been shown to be an effective form of aerobic exercise for SCI patients (Williams et al., 2020; Devillard et al., 2007), with some studies commenting on its ability to improve sitting balance (Williams et al., 2020; Bjerkefors, Carpenter and Thorstensson, 2007; Grigorenko et al., 2004; Tsang et al., 2015). Arm-cycling exercise challenges trunk muscles in stabilising posture as a result of trunk movement during pedalling (Hill et al., 2018; Di Blasio et al., 2009). Williams et al., (2020) demonstrated arm-cycling exercise to be effective in engaging trunk muscles and found that a five-week, thrice weekly, exercise programme improved static sitting balance. They found that unsupported arm cycling improved cardiopulmonary fitness whilst also being effective in evoking trunk muscle activity as measured by surface EMG. They found significantly improved static sitting balance with eyes closed as seen by reduced COP velocity and area. An arm-cycle ergometer could therefore provide an accessible intervention that does not require specialist support for trunk function. Adaptive sports and upper body training programmes have been found to improve overall quality of life, cardiovascular fitness and muscle strength (Martin Ginis, Jörgensen and Stapleton, 2012; Devillard et al., 2007).

Although regular, supervised arm-crank ergometry (ACE) has been shown to have benefits in improving static sitting balance (Williams et al., 2020; Hill et al., 2018), whether these same effects can be seen in a home-based, patient-driven, unsupervised environment is unknown. Although arm-cycling is often utilised to improve cardiopulmonary fitness, further research is needed to investigate whether it can improve disability and other clinical outcomes, such as QOL. Furthermore,

previous research has not investigated the underpinning mechanisms leading to cycling-induced improvement in balance control. Hence, the aims and hypotheses of this study were to investigate whether a 6-week, home-based arm-cycling intervention is a feasible rehabilitation protocol for improving trunk control after SCI and its underlying mechanisms. We also aimed to investigate psychological and self-perceived improvements and benefits during a focus group conducted at the end of the study. We hypothesised that arm cycling training increases corticospinal drive to the trunk muscles via the crossed facilitatory interactions between the arms and the trunk, resulting in improved trunk control alongside perceived self-improvements.

2. Methods

2.1 Ethics

The study was approved by the Health Research Authority, Health and Social Care Research Ethics Committee (19/NI/0075) to recruit patients from the Midland Centre for Spinal Injuries (MCSI) and people living in the local community. Prior to study commencement, participants were given a study information booklet (Appendix 1), and were subsequently invited to the University as an opportunity for them to see the laboratories and ask questions. They were given appropriate time to consider their participation in the study. Those who agreed to take part provided written, informed consent prior to the experiment. Participants were informed on their right to withdraw from the study at any time and were asked to keep the researchers informed on any changes in health.

2.2 Study design

A prospective, longitudinal study, involving four experimental visits to the University, were conducted over a six week period, all visits at two-week intervals. Functional and neurophysiological assessments were carried out prior to (week 1) and after (week 6) the six week exercise intervention. Additional neurophysiological assessments (week 2 and week 4) were performed to monitor progressive changes in corticospinal function (Figure 1). It is logical to expect neuroplasticity comes before functional improvements with research demonstrating training-induced neuroplasticity leading to functional improvements (Fouad and Tetzlaff, 2012).

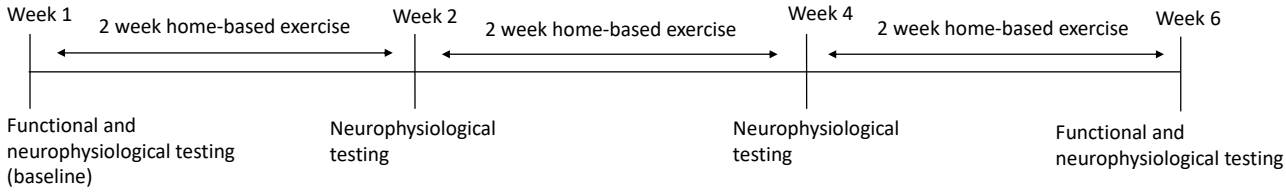

Figure 1: The study layout

2.3 Participants

Individuals with chronic (≥ 1 year), incomplete (categorised as C or D by the American Spinal Injury Association Impairment Scale, ASIA) cervical or thoracic spinal cord injury (SCI) were recruited. Participants were only included in the study if they could maintain independent sitting balance for at least 30 seconds and if they had functional use of their upper to limbs to allow for completion of the arm cycling. Individuals with contraindications to the TMS (e.g. epilepsy or a family history of epilepsy, recurrent or unexplained loss of consciousness) were excluded (Rossi et al., 2011).

A convenient sample size of 15 participants was used for this pilot study. The study recruitment started in October 2019 but was suspended in March 2020 due to covid-19 pandemic. Hence, seven individuals with SCI were recruited in the study (56.6 years±14.5; cervical SCI: 6; thoracic SCI: 1; Table A and B). Six participants were recruited from the MCSI, one participant was recruited from the community via online advertisements.

All seven participants completed the neurophysiological assessment; six participants underwent the functional assessment, with one participant being excluded as they were unable to transfer safely from their wheelchair for balance assessments.

A

	Mean	SD	Range
AGE (YEARS)	56.6	14.5	40-80

TIME SINCE INJURY (YEARS)	12.4	20.6	3-59

Table A: Demonstrates group participant characteristics of our SCI participants

B

	LEVEL OF INJURY	ASIA SCORE	Time since injury (years)	Type of injury
P01SS	C5/6	ASIA C	4	Traumatic
P02PB	T4	ASIA D	7	Non-traumatic
P03SS	C6/7	ASIA D	81	Traumatic
P04MB	C5/6	ASIA C	3	Traumatic
P05ML	C3/4	ASIA D	5	Traumatic
P06MN	C5/7	ASIA C	4	Traumatic
P07AS	C3/4	ASIA D	5	Traumatic

Table B: Individual characteristics of our SCI participants

2.4 Instrumentation

Part i: Functional assessment

a) Motion and force plate

A 3-D motion capture system (BTS Bioengineering S.p.A., Milanno, Italy; SMART-Suite, SMART-DX6000) was used for functional assessment to record movement trajectories. Reflective markers were placed on the spinous process at the 1st thoracic vertebral level (T1) and the ulnar styloid of the forearm bilaterally to record trunk and wrist movements respectively (Field-Fote and Ray, 2010). A force plate was used to record sway of Centre of Pressure (CoP) (BTS Bioengineering S.p.A., Milano, Italy; BTS P-6000; 40x60cm). Motion and force platform data were both sampled at 250Hz and recorded for data analysis.

b) High-density electromyography (HDEMG):

Activity of erector spinae (ES) muscles was detected using two 13x5 cm HDEMG electrodes (Quattrocento, OT Bioelettronica, Italy) bilaterally placed over the muscle bellies. Using surface palpation, the caudal medial-lateral edge of the electrode was

placed at the 12th thoracic level, allowing the electrodes to cover T12 to T6, the selection of this region allows us to understand improvements in muscle activation and movement patterns below the level of injury in our participants. Prior to electrode placement the skin was prepared using gentle skin exfoliation and alcohol wipes to reduce impedance. A double-sided adhesive foam was then attached to the electrode surface (SPES Medica, Genoa, Italy), followed by the application of a highly conductive-adhesive paste to fill the electrode chambers (AC-CREAM, SPES Medica, Genoa, Italy).

The electrode signals were all processed through a bioelectrical amplifier. The HDEMG signals were recorded in the monopolar montage and converted via the amplifier with a 16-bit analogue-digital convertor, with a gain of 150 and sampling frequency of 2048 Hz. The signals were recorded with a band-pass filter with a cut-off frequency between 10-450 Hz.

Part ii: Neurophysiological assessment

a) Bipolar EMG

Activity of the ES muscles were recorded bilaterally using surface bipolar EMG during TMS data collection (Delsys® Bagnoli-EMG system). A pair of recording bars (19.8mm X 35 mm) were placed over the muscle bellies of the ES at 12th thoracic vertebral level, found via the same surface palpation. Muscle activity was also recorded from biceps brachii (BB) bilaterally. Ground electrodes were placed at C7 and the left olecranon. EMG signals were pre-amplified (1000x) and band-passed filtered between 20 and 450 Hz before being sampled at 1 kHz by a micro 1401 (CED, Cambridge, UK). Data was acquired, stored and analysed by Signal software (version 6, CED, Cambridge, UK).

b) Transcranial magnetic stimulation (TMS)

TMS was delivered using a Magstim 200^2 stimulator with a monophasic current waveform connected to a double-cone coil (outside coil diameter: 110mm; The Magstim Company Ltd, UK). The coil handle was pointed vertically upwards (Chiou et al., 2016; Chiou et al., 2018). The coil was moved around the trunk representation area of the primary motor cortex (M1) until visible MEPs that can be distinguished from the background EMG could be recorded in the contralateral ES muscle using bipolar EMG (figure 2). We did not assess motor threshold because the majority of our participants required high TMS intensity and would not tolerate further testing. The hemisphere in which the largest and most reliable MEPs could be obtained from the contralateral ES muscle was decided as the targeted hemisphere. When a visible MEP could not be elicited by stimulating either hemisphere, the coil was placed on the vertex of the head (N=2) in order to stimulate both hemispheres at the same time, to give no bias towards a hemisphere. The position of the coil was recorded using a neuro-navigation system (Brainsight 2, Brainbox, Ltd, UK; figure 3) and used throughout the experiment. The same coil position was also used at subsequent visits to reduce coil placement variability as a confounding variable. Stimulus intensity was chosen individually to elicit visible MEPs in the contralateral ES muscles (intensity: mean±SD % maximum stimulator output (MSO)).

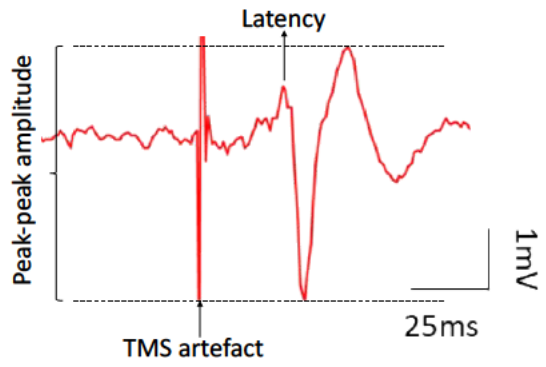

Figure 2: An example of an ES MEP elicited by TMS over the primary motor cortex (M1), demonstrating TMS artefact, latency and peak-peak amplitudes

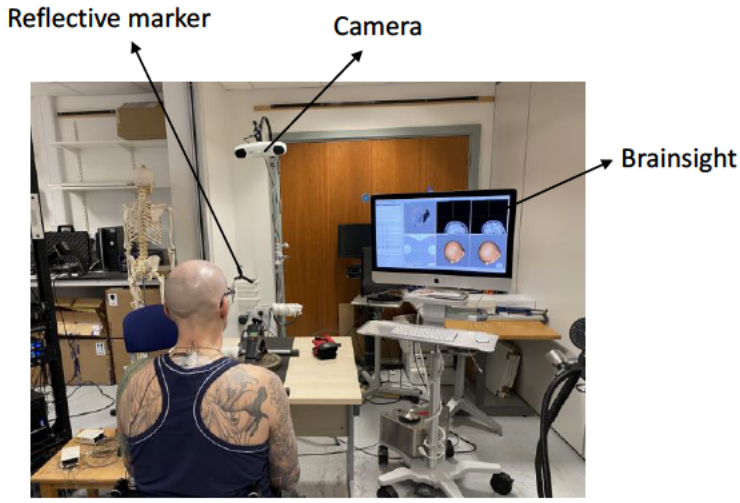

Figure 3: The laboratory set up for the Brainsight.

2.5 Assessments

Part i: Functional testing

To examine trunk motor control, participants were seated on a custom-made chair with an embedded force plate. Their torso was unsupported, hips and knees flexed at 90°, and feet placed on the floor. They were asked to undergo a number of tasks: 1) multidirectional reaching, 2) perturbation task, and 3) rapid shoulder flexion (RSF). Participants were given a description and demonstration of each task by the researcher, but not allowed to practise the task. All participants were supervised on the force-platform at all times by at least one researcher to ensure safety. Although

during our study, participants had their feet on in-floor force platforms, the signals were small and unclear, suggesting that there was not significant weight distribution through the lower limbs. However, future studies could incorporate more sensitive force platforms during the lower limbs to investigate this further.

a) Multidirectional reaching tasks

Participants were asked to reach forward (figure 4), and to left and right directions (figure 5) without assistance. The instruction was '*with your arm starting at your side, bring it up to 90° and reach as far as you can, then bring your arm back into the starting position and lower it down to your side*'. Participants completed reaching towards each direction three times.

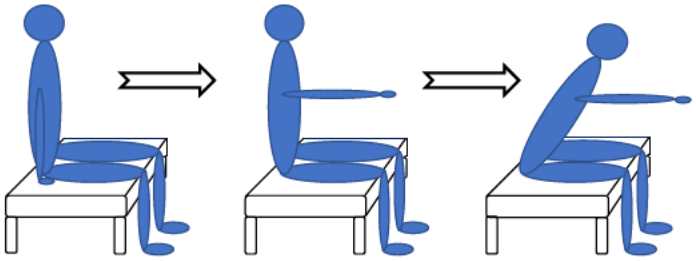

Figure 4: The forward reaching task whilst sat on the force platform

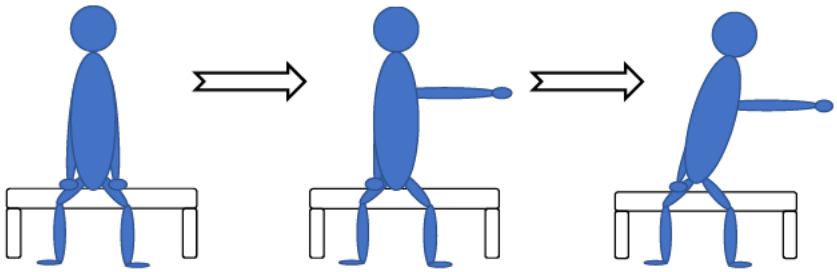

Figure 5: The lateral reaching task whilst sat on the force platform

b) Perturbation task

To examine postural adjustments of the trunk to an external perturbation, we used a previously described method using a pendulum; involving a weight of 10% of

the body mass of the individuals being released form a 45° angle towards an extended arm of the participants (figure 6) to create the external perturbation (Aruin et al., 2015). All participants used their right arm as their target arm, maintaining sitting balance can be difficult for this population whilst having both arms extended out, therefore one arm was used, with the right arm for all participants allowing for standardisation. They were seated upright and held the target arm straight at 90° of shoulder flexion; the other arm was rested on their thigh. They were instructed to maintain their balance, not allowing the weight to move them. The length of the pendulum was adjusted to be levelled to the shoulder height of the participants. A tri-axial accelerometer was attached to the weight to indicate the timing of the pendulum impact. The task was repeated 5 times. The task was designed to replicate external postural perturbations in response to an external stimulus, i.e. the pendulum weight coming into contact with the participants outstretched arm. Compensatory postural adjustments (CPAs) are the sensory feedback response to external postural perturbations (Alexandrov et al., 2005), therefore due to the nature of this task we would expect it to induce CPA responses. The CPA window was defined as the changes occurring between (100, 400) ms after the stimulation (Ariun and Latash, 1995) (figure 8).

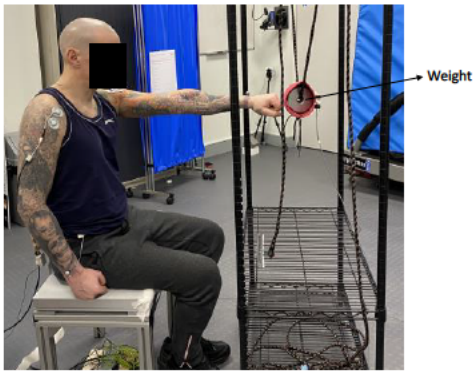

Figure 6: The perturbation task

c) Rapid shoulder flexion

Anticipatory postural adjustments (APAs) are utilised to reduce the consequences of a predicted perturbation (Bouisset and Zattara, 1987); this test therefore is designed mainly to investigate APAs as it involves self-initiated perturbations induced by bilateral rapid shoulder flexion. Participants were seated upright with arms by their sides. They were instructed to raise both arms up to 90° of shoulder flexion as fast as possible in response a visual cue (LED light) at eye level, at a set distance away (figure 7). The LED light was controlled by a research by a button press. A verbal warning cue '*Ready*' was given each time prior to the visual cue. The task was repeated 5 times, with a random inter-trial interval. The dominant arm was then defined as the arm with the fastest reaction time. The APA window was defined as the changes occurring between (-200, 100) ms of the stimulus (Ariun and Latash, 1995) (figure 8).

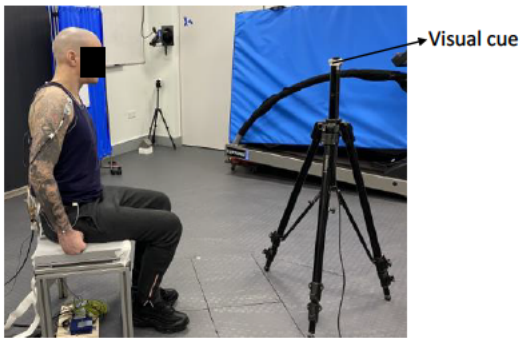

Figure 7: The RSF task

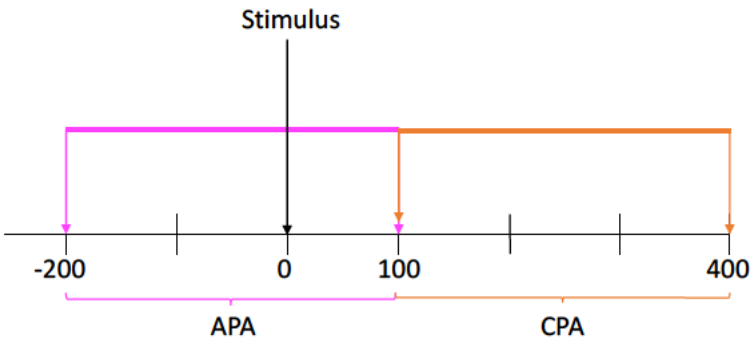

Figure 8: Constructed by the researchers, this demonstrates how APA and CPA windows were calculated, the stimulus was either the pendulum making contact with the participants hand or the LED flashing on. The APA window was then defined by (-200, 100) and the CPA window define as (100, 400).

Part ii: Neurophysiological assessment

To examine the effect of arm cycling on corticospinal excitability of the ES muscle, motor evoked potentials (MEPs) in the ES muscle was elicited before, at completion of, and 10 minutes, 20 minutes and 30 minutes after the arm cycling using single-pulse TMS. Participants were relaxed in their wheelchair during the assessment. Ten MEPS were delivered at each time point (figure 9). This assessment was repeated every two weeks.

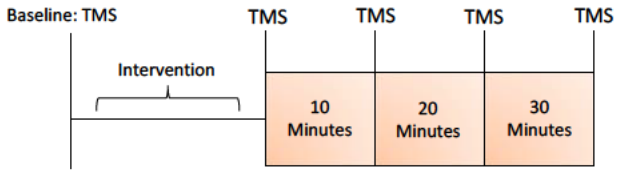

Figure 9: The neurophysiological protocol.

2.6 Intervention

a) Laboratory set-up:

A stationary arm bike was used for arm cycling (AGM Mini Exerciser Bike). Participants were instructed to sit forward without resting on the backrest of their wheelchair when performing arm cycling (figure 10). If participants were unable to

maintain upright seated position, cushioning was provided to support the trunk (N=1). The arm bike was placed on a table in front of the participant at a distance so participants reached to the maximal pedal position with the elbow fully extended. Participants were allowed to adjust their own position and the distance in relation to the arm bike for comfort. Participants underwent three brief maximal voluntary contractions (MVCs) of the elbow flexors. Based on previous work (Chiou et al., 2018), the size of ES MEPs increased during 20% MVC of the BB. To ensure that this facilitation was induced by the arm cycling, the resistance was set at the level that required ~20%MVC of BB. Participants were also asked to perform the arm cycling with a speed at 60 rpm (Lockyer, Soran and Power, 2020), displayed on the ergometer electronic screen. They underwent the arm cycling in a total of 30 minutes; breaks were allowed if needed. A modified Borg scale (Appendix 2) was used to monitor exercise exertion to ensure that the exercise intensity was not exceeding the moderate level (3-4/10) to avoid fatigue.

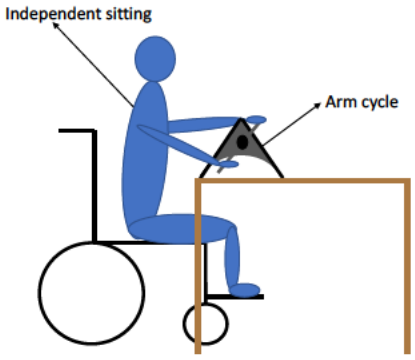

Figure 10: The laboratory set-up and arm-cycling sitting position. Not to scale.

b) Home-based exercise programme:

After completing their first session of arm cycling in the lab, participants were instructed to continue the exercise with the same equipment and setup at home, five consecutive days per week, for six weeks. They were given identical arm bikes in

which they would use to exercise at home. They were required to document time duration of exercise, number of breaks, number of revolutions, and RPM for their exercise in an exercise diary (Appendix 3) provided by the researchers. They were also asked to document any study-related adverse events in the diary. The modified Borg scale was given to the participants for self-monitoring the exercise intensity at home. Participants were also given an exercise instructions sheet (Appendix 4) for reference.

2.7 Focus group:

Following completion of the six week arm cycling programme, participants were invited to participate in a virtual focus group, held on Zoom (N=3). Two moderators (EA and SYC) facilitated the discussion based on a semi-structured topic guide. The focus group started from an introduction of the format of the discussion and the context of the questions. Confidentiality of the information exchanged was emphasised to all participants by the moderators. Questions included; the study protocol, application of home-based exercise intervention, and future recommendations and practicality in an NHS setting. The discussion was recorded and verbatim transcribed by one of the moderators (EA) to allow subsequent analysis.

2.8 Data analysis

Data is presented as mean±SD in the text and as mean± the standard error of the mean (SEM) in the figures, with error bars indicating SEM. At each time point, peak-to-peak amplitudes of 6-10 MEPs were averaged. As raw MEP amplitudes vary between individuals, the averaged amplitudes of MEPs were also calculated and

expressed as a percentage of the amplitudes of MEPs at baseline to help visualisation of the results in figures. A 100ms window prior to the stimulus was used to calculate amplitudes of root-mean-square (RMS) of the pre-stimulus EMG in the ES muscle. MEP latency was visually determined from the average rectified EMG activity when the amplitude of ES exceeded 2 SD of the mean pre-stimulus EMG value (Chiou et al., 2016; Chiou et al., 2018; Hodges, Cresswell and Thorstensson, 1999) (figure 11). The kinetic and kinematic data were analysed using MATLAB R2017b (The MathWorks, Inc.). The reaching distance and trunk movement were measured from maximal displacement of the wrist marker and of the trunk marker, respectively (Field-Fote and Ray, 2010). The maximal displacement and the area of the COP in anterior-posterior and in medial-lateral directions in reaching were also calculated (Lemay et al., 2014). Furthermore, reaction time during the RSF task was determined by the onset of the displacement of the wrist marker with respect to the LED light. The APA window was defined as the changes occurring between (-200, 100) ms of the stimulus with the CPA window being defined as the changes occurring between (100, 400) ms after the stimulation (Ariun and Latash, 1995) (figure 8).

The HDEMG signals were recorded and analysed offline using MATLAB scripts. The signals were re-referenced to form 59 bipolar channels in the presumed direction of the ES muscle fibres (Falla et al., 2014). Prior to analysis, the signals were band-pass filtered at 20-350 Hz (Martinez-Valdes et al., 2019). The bipolar channels were visually inspected and removed dependent on signal-to-noise ratio secondary to impaired electrode-skin interfaces or movement artefacts (Murillo et al., 2019). EMG amplitude (Root Mean Square (RMS)) was then calculated during each movement and averaged across the 59 channels to obtain a single value for the left

and right ES muscle. Background RMS-amplitude was also examined in a 100ms window prior to movement commencement to allow for normalisation, with the results being expressed as a normalised value to the background activity (%). Modified entropy was also calculated to allow for examination of muscle activity heterogeneity (Farina et al., 2008) across and between left and right ES electrodes. During each movement the y coordinate of central EMG activity barycentre was also calculated using a topographical map of ES EMG amplitude (Abboud et al., 2014).

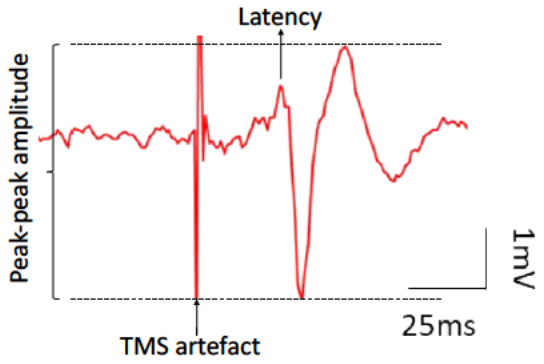

Figure 11: An example of an ES MEP elicited by TMS over the primary motor cortex (M1), demonstrating TMS artefact, latency and peak-peak amplitudes

2.9 Statistical analysis

Statistical program for the Social Sciences (SPSS v.25, IBM Corp, Armonk, NY, USA) was used for statistical analysis. Normal distribution of each parameter was tested using the Shapiro-Wilk test. When data were not normally distributed ($p<0,05$), non-parametric tests were utilised. When data were not sphericity assumed, Greennhouse-Geisser correction was used. Repeated measures ANOVA was performed to examine the effect of TIME (baseline, 10, 20 and 30) on MEP size, MEP latency and pre-stimulus EMG. Repeated measures ANOVAs were also used to examine the effect of WEEK (week 1, week 2, week 4 or week 6) on MEP size, MEP latency and pre-stimulus EMG. For kinetic and kinematic data, paired-t tests were used to compare the reaching distance, reaction time, trunk movement, COP

displacement and COP area between pre exercise intervention at week 1 and post exercise intervention at week 6. For the HDEMG data, and in circumstances where data sets were limited due to equipment error and not being able to access the laboratory during the covid-19 pandemic, data was analysed descriptively using means and standard deviations. Paired t-tests were utilised for statistical comparisons for each parameter independently (RMS-amplitude, entropy and y barycentre). Significance was set at $p < 0.05$, Bonferroni correction was used for multiple comparisons.

3. Results

3.1 Excluded data

Seven participants were recruited and participated in the TMS data collection, one was unable to transfer safely onto the force platform for functional data testing. Therefore, there were six participants that participated in the HDEMG and motion data collection. For the multidirectional reaching, data was collected for the six participants for the motion and HDEMG data. For the RSF, there were six data sets for the HDEMG data but five for the motion data due to equipment failure during the testing of one participant. For the perturbation task, there were three data sets for the HDEMG and motion data due to experimental and equipment failure, alongside the inability to re-analyse data during the lockdown situation.

3.2 Multidirectional reaching tasks and trunk function

For the forward reaching task, paired t-tests demonstrated no significant difference in reaching distance ($t(5)= 0.246$, $p=0.816$), trunk displacement ($t(5)= 0.340$, $p=0.748$), COP displacement ($t(5)= 0.521$, $p=0.625$) or COP area ($t(5)= -0.365$, $p=0.730$) following the exercise intervention.

For the left reaching task, Wilcoxon signed rank test showed a significant increase in reaching distance (before: 164.18mm ± 80.96; after: 205.55mm ± 132.76; $Z= -1.992$, $p= 0.046$; figure 12A), COP area (before: 2785.80mm^2 ± 3143.50; after: 3718.3 mm^2 ± 3856.8; $Z= -1.992$, $p= 0.046$; figure 12B) and COP displacement (before: 65.87mm ± 35.42; after: 79.08mm ± 37.25; $Z= -2.201$, $p=0.028$) after the intervention. Although there was a trend for increased trunk displacement (N=5), there was no significant difference seen (before: 180.71mm ± 78.85; after: 214.11mm ± 119.37; $Z= -1.782$, $p=0.075$; figure 13).

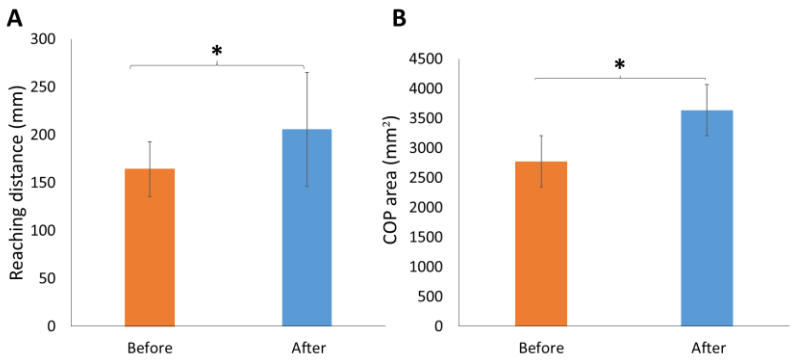

*Figure 12: Group mean data found a significant increase in reaching distance (A) and COP area (B) following the exercise intervention, in the left reaching direction. Wilcoxon test *p<0.05 significance level. Error bars indicate the standard error of the mean (SEM).*

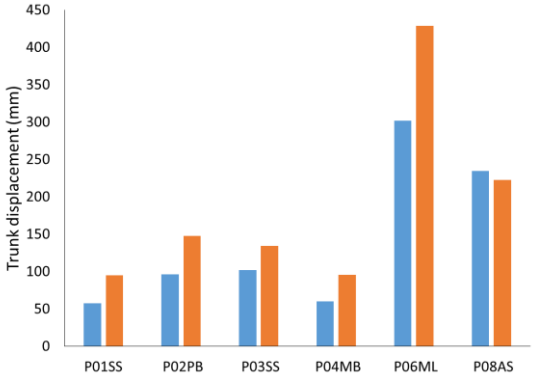

Figure 13: Individual participant data demonstrating the majority of participants following the trend of increased trunk displacement following the exercise intervention in the left reaching direction.

For the right reaching task, paired t-tests showed significant increases in COP displacement (before: 65.38mm ± 44.24; after: 89.03mm ± 47.87; t(5)= -2.380, p= 0.033; figure 14A) and COP area (before: 2598.42units ± 2555.14; after: 4462.15units ± 5134.27; Z= -1.992, p= 0.046; figure 14B) after the intervention. On the contrary, neither reaching distance nor trunk displacement was increased after the intervention (before: 158.56mm ± 93.98; after: 196.37mm ± 125.35; t(5)= -2.369, p= 0.064; figure 15), although there was a trend for increased reaching distance (N=5) and trunk displacement (N=4), with the majority of participants following this trend.

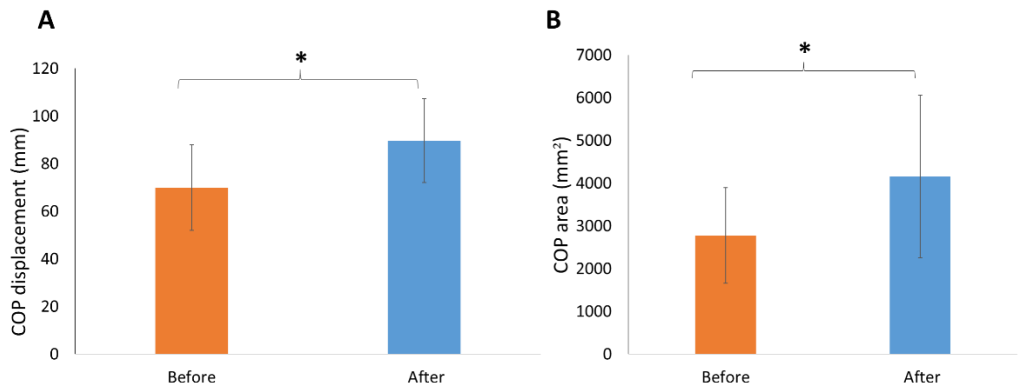

*Figure 14: Group mean data demonstrating a significant increase in COP trajectory (A) and COP area (B) after the exercise intervention, in the right reaching direction. Paired t- test *p<0.05 significance level. Error bars indicate the standard error of the mean (SEM).*

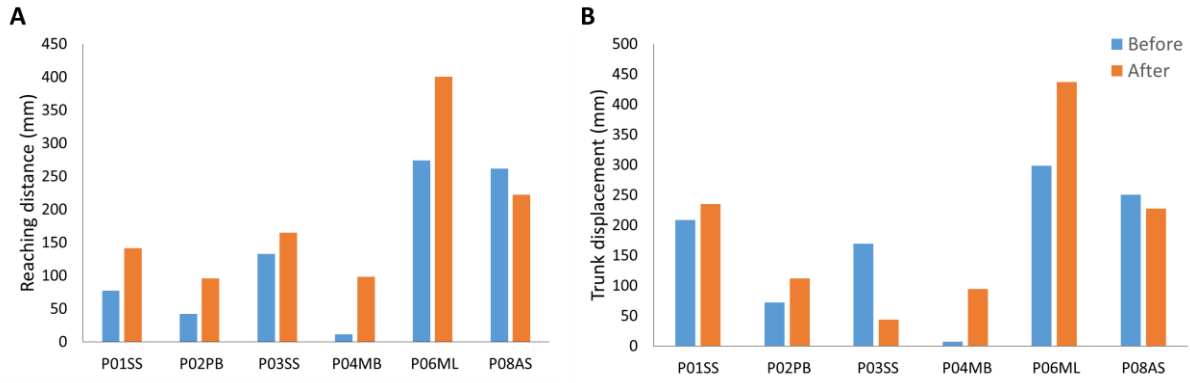

Figure 15: Individual participant data demonstrating the majority of participants following the trend of increased reaching distance (A) and trunk displacement (B) following the exercise intervention in the right reaching direction.

Our results demonstrated that during lateral reaching participants had improved postural control following the exercise intervention.

3.3 Postural adjustments of the trunk to the perturbations

During rapid shoulder flexion a paired t-test showed a significant difference for the dominant arm in reaction time ($t(4)= 4.106$, $p= 0.015$), demonstrating that following the exercise intervention the participants were able to react with dominant arm significantly faster, compared to before (before: 237.33ms ± 21.25; after: 192ms ± 20.08; figure 16A). Although non-significant, there was also a trend for the non-dominant arm to also react faster after the exercise intervention compared to before (before: 244ms ± 32.62; after: 213.6ms ± 27.54; figure 16B), with the majority of

participants following this trend (N=3), of the available data (t(3)=2.567, p=0.083). Paired t-test found no significant difference for total T1 trajectory (before: 107.16mm ± 58.08; after: 151.82mm ± 67.57; t(4)= -1.590, p= 0.187) or maximum posterior COP displacement (before: 8.18mm ± 4.81; after: 11.42mm ± 6.27; t(5)= -1.120, p=0.314). The findings suggest that while participants improved their reaction time of the arms, there was no change in how they used their trunk or moved their body to complete the task after the intervention.

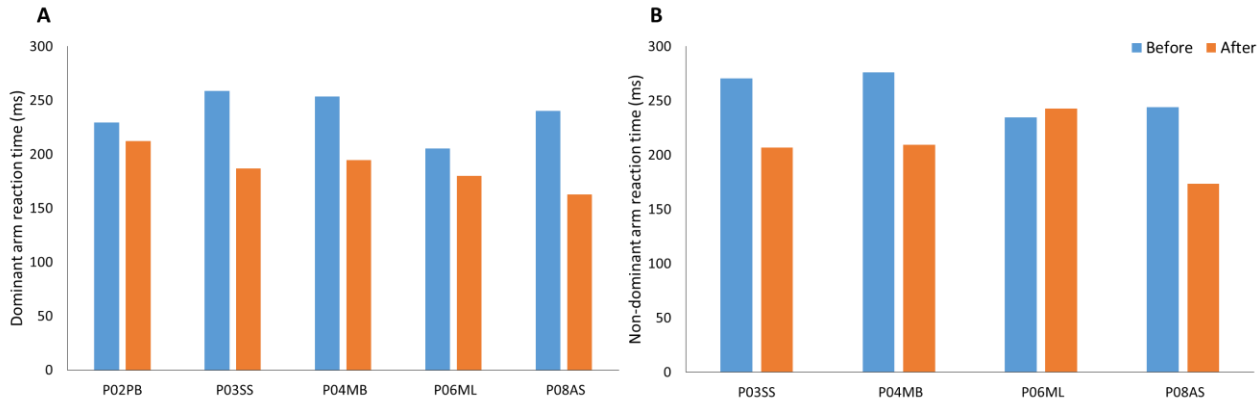

Figure 16: Individual participant data demonstrating the majority of participants demonstrating an improved reaction time for the dominant arm (A) and the non-dominant arm (B)

Note that for the perturbation task, there was available data from only three participants. During the APA and CPA window, there was no significant difference in any of the kinematic measurements. During APA there was a trend for decreased T1 maximum posterior displacement, (before: 5.62mm ± 3.70; after: 0.62mm ± 0.75; t(2)= 1.986, p= 0.185; figure 17A), decreased COP area (before: 34.07mm² ± 17.46; after: 24.08mm² ± 21.57; t(1)= 3.432, p= 0.180; figure 17B), with all three participants following this trend and two of the participants had decreased COP maximum posterior displacement (before: 7.81mm ± 0.96; after: 4.23mm ± 4.22; t(1)= 0.977, p= 0.508). This demonstrates the potential for an improvement in trunk stability as there was a trend for reduced COP displacement and a trend for improved upright

trunk control demonstrated by the reduced trunk marker displacement. During the CPA window, although not significant, we saw a trend with all three participants demonstrating decreased trunk maximum posterior displacement (before: 11.03mm ± 6.39; after: 7.32mm ± 4.46; t(2)= 3.259, p= 0.083; figure 18A) and two participants demonstrating decreased COP maximum posterior displacement (before: 5.05mm ± 5.52; after: 3.57mm ± 3.14; figure 18B). This demonstrates that following the exercise intervention some participants improved their CPA in response to external perturbation, indicating the potential of improved trunk control.

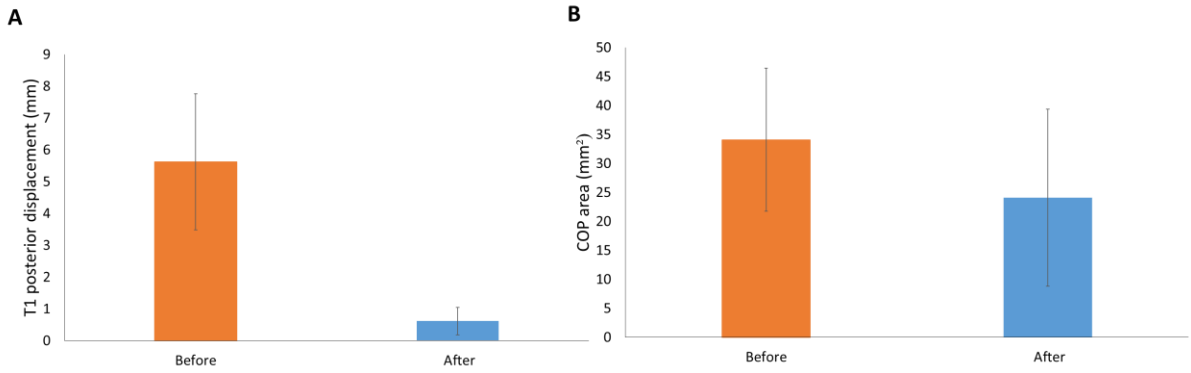

Figure 17: Group mean data demonstrating reduced trunk posterior displacement (A) and COP area (B) during APA. Error bars indicate the standard error of the mean (SEM).

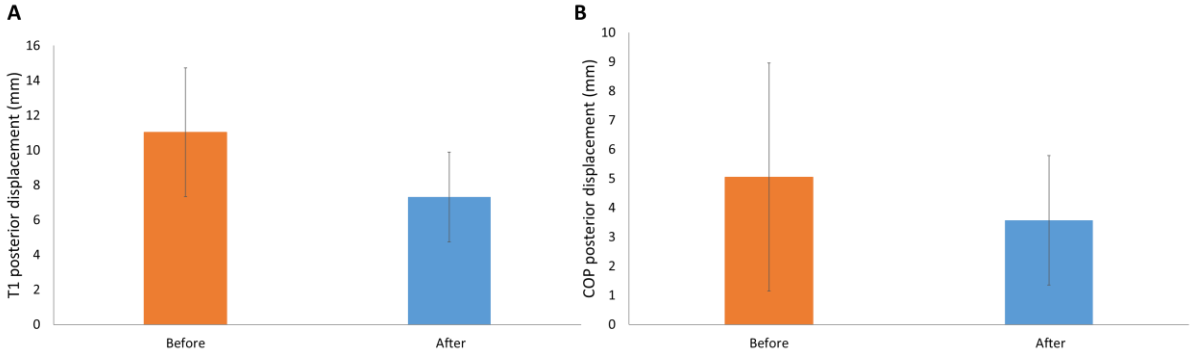

Figure 18: Group mean data demonstrating the reduced trunk (A) and COP (B) posterior displacement during CPA. Error bars indicate the standard error of the mean (SEM).

3.4 Neuromuscular function of the trunk

a) Forward reaching:

During forward reaching, there were no significant differences in the contralateral ES muscle for RMS-amplitude (t(5)= -1.045, p=0.344), entropy (t(5)= -1.208,

p=0.281) or y barycentre (t(5)= -0.780, p=0.471). In the ipsilateral ES muscle there were also no significant changes for RMS-amplitude (t(4)= -0.440, p=0.683), entropy (t(5)=-1.804, p=0.131) or y barycentre (t(5)=0.275, p=0.794).

During descriptive analysis we noticed that the average group data showed increased RMS-amplitude following the exercise intervention for the contralateral (before: 98.572(%) ± 60.011; after 128.69(%) ± 33.538; N=5) and ipsilateral (before: 147.16(%) ± 44.271; after: 166.00(%) ± 75.713) ES muscles (figure 19), suggesting increased muscle activity, although these changes were not significant..

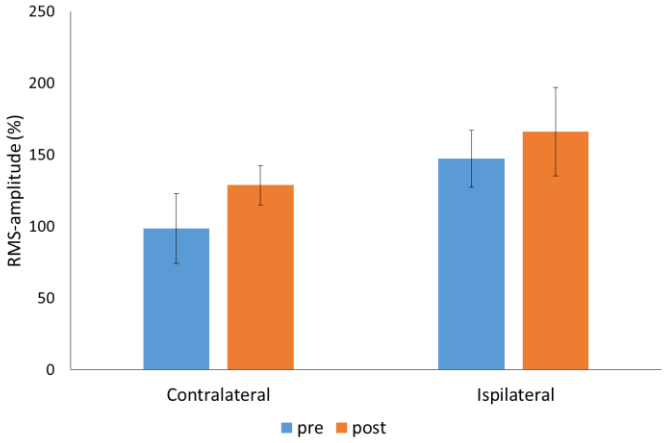

Figure 19: Group mean data demonstrating increased RMS-amplitude in the contralateral and ipsilateral ES muscles following the exercise intervention. Error bars indicate the standard error of the mean (SEM).

Although there was no significant difference, our average group data also demonstrated an increase in entropy for the contralateral (before: 4.328(A.U.) ± 0.949; after: 5.068(A.U.) ± 0.677; t(5)= -1.208, p=0.281)) and ipsilateral (before: 4.674(A.U.) ± 0.925; after: 5.497(A.U.) ± 0.215; t(5)=-1.804, p=0.131) ES muscles following the exercise intervention (figure 20). Our findings suggest more homogenous activity across the muscle.

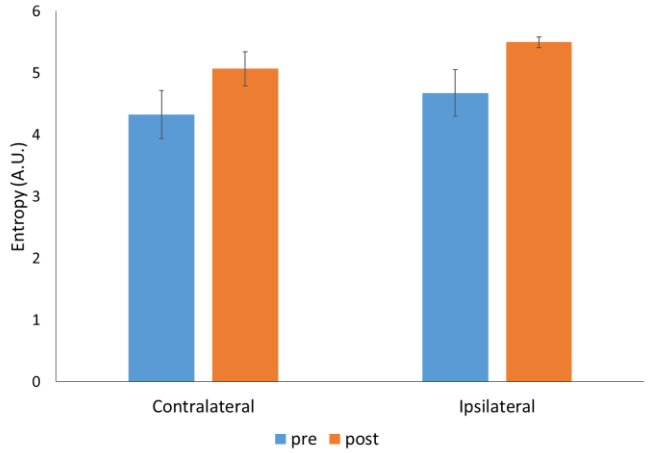

Figure 20: A Group mean data demonstrating increased entropy for in the group average data for the contralateral and ipsilateral ES muscles. Error bars indicate the standard error of the mean (SEM).

An interesting finding when analysing the y barycentre is that before the exercise intervention the average difference between the contralateral and ipsilateral y barycentre was 8.02mm ± 4.85, after the exercise intervention the average difference was 5.18mm ± 4.48 ($t(5)=0.962$, $p=0.380$; figure 21). This demonstrates that following the exercise intervention the participants were able to recruit their ES more symmetrically during the tasks, which could contribute in an improved ability to maintain an upright sitting position.

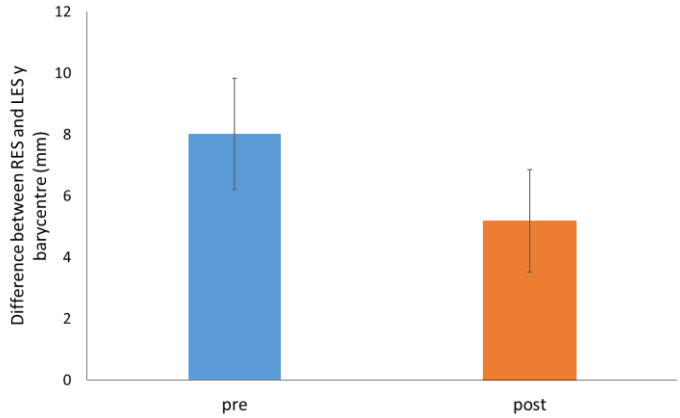

Figure 21: Group mean data demonstrating the average difference in y barycentre's in the between the contralateral and ipsilateral ES muscles. We can see a decreased difference indicating increased symmetry in activation. Error bars indicate the standard error of the mean (SEM).

b) Left reaching:

In the contralateral ES muscle there were no significant differences for RMS-amplitude $t(5)=0.036$, $p=0.973$), entropy ($t(5)=-1.594$, $p=0.172$) or y barycentre

(t(5)=2.033, p=0.98). In the ipsilateral ES muscle there were also no significant differences for RMS-amplitude (t(5)=-0.350, p=0.714), entropy (t(5)=-1.426, p=0.213) or y barycentre (t(5)=-1.016, p=0.356).

During descriptive analysis, we found our average group data demonstrated an increase in entropy for the contralateral (before: 4.896(A.U.) ± 0.314; after: 5.162(A.U.) ± 0.249; t(5)=-1.594, p=0.172) and ipsilateral (before: 4.733(A.U.) ± 0.729; after: 5.228(A.U.) ± 0.624; t(5)=-1.426, p=0.213) ES muscles following the exercise intervention (figure 22), suggesting more homogenous activity across the muscle.

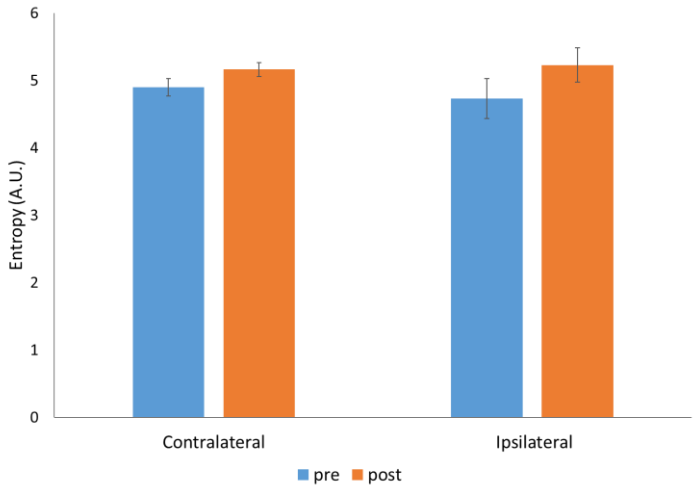

Figure 22: Group mean data demonstrating increased entropy for in the group average data for the contralateral and ipsilateral ES muscles. Error bars indicate the standard error of the mean (SEM).

c) Right reaching:

In the contralateral ES muscle there were no significant differences for RMS-amplitude (t(3)=-1.529, p=0.224) or y barycentre (t(5)=0.940, p=0.391). We did find a significant increase in entropy following the exercise intervention (t(5)=-2.591, p=0.049) in the contralateral ES muscle following the exercise intervention. In the ipsilateral ES muscle there were no significant differences for RMS-amplitude (t(5)=1.530, p=0.186) or entropy t(5)=-2.386, p=0.63). We did find a significantly

more caudal displacement of the y barycentre following the exercise intervention (t(5)=2.924, p=0.033).

A significant increase in entropy for the contralateral ES muscle following the exercise intervention suggests improved homogeneity of muscle activity across the muscle (before: 4.332(A.U.) ± 1.057; after: 4.741(A.U.) ± 1.121; figure 23). Our average group data also demonstrated an increase in entropy in the ipsilateral ES muscle (before: 4.710(A.U.) ± 0.780; after: 5.518(A.U.) ± 0.121) following the exercise intervention, also suggesting more homogenous activity across the muscle.

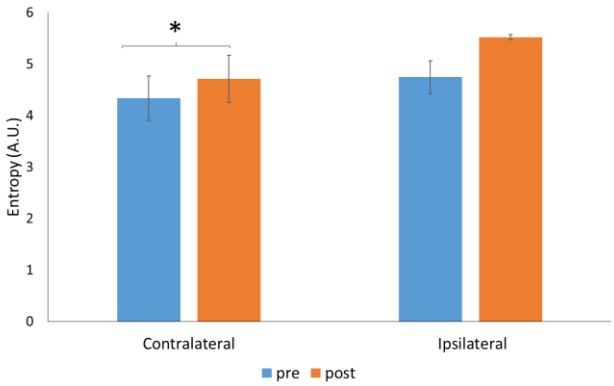

*Figure 23: Group mean data demonstrating the improvements in entropy following the exercise intervention (*p<0.05). Error bars indicate the standard error of the mean (SEM).*

Our data demonstrated a significantly lower centre of activity for the y barycentre in the ipsilateral muscle group (before: 48.963(mm) ± 4.239; after: 43.947(mm) ± 2.371; figure 24) indicating that the following the exercise intervention our participants recruited more ES muscle activity caudally during the right reaching direction.

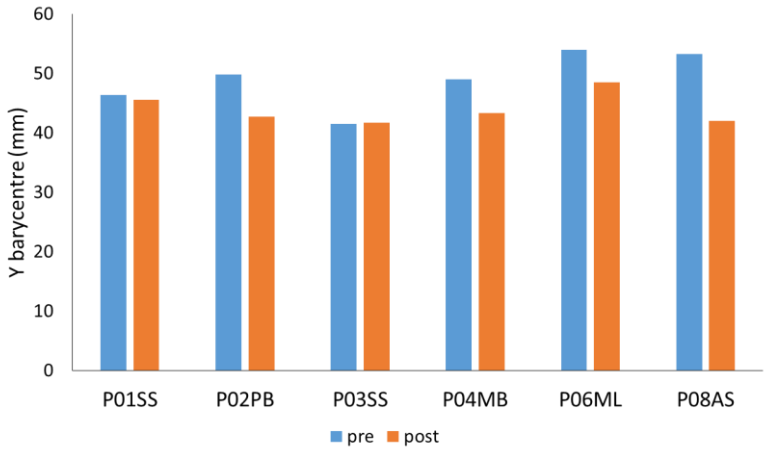

Figure 24: Individual participant data demonstrating the y barycentre (mm) for each participant in the ipsilateral ES muscle before and after the exercise intervention.

d) Rapid shoulder flexion (RSF):

During the APA window of RSF, we found a significant increase in RMS-amplitude in the LES muscle (t(5)=-9.932, p=0.000). We found no significant differences in RMS-amplitude in the RES muscle (t(5)=-0.235, p=0.823), although our average group data found increased RMS-amplitude for RES following the exercise intervention (before= 147.105(%) ± 22.809; after= 152.692(%) ± 37.800) (figure 25).

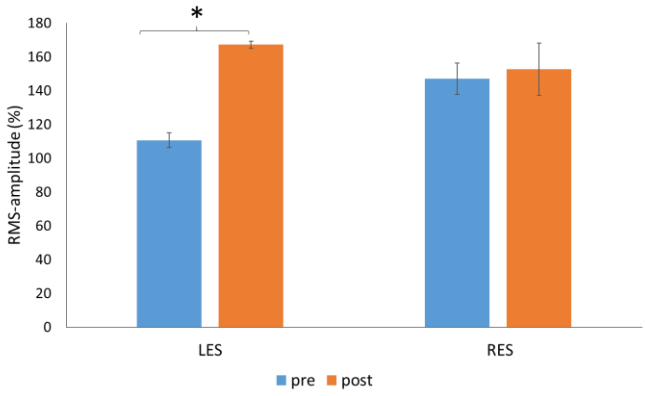

*Figure 25: Group mean data demonstrating increases in RMS-amplitude during the APA phase of RSF for the LES and RES muscles (*p<0.05). Error bars indicate the standard error of the mean (SEM).*

Although we found no significant differences for entropy during APA for LES (t(5)=-1.166, p=0.296) or RES (t(5)=-1.698, p=0.150) muscles during RSF, our average group data found increased entropy for LES (before= 4.960(A.U.) ± 0.590;

after= 5.293(A.U.) ± 0.770) and RES (before= 4.884(A.U.) ± 0.751; after= 5.483(A.U.) ± 0.150) following the exercise intervention during the APA phase of RSF (figure 26) for increased homogeneity of muscle activity (figure 27).

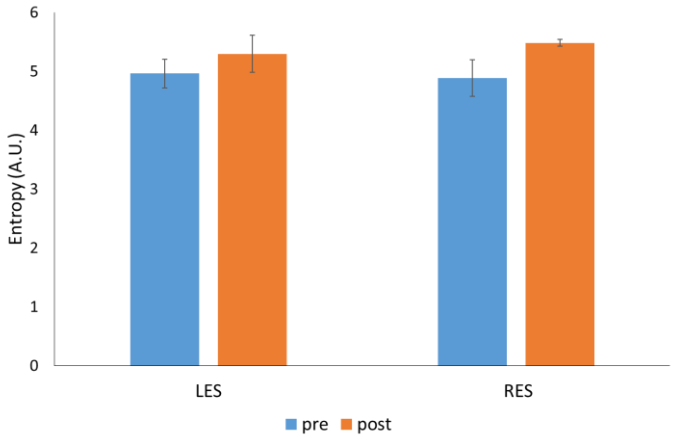

Figure 26: Group mean data demonstrating increased in entropy during the APA phase of RSF for the LES and RES muscles. Error bars indicate the standard error of the mean (SEM).

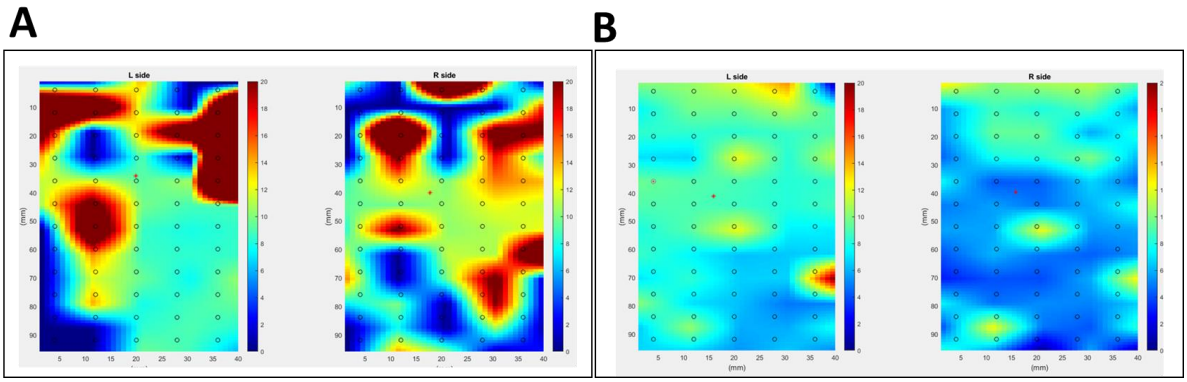

Figure 27: A heat map during APA before (A) and after (B) the exercise intervention from a representative participant. We can see that the LES and RES muscle activity has become more homogenous across the ES muscle.

During the CPA window of RSF, we found a significant increase in RMS-amplitude in the LES muscle (t(5)=-4.559, p=0.006). No significant differences were seen for RMS-amplitude in the RES muscle (t(5)=-0.548, p=0.607), however our average group data did find increased RMS-amplitude for RES following the exercise intervention (before= 197.140(%) ± 85.544; after= 229.029(%) ± 98.672). Furthermore, the magnitude of activity becomes more similar between the LES and

RES muscle following the exercise intervention, demonstrating the ES muscles activating to a similar amount bilaterally (figure 28).

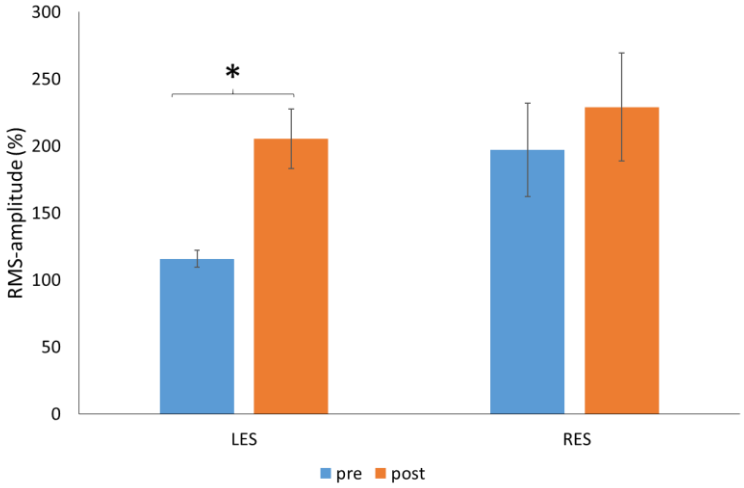

*Figure 28: Group mean data demonstrating increases in RMS-amplitude during the CPA phase of RSF for the LES and RES muscles (*p<0.05). Error bars indicate the standard error of the mean (SEM).*

Although we found no significant differences, our average group data found increased entropy for LES (before= 4.963(A.U.) ± 0.548; after= 5.349(A.U.) ± 0.699; t(5)=-2.073, p=0.093) and RES (before= 4.775(A.U.) ± 0.828; after= 5.445(A.U.) ± 0.279; t(5)=-1.582, p=1.75) muscles following the exercise intervention during the CPA phase of RSF following the exercise intervention (figure 29), suggesting improved homogeneity of muscle activity (figure 30).

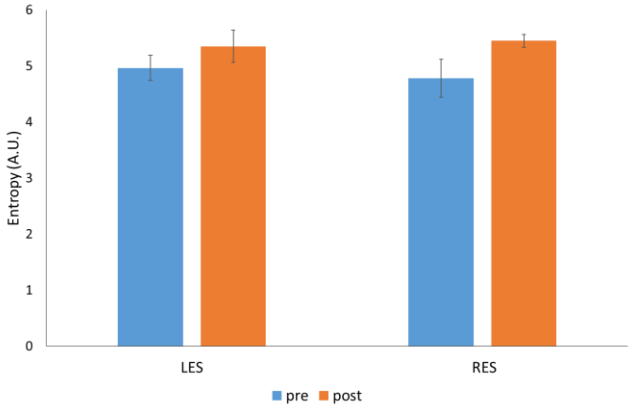

Figure 29: Group mean data demonstrating increase entropy during the CPA phase of RSF in the LES and RES muscles. Error bars indicate the standard error of the mean (SEM).

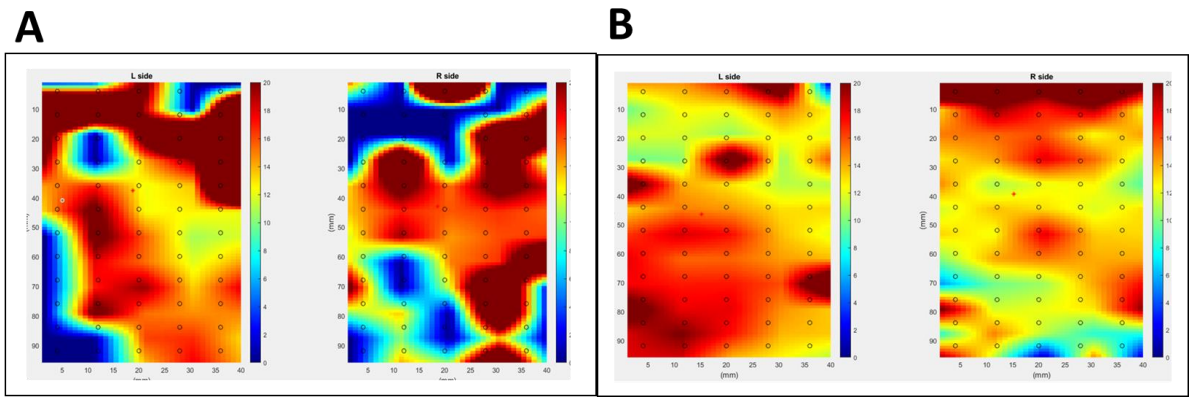

Figure 30: A heat map during CPA from a representative participant.. When comparing before (A) and after (B) the exercise intervention, for the LES and RES ES muscle, the activity has become more homogenous.

An interesting finding when analysing the y barycentre is that before the exercise intervention the average difference between the contralateral and ipsilateral y barycentre was 6.04mm ± 6.89, after the exercise intervention the average difference was 3.81mm ± 2.75 ($t(2)=3.613$, $p=0.069$; figure 31). ES is a longitudinal muscle therefore if the y barycentre for the contralateral and ipsilateral muscle are more similar following the exercise intervention, it is possible that the participants are recruiting the muscle at a similar region of the ES muscle during the task, this would however need to be further investigated in further studies.

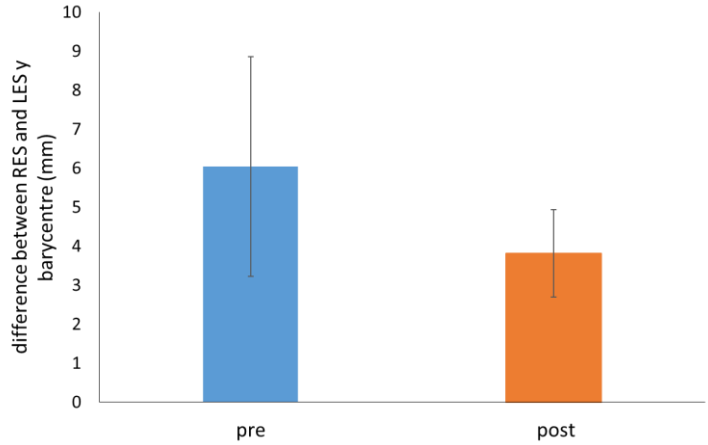

Figure 31: Group mean data demonstrating the average difference in y barycentre's in the between the LES and RES ES muscles. We can see a decreased difference indicating increased symmetry in activation. Error bars indicate the standard error of the mean (SEM).

e) Perturbation task:

During the APA phase of the perturbation task we found no significant differences for RMS-amplitude for LES ($t(2)=-1.063$, $p=0.399$) or RES ($t(2)=2.916$, $p=0.100$), y barycentre for LES ($t(2)=0.444$, $p=0.700$) or RES ($t(2)=0.514$, $p=0.659$), or entropy for LES ($t(2)=0.850$, $p=0.485$) or RES ($t(2)=-1.388$, $p=0.300$).

During the CPA phase of the perturbation task we found no significant differences for RMS-amplitude for LES ($t(2)=-0.496$, $p=0.669$) or RES ($t(2)=2.524$, $p=0.128$), y barycentre for LES ($t(2)=0.498$, $p=0.668$) or RES ($t(2)=0.586$, $p=0.617$), or entropy for LES ($t(2)=0.933$, $p=0.449$) or RES ($t(2)=-1.198$, $p=0.354$).

3.5 Corticospinal excitability of the ES muscle

Stimulus intensity was chosen individually to elicit visible MEPs in the contralateral ES muscles (intensity: 91.14±4.18 % maximum stimulator output (MSO)) (table C). The intensity was similar to that reported in previous work (Chiou et al., 2020).

	Mean	SD	Range
TMS intensity (% maximum stimulator output (MSO)	91.14	4.18	85-100

Table C: Demonstrates TMS intensity utilised during the study.

Repeated measures ANOVA found no significant effect for TIME ($F_{4,16}$ = 1.631, p= 0.215) or WEEKS ($F_{4,16}$= 1.381, p= 0.296) for background EMG activity in the ES muscle, indicating motoneuronal excitability remained the same across all time points.

Overall, repeated measures ANOVA showed no significant effect of TIME ($F_{4.12}$= 1.287, p=0.329) or WEEKS ($F_{3,9}$= 0.399, p= 0.757) on the size of MEPs in the

ES muscle, suggesting that corticospinal excitability projecting to the ES muscle did not change significantly along the time course of the exercise intervention.

Due to small sample size (N=7), descriptive statistics were additionally performed to allow for appreciation of details of the dataset. During the week 1 (figure 32) and week 2 testing, there was the largest amount of facilitation occurring immediately after 30 minutes of arm cycling (week 1: 160.35% ± 91.79; week 2: 169.63% ± 131.33). The facilitation then decreases towards the 30 minute post exercise time point (week 1: 118.80% ± 64.11; week 2: 135.53% ± 79.95). During week 4 and week 6, although there is facilitation immediately after the exercise (week 4: 148.25% ± 79.38; week 6: 112.37% ± 20.23), there is an upward trend of facilitation towards the 30 minute post exercise time point (week 4: 165.21% ± 86.66; week 6: 138.80% ± 61.39). This means that from week 4 onwards there is a tendency for the corticospinal excitability to be elevated and the excitability remains for a longer period of time, hence possible neuroplasticity (figure 33).

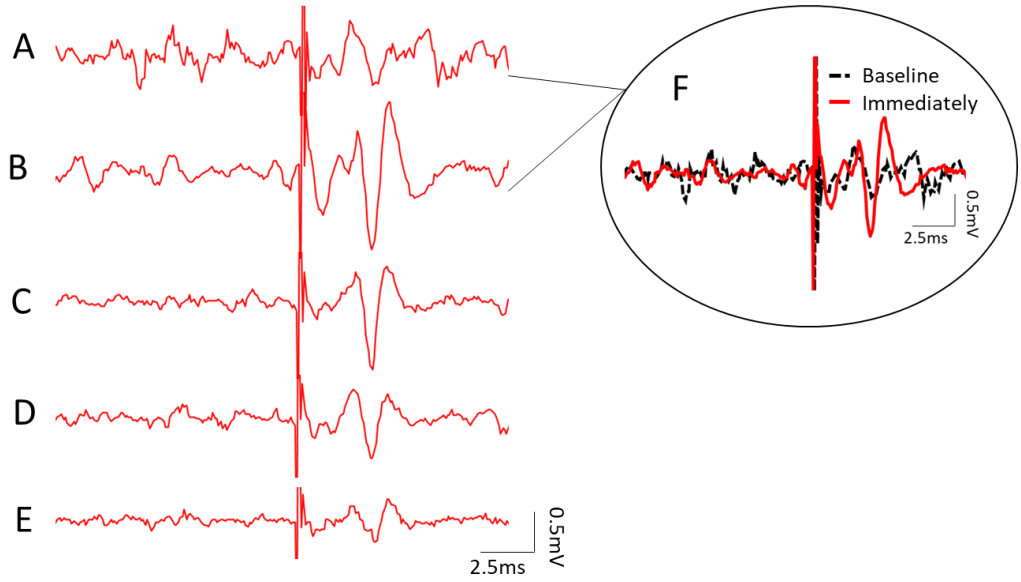

Figure 32: 5 averaged, raw MEP traces for an individual participant during week 1 for baseline (A), immediately (B), 10 minutes (C), 20 minutes (D), 30 minutes (E) after the exercise intervention. We can see that the ES MEP size increases following the exercise intervention and subsequently deceases in size towards 30 minutes. (F) demonstrates the raw baseline and immediately trace overlaid to demonstrate the increase in size and increase clarity of the MEP.

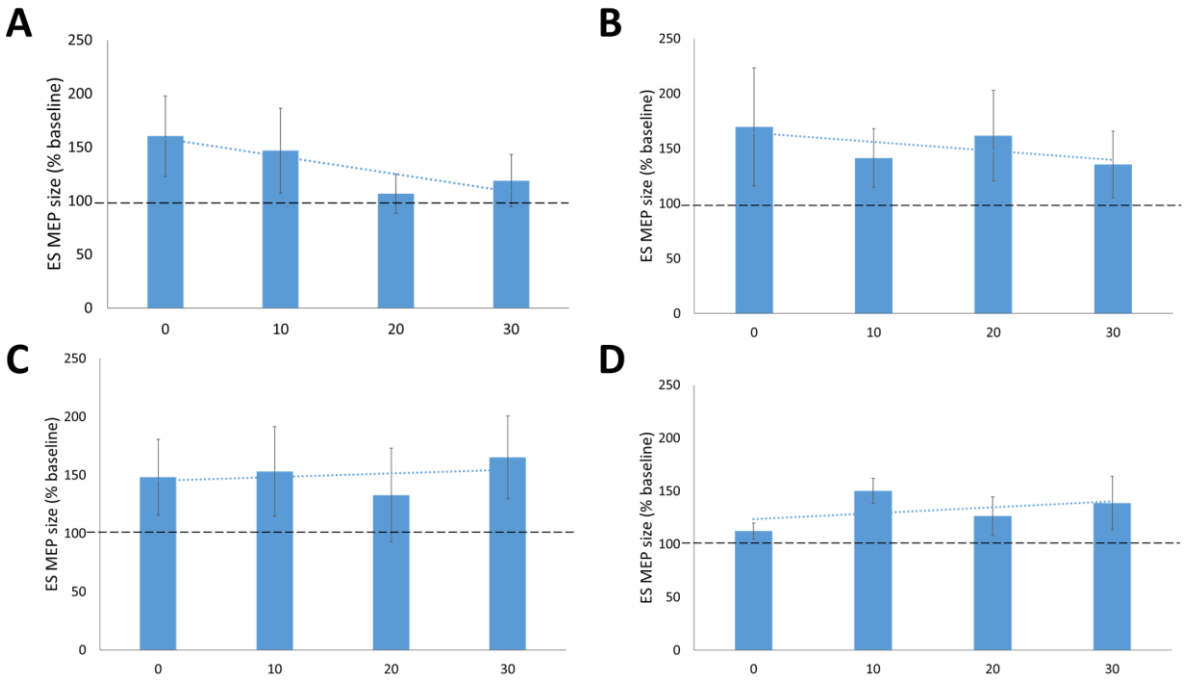

Figure 33: Group mean data demonstrating the trend of facilitation immediately, 10 minutes, 20 minutes and 30 minutes following the exercise intervention, normalised to the baseline MEP, for the baseline week (A), week 2 (B), week 4 (C) and week 6 (D). Error bars indicate the standard error of the mean (SEM). The blue line demonstrates the trend of the data with the dotted line demonstrates the baseline MEP as in 100%.

When comparing the facilitation trend at week 1 and at week 6, we observed a greater increase in ES MEP immediately after the exercise at week 1 in comparison to week 6 (week 1: 160.35% ± 91.79; week 6: 112,37% ± 20.23). A similar facilitation size was found at 10 minutes after the exercise (week 1: 146.71% ± 97.24; week 6: 150.15% ± 31.16). However, the size of ES MEP was greater at 20 minutes (week 1: 106.46% ± 40.87; week 6: 126.35% ± 48.42) and 30 minutes (week 1: 118.80% ±64.11; week 6: 138.90% ± 61.39) after the exercise at week 6 compared with week 1. These results suggest a tendency of the exercise-induced facilitatory effect on ES MEPs outlasting longer after 6 weeks of the intervention (figure 34 and figure 35).

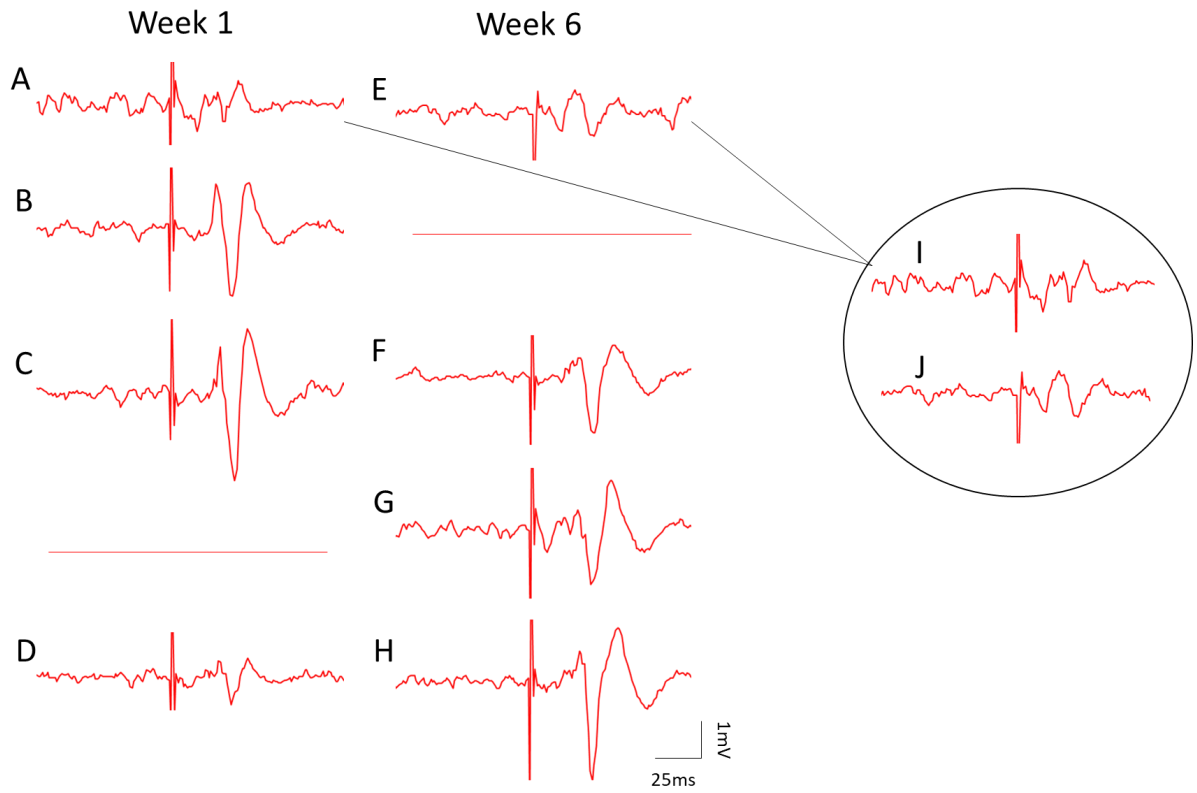

Figure 34: A representative participant's averaged raw MEP traces from week 1 baseline (A), immediately (B), 10 minutes (C) and 30 minutes (D) post exercise and week 6 baseline (E), 10 minutes (F), 20 minutes (G), and 30 minutes (H). The missing data points are due to an artefact overlaying the MEP giving an incorrect reading. The diagram demonstrates that the MEP at week 6 remains facilitated to a greater extent at 30 minutes. (I) and (J) demonstrate a closer look at the baseline MEPs with (I) being the baseline MEP at week 1 and (J) being the a larger baseline MEP at week 6.

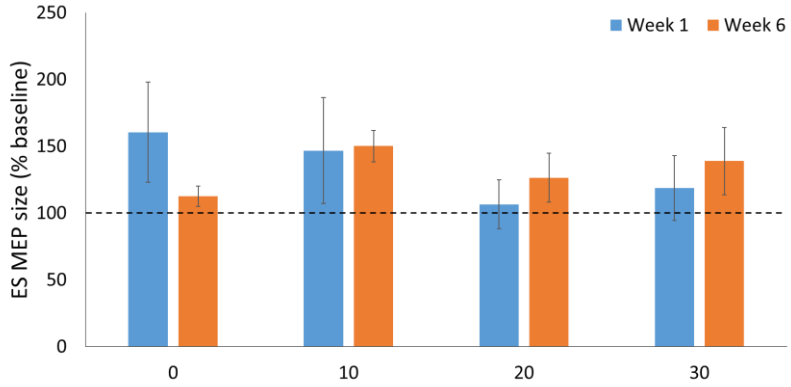

Figure 35: Group mean data demonstrating differences between the baseline week and 6, across immediately after, 10 minutes, 20 minutes and 30 minutes after the exercise intervention. Error bars indicate the standard error of the mean (SEM).

Further, we compared the ES MEP prior to arm cycling (baseline) along the course of the exercise intervention. There was no significant effect of WEEKS on the size of ES baseline MEP ($F_{4,16}$= 5, p= 0.202). Descriptive statistics showed that ES baseline MEPs obtained at week 2 (105.75% ± 37.56) and week 4 (103.86% ±

44.59) were similar when compared to those obtained at week 1 (the baseline week). However, at week 6 there was a visible increase in ES MEP size (157.11% ± 31.07) compared with week 1 (the baseline week) (N=4) (figure 36). These results again suggest the possibility of inducing neuroplasticity in the corticospinal tract projections to the ES muscle by 6 weeks of arm cycling exercise (figure 37).

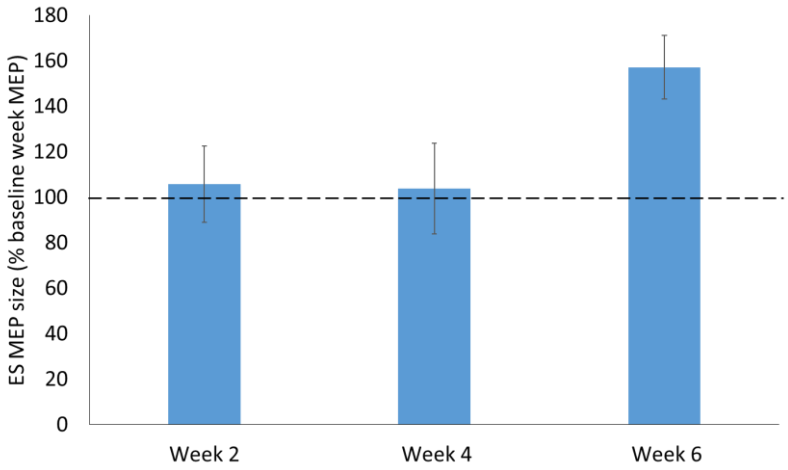

Figure 36: Group mean data demonstrating the baseline ES MEP values across the weeks, normalised to week 1 (baseline week) value. Error bars indicate the standard error of the mean (SEM).

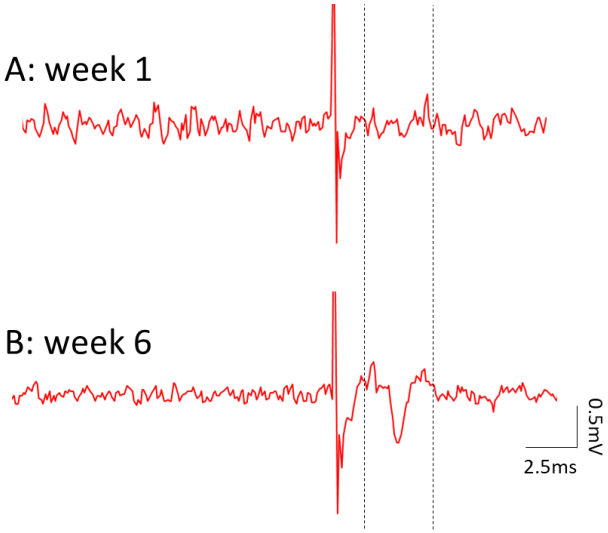

Figure 37: A representative participants 5 averaged raw MEP traces. At week 1 baseline (A) there was no visible MEP, we can see that at week 6 baseline (B) there is clear, visible MEP.

3.6 MEP latency across the time points

Repeated measures ANOVA found no significant effect for TIME at week 1 ($F_{4,16}$= 7.15, p= 0.594), week 2 ($F_{4,16}$ = 0.462, p= 0.763), week 4 ($F_{4,16}$ = 1.123, p= 0.381) or week 6 ($F_{4,16}$ = 0.299, p=0.875). However, we can visually interpret a general trend for decreased MEP latency across the timepoints in each week (figure 38). We can also visually interpret changes in MEP latency between week 1 and week 6 across all time points (figure 39).

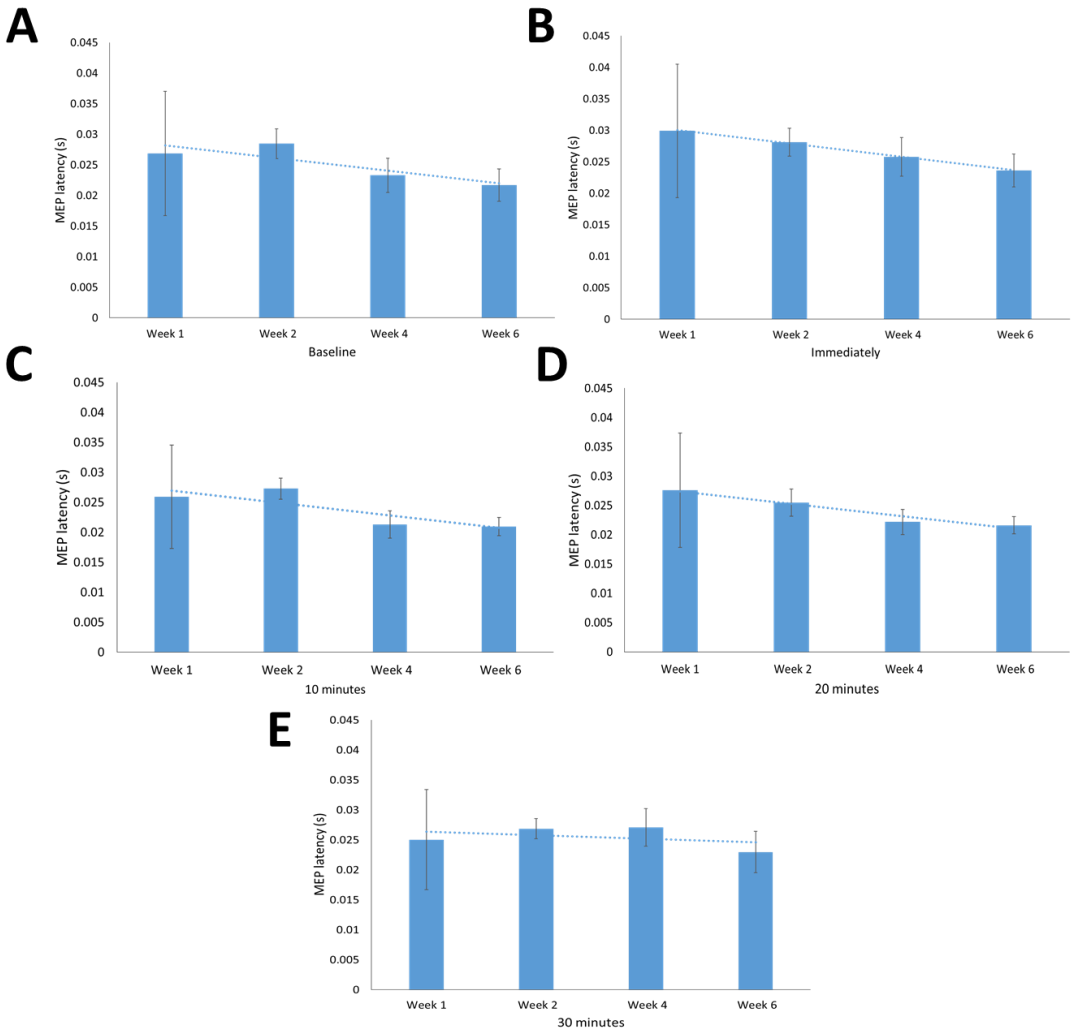

Figure 38: Group mean data visually demonstrating the trend of the MEP latency to decrease across the weeks for (A) baseline, (B) immediately, (C) 10 minutes, (D) 20 minutes and (E) 30 minutes timepoints. Error bars indicate the standard error of the mean (SEM).

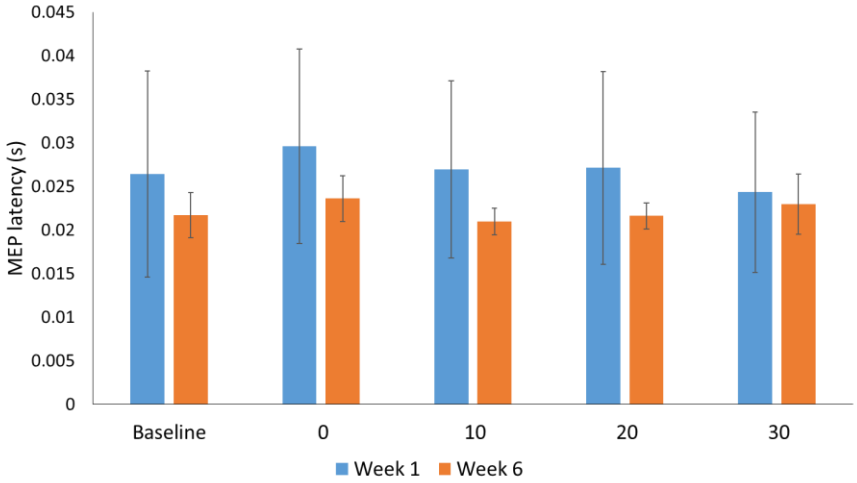

Figure 39: Group mean data to visually compare the MEP latencies for week 1 and week 6 across the timepoints. Error bars indicate the standard error of the mean (SEM).

3.7 Feasibility

Analysis of the participants' daily diaries across the six week intervention protocol found that 94% adhered to the study protocol meaning the vast majority of participants completed five consecutive arm cycling sessions for a total of 30 minutes. It is important to consider that one participant did not provide a daily diary for week 4 or 6, which was recorded as 0 in the analysis; the participant verbally confirmed completion of the home sessions.

Participants were encouraged to note any adverse events during each session, and were reported as follows; shoulder pain (N=4 sessions), neck pain (N=4 sessions), low back pain (N=1 sessions) and nausea (N=1 sessions), all of which were reported from different participants. Adverse events were therefore reported in 4.76% of sessions.

Total adherence and adverse events data demonstrates that the participant complied with the exercise intervention and suggests a feasible programme with limited risk of adverse events.

3.8 Focus group

During the focus group, five main themes arose; overall experience, physical benefits, psychosocial benefits, feasibility and recommendations. These themes were split down further into subthemes. The table below lists the subthemes with the number of participants in agreement and a quote from a representative participant (Table D).

Our participants found the intervention to be beneficial for their physical and mental health. One participant commented; *'I don't know whether it was because I gained a little bit of strength or a little bit more coordination or control… but towards the end I could hold myself in a much better posture',* highlighting the perceived benefits on their physical function. Another participant commented; '*I think the most important improvement was in my mood, it lifts your spirits, you know you are doing something and if you feel like that you do improve, other things improve do you know what I mean',* demonstrating the potential for the intervention to improve mental health. Our participants found the exercise protocol to be feasible and enjoyed the process of the intervention; *'I found it amazing what you were actually trying to achieve with the kit you've got'.*

Table D

Theme	Sub-theme	Number of participants	Quotes
Physical benefits	Functional improvements	3	*ML: 'I don't know whether it was because I gained a little bit of strength or a little bit more coordination or control… but towards the end I could hold myself in a much better posture'*
	Aerobic improvements	2	

			ML: 'I certainly noticed that I got a bit fitter and I certainly got a bit stronger, and built my stamina'
Psychosocial benefits	Psychosocial improvements	3	*PB: 'I think the most important improvement was in my mood, it lifts your spirits, you know you are doing something and if you feel like that you do improve, other things improve do you know what I mean'*
Feasibility	Exercise diaries/ compliance	2	*ML: 'I suppose how it worked with having the little diary itself, I think that gives you more focus to get it completed'*
	Barriers	2	*ML: 'I just had to try a couple of different chairs to get the right height to make sure it was right whilst I was doing it'*
	Ease of use/ independence	3	*MB: 'once you have it set-up, and you know what you are doing… it's a good piece of kit to be honest'*
	Cost effectiveness	2	*MB: 'you don't have to go and buy all these fancy thousands pounds worth of machines to do it, its something as*
	Hospital implementation	2	

			simple as that and as easy as that' *MB: 'all the time that I was in hospital they could have gave me one of these just to get my arms going; cause either they hadn't thought about it or it wasn't high on their agenda'*
Recommendations	Rehabilitation duration	3	*ML: 'I see changes in multiples of months and not weeks because progress is potentially so slow, so you know if I had done it for 6 months, I think you would only ever see progression in a longer term, whereas in six weeks you only seen progression in a snapshot'*

4. Discussion

4.1 Summary of results

This pilot study aimed to investigate whether a 6-week, home-based arm-cycling intervention is a feasible rehabilitation protocol for improving trunk control after SCI and aimed to investigate possible underlying mechanisms of improvements. We also aimed to investigate the impact of the exercise on psychological and self-perceived improvements in function and quality of life. Our key findings included a significant increase in reaching distance, COP area and COP displacement in the left reaching task with a significant increase in COP displacement and COP area in the right reaching task. This demonstrates that SCI participants improved dynamic sitting balance after the exercise intervention. Another key finding was faster reaction time of the dominant arm and increased activity of the ES muscle during the reaction time task. This demonstrates improved volitional control of the ES muscles and performance of functional arm movements after the exercise intervention. Although our TMS data did not find significant changes, we observed clear trends for improved corticospinal excitability immediately after the exercise intervention with the increase lasting a longer period of time towards the end of the six weeks. We also found a trend for the baseline MEP value to be increased by week 6 as well as a trend for improved MEP latency. These findings potentially indicate neuroplasticity in corticospinal pathways projecting to the muscles below the level of injury after the arm cycling intervention. Our focus group also highlighted that participants believe this protocol to be feasible as a home-based exercise intervention and found self-perceived improvements in mood, functional abilities and exercise tolerance. Although further research is needed for this study to be conducted on a wider scale, our results have

demonstrated that our research proposal and methodology is able to investigate improvements in function, neuromuscular control, corticospinal excitability and psychologically perceived factors when utilising a six week arm-cycling exercise programme.

4.2 Corticospinal excitability and crossed corticospinal facilitation

Our results demonstrate a trend that 30 minutes of rhythmic arm cycling has the potential to increase corticospinal excitability, as observed visually during descriptive analysis, which could be attributed to the phenomenon known as cross transfer effect (Carson et al., 2004, Lee et al., 2010; Carroll et al., 2008). We found a trend across all time points, at each week, for rhythmic arm cycling to increase corticospinal excitability when normalised to the baseline ES MEP. Hess et al., (1986) was the first to demonstrate the ability of MEPs in the resting abductor digiti minimi to be increased by strong contractions of the homologous muscles. Further studies have demonstrated that MEP size of a relaxed, untrained muscle can be facilitated through unilateral tonic contractions (Perez and Cohen, 2008; Muellbacher et al., 2000; Meyer et al., 1995; Stedman, Davey and Ellaway, 1998; Chiou et al., 2013). However, the exact mechanisms of how unilateral training increases MEP size of the contralateral muscle is not fully understood (Carroll et al., 2008). It has been suggested that the neural adaptions that occur with improved performance of the trained muscles are contained within the CNS in an area accessible to the contralateral limb (Imamizu and Shimojo, 1995; Laszlo, Baguley and Bairstow, 1970; Taylor and Heilman, 1980). Additional theories suggest that the practice of a task induces bilateral neural adaptions (Parlow and Kinsbourne, 1989), with the contralateral M1 activity having the potential to alter ipsilateral M1 activity (Carson,

2005). Unilateral tasks have also been demonstrated to modify inhibitory mechanisms between the hemispheres (Hortobágyi et al., 2011), with interhemispheric inhibition decreasing from the active M1 (Perez and Cohen, 2008). Studies also found increased ipsilateral M1 activation and corticospinal excitability targeting homologous muscles during unilateral voluntary contractions (Urbano et al., 1998; Salmelin et al., 1995; Hortobágyi et al., 2003; Muellbacher et al., 2000), which could also be a possible underlying mechanism for cross education between the hemispheres. Although the specific neuronal mechanisms attributed to the increased corticospinal output remain unclear (Perez and Cohen, 2008), understanding these underlying principles will have huge clinical implications for neuro-rehabilitation as interventions can become more targeted at neurophysiology to potentially allow for greater functional improvements.

Additional to tonic contractions, research has demonstrated unilateral training can increase MEP size of the contralateral limb (Carson et al., 2004, Lee et al., 2010). Carroll et al., (2008) demonstrated unilateral ballistic motor learning is accompanied by bilateral increases in corticospinal excitability. Rhythmic movements have also been shown to facilitate corticospinal excitability; Carson et al., (2004) found unilateral rhythmic movements of the wrist (i.e. flexion and extension) increased the MEPs evoked by the homologous muscles of the opposite limb. We previously found 30 minutes of unilateral rhythmic arm cycling facilitated corticospinal excitability of the ES muscle and reduced intracortical inhibition, with no changes in CMEPs (Chiou et al., 2020b), indicating that the facilitation occurs, at least in part, at the cortical level. Although previous studies have demonstrated ES MEP is increased during tonic, unilateral, upper-limb muscle contractions (Chiou et al., 2018b; Davey et al., 2002), our study is the first to demonstrate that bilateral

rhythmic arm movements can also increase corticospinal excitability of an untrained muscle, in this instance the ES muscle.

4.3 MEP latency

Another key finding in this present study is the trend for decreased MEP latency for each time point across the six week exercise intervention. MEP latencies are prolonged following SCI (Smith et al., 2000) with paravertebral muscle MEP latencies being delayed by around 7-8ms (Cariga et al., 2002). The delay could be due to demyelination of corticospinal axons which often occurs following spinal cord injury (Bunge et al., 1993) as well as the degeneration of uninjured corticospinal axons (Bronson et al., 1978; Fishman, 1987; Yamamoto et al., 1989). Shortened, thus improved, MEP latency may be as a result of faster conductions along the corticospinal pathway (Kobayashi and Pascual-Leone, 2003). Although there is limited research on shortened MEP latencies in SCI, it is associated with improved functional recovery in stroke (Turton et al., 1996; Barker et al., 2012; Beaulieu et al., 2014) and also linked to improved motor performance (Turton et al., 1996; Beaulieu et al., 2014). In stroke populations, shorter MEP latencies have been reported following repetitive, task-orientated exercise (Beaulieu and Milot, 2018). Beaulieu and Milot (2018) suggest that MEP latency may be an improved outcome measure for training-induced neuroplasticity, with shortened MEP latency often correlating with increased corticospinal excitability and function (Beaulieu and Milot, 2018) which can be attributed to our findings. We can therefore deduce a six week arm cycling intervention has the potential to increase corticospinal excitability and induce increased conduction along the pathway, however further research is needed.

4.4 Neuroplasticity

Neuroplasticity is a complex process (Hötting and Röder, 2013) and the exact neuronal mechanisms are not completely understood (Kelly and Garaven, 2005). Neuroplasticity allows for recovery following neurological injury (Dancause and Nudeo, 2011; Taub et al., 2002) with increasing evidence emerging that regular exercise enhances motor cortex plasticity in humans (Cirillo et al., 2009). Following incomplete spinal cord injury, the spinal cord tissue has some potential for recovery (Loy and Bareyre, 2019). Neuroplasticity and increased sprouting of axonal connections influences brain-spinal cord connectivity (Loy and Bareyre, 2019) and how rehabilitation influences this is a critical question. McDonnell et al., (2013) found 30 minutes of low-intensity exercise in healthy adults, promoted continuous theta burst simulation (cTBS)-induced neuroplasticity, demonstrating modulated motor cortical plasticity. Our results suggest that arm cycling has the potential to facilitate excitability in the descending pathway after SCI and induce neuroplasticity. When comparing week 1 and week 6 corticospinal facilitation in more detail, we deduced a greater increase immediately following arm cycling during week 1. This could suggest that a single session of arm cycling has the potential to facilitate an increase in corticospinal excitability in isolation. However, at the 30 minute time point corticospinal excitability was facilitated to a greater extent during week 6, demonstrating the exercise-induced faciliatory effect outlasted longer following the intervention thus suggesting neuroplasticity. Furthermore, when comparing the baseline ES MEP values prior to arm cycling, the ES MEP size was 157.11% larger at week 6 when normalised to the week 1 ES MEP. Again, this trend could possibly be attributed to neuroplastic changes occurring along the corticospinal pathway following six weeks of an arm cycling intervention. Although our results were unable

to consistently demonstrate significant differences, recent research suggests that there are age-related reductions in neuroplastic changes for older adults compared to young and middle-aged adults (Freitas et al., 2011). Therefore, although we were able to show some trends in our data to indicate that arm cycling can influence neuroplasticity, it is possible that these improvements would have been projected further in a younger population.

Training-induced neuroplasticity can lead to functional improvements through the upregulation of neurotransmitters and enhanced collateral sprouting (Fouad and Tetzlaff, 2012). Rodent studies have demonstrated neuroplasticity at a cellular level with improvements in function during locomotor rehabilitation (Tillakaratne et al., 2002; Hutchinson et al., 2004), which has now been successfully implemented into clinical practice for incomplete SCI to promote functional recovery (Dietz and Harkema, 2004; Behrman, Bowden and Nair, 2006; Behrman et al., 2005). Intense, repetitive training after cervical SCI have also been shown to promote cortical plasticity (Beekhuizen and Field-Fote, 2005; Hoffman and Field-Fote, 2007; Winchester et al., 2005). Our exercise intervention allowed for some functional improvements, with neuroplasticity being a feasible explanation for this.

It is known that during and following exercise cessation plasticity of spinal cord circuits is not isolated to the moving muscle (Brooke et al., 1997). Bilateral arm cycling has been shown to reduce the amplitude of Hoffmann (H-) reflex in soleus muscles (Frigon, Collins and Zehr, 2004; Zehr and Duysens, 2004) with the effect outlasting the duration of activity (Javan and Zehr, 2008). Rhythmic arm cycling has been shown to significantly suppress soleus H-reflex amplitudes in neurologically intact participants (Frigon, Collins and Zehr, 2004; Loadman and Zehr, 2007). This interlimb effect may be generated in circuits activated during rhythmic arm

movements, namely spinal circuits (Zehr and Duysens, 2004). Arm cycling may therefore have the potential to supress reflexes and spasticity following neurological injury (Aymard et al., 2000). Barzi and Zehr (2008) conducted a study which demonstrated that arm cycling significantly suppressed soleus H-reflexes in stroke patients. Although the suppression was to a lesser extent than that observed in neurologically intact participants, their research demonstrated that even following neurological injury, spinal control mechanisms can still be influenced via interlimb pathways. It is therefore possible that during our study, spinal circuits may have contributed to neuroplasticity. Ostadan et al., (2016) also found that exercise promoted increased corticospinal excitability which remained for 2 hours following exercise cessation, with the amplitude of corticospinal excitability correlating with the magnitude of off-line gains in skill level. It is likely that with further data collection from an increased number of participants we would have seen clearer trends and correlations between functional improvements and neuroplasticity.

4.5 Neuromuscular control and muscle recruitment

Our results demonstrate some potential for neuroplasticity induced functional changes as demonstrated by our neuromuscular data. Following SCI, neuromuscular control of muscles is impaired often leading to patients having un-coordination movement, spasticity and reduced muscle activity (Jordanic et al., 2016). It is well documented that SCI patients have altered muscle strategies leading to compensatory movement. SCI patients also have a tendency to recruit non-postural muscles due to trunk instability (Chen et al., 2003; Larson et al., 2010). Potten et al., (1999) found during reaching tasks, SCI patients have a tendency to posteriorly rotate their pelvis to allow for increased stability utilising cranial muscles. They also

found that during upright posture, SCI patients have an increased tendency to activate their pectoralis major to stabilise the shoulder girdle and enabling latissimus dorsi and trapezius to become more activate. However, they found that even when utilising this non-postural muscle recruitment, they could not compensate for the loss of ES muscle activity as the SCI participants still had increased postural instability compared to controls.

Although compensatory muscle strategies are well documented, there is currently limited understanding of trunk function following SCI (Chen et al., 2003; Gauthier et al., 2012; Larson et al., 2010; Field-Fote and Ray, 2010). It has been suggested that SCI patients have a reduced ability to stabilise their trunk muscles which leads to the altered muscle patterns compared to neurologically intact individuals (Reft and Hasan, 2002). Rehabilitation has been shown to have the potential to partially regain muscle functioning (Jordanic et al., 2016). Entropy can be used to evaluate the spatial distribution of muscle recruitment with higher levels of entropy indicating a more uniform muscle activity distribution (Sanderson et al., 2020). Increased caudal muscle recruitment, as seen by increased distribution across the muscle, and thus increased entropy, allows for increased utilisation of muscle fibres and the creation of a longer movement lever (Bogduk, 2005). Longer muscle levers allow for more effective motor strategies and advantages in biomechanical movement (Bogbuk, 2005). Research in low back pain populations have found symptomatic patients have more cranial and less diffused muscle activation in comparison to asymptomatic patients (Sanderson et al., 2020; Sanderson et al., 2019). Currently, there are no studies investigating spatial distribution of ES muscle activation following SCI. However, Reft and Hasan (2002) reported increased energy expenditure during upright posture following SCI, which

would suggest heterogenous muscle activity, with more sections of the muscle working at higher rates, in comparison to the muscle working as a unit. During right reaching, we found significantly increased entropy in the contralateral ES muscle with a trend for increased entropy in the ipsilateral ES muscle, indicating more homogenous ES muscle activity, with a significantly more caudal displacement of the y barycentre. This occurred alongside a significant increase in COP displacement and COP area, with a trend for increased reaching distance and increased trunk displacement. Similar changes were also observed during left reaching; we found a trend for increased entropy in the contralateral and ipsilateral ES muscle alongside significantly increased reaching distance, COP area and COP displacement with trends for increased trunk displacement. Muscle activity redistribution minimises muscle fatigue and improves muscle endurance (Farina et al., 2008; Gallina et al., 2013; Falla et al., 2014). This is advantageous as SCI patients are constantly using their upper limbs during ADLs so improved endurance would allow for increased, accurate completion of tasks.

It is therefore possible that following our arm cycling intervention participants who had injuries above the level of T6, improved both corticospinal drive and neuromuscular control to the muscles below the level of injury. Further research utilising correlation analysis is needed to investigate relationships between these improvements and to decipher whether improvements in corticospinal excitability correlates to improvements seen in function.

It is important to consider when looking at our heat maps used to visually demonstrate changes seen in RMS-amplitude and entropy that the hotspots observed could be as a result of noise or muscle spasm or altered motor control. The heat maps utilised are during the RSF task which is a dynamic task requiring fast

movements, potentially triggering spasticity with no current standard assessment to quantify spasticity. Further research is needed to investigate spasticity and HDEMG heat maps in this population.

4.6 Anticipatory and compensatory postural control

Anticipatory and compensatory postural adjustments occur in preparation and in response to perturbations respectively to maintain balance (Alexandrov et al., 2005; Hall et al., 2010). During APAs there is increased muscle activity of postural muscles (Belenkill et al., 1967), alongside movement strategies accompanied by ES activation to minimise disturbances caused by perturbations (Aruin and Latash, 1995; Hodges and Richardson, 1997a). CPAs also cause changes in muscle activity following perturbations to restore balance (Park et al., 2004; Alexandrov et al., 2005) and are controlled by feedback control mechanisms (Kanekar and Aruin, 2014). Kanekar and Aruin (2014) reported delayed anticipatory muscle recruitment in older adults, causing larger compensatory movements as seen by larger COP displacements, indicating postural instability. The role of APAs and CPAs following SCI in maintaining postural control is scarcely reported. During the preparatory phase of movement, corticospinal output is modulated but whether this is preserved, and to what extent, following SCI needs further research (Chen et al., 1998; Leocani et al., 2000). SCI patients have shown a decreased ability to modulate corticospinal excitability during a motor tasks (Barry et al., 2013; Bunday et al., 2014) and often have decreased corticospinal amplitudes and prolonged latencies during voluntary movement (Davey et al., 1998; Perez, 2012). These deficits can then extend into changes in preparatory movement phases (Federico and Perez, 2017). SCI patients have prolonged reaction times in the response to a given signal (Labruyère and van

Hedel, 2011; Labruyère and van Hedel, 2013) possibly as a result of altered synchronicity of descending corticospinal volleys (Cirillo, Calabro and Perez, 2016). Following our exercise intervention our participants had significantly improved reaction times of their dominant arm and a trend for improvement of their non-dominant arm. Although there were no other clear trends in COP or trunk displacement data, we found a significant increase in RMS-amplitude in contralateral ES muscle, to the dominant arm, during the APA and CPA phase of RSF, with a trend for increased RMS-amplitude in ipsilateral ES muscle, to the dominant arm. This could suggest an improved ability to modulate the corticospinal pathway to allow for improved neuromuscular control of postural adjustments and reaction times.

External perturbation paradigms, such as the pendulum during the perturbation task in this study, eliminate the influence of movement on postural control that exists with the rapid shoulder flexion task (Kanekar and Aruin, 2014). This could mean more accurate analysis of APAs and CPAs in SCI populations. Research has found that as long as the perturbation is predictable, APAs are observed in both externally and internally perturbed conditions. Effective APAs, allow for smaller COP peak displacements in response to external perturbation in older adults (Kanekar and Aruin, 2014). Our small sample size does not currently allow for reliable conclusions to be drawn, further research using this paradigm is required to further develop understanding.

4.7 Dynamic sitting balance

We found that following our six week exercise intervention of regular, rhythmic arm cycling, participants were able to demonstrate improved postural control during

dynamic sitting balance. Hill et al., (2018) found that a six week, thrice weekly, supervised arm-crank ergometry (ACE) improved functional performance of healthy, older adults, with marked improvements in functional reach. This is in support of our study as we found that following the exercise intervention, the SCI participants could reach significantly further in the left direction, with a trend towards significant increase in the right direction. Increased reach distance has important clinical implications for SCI as reach distance defines the workspace available (Field-Fote and Ray, 2010). It also means when reaching for an object, after the exercise intervention, the participants would be able to do this more successfully, improving independence.

Indirect trunk strengthening is likely to occur as a result of ACE, (Hill et al., 2018) which could have contributed to increased trunk movement. We found that following the exercise intervention, participants showed a trend for increased trunk marker distance during lateral reaching, indicating increased reach distance and trunk movement. Williams et al., (2020) found that during unsupported ACE, participants were able to significantly increase their trunk muscle activation, even in those with motor-complete injuries, to a comparable level to their trunk maximal voluntary contraction. This demonstrates that ACE is an effective modality to engage the trunk muscles and act as a trunk strengthening exercise. In our study, we have successfully implemented this as an independent, home-exercise intervention that does not require specialist equipment or the presence of a therapist. Hill et al., (2018) recommended that ACE training could be used as an effective adjunct to physiotherapy interventions such strength and balance training. Using our findings that arm cycling alone induced neuroplasticity and allowed for functional improvements, it is therefore reasonable to assume that if combined with additional

physiotherapy techniques, there would be larger, accumulative, improvements in corticospinal excitability and function. In future studies, an isometric ES contraction test could be used to further investigate ES strengthening.

4.8 Psychosocial improvements

SCI has massive implications on a individuals QOL (Tulsky and Kisala, 2015). Depression is closely linked to lower QOL (Hartoonian et al., 2014; Dijkers, 2005) and is a huge problem in this patient population with higher rates than in the general population (Hartoonian et al., 2014; Elliott and Frank, 1996; Fuhrer et al., 1993; Kessler et al., 2003; Frank et al., 1992). Our focus group highlighted the psychological benefits of participating in a six week exercise intervention. A participant commented on the arm cycling lifting their mood and motivating them to become more active. This demonstrates not only the ability to improve mental health but also in improving sedentary behaviour. This is important as research suggests SCI patients perform little to no physical activity (Nightingale at al., 2017; Washburn et al., 2002; Tanhoffer et al., 2014; Tanhoffer et al., 2015). A main barrier for SCI patients participating in physical activity is a lack of energy and motivation (Williams, Smith and Papathomas, 2014), this demonstrates that arm cycling could be used as a tool to influence a participants perception of exercise.

Upper limb exercise has been shown to be effective form of aerobic exercise for SCI patients (Williams et al., 2020; Devillard et al., 2007), and although we did not directly measure aerobic fitness, our participants commented that they felt the intervention improved their stamina. Participants in our focus group also discussed self-perceived improvements in strength, coordination and posture. Previous research has shown that SCI being physically active led to reduced perceived levels

of MSK and neuropathic pain, as well as increased function in transfers allowing for greater subjective wellbeing (Buchholz et al., 2009; Martin Ginis, Jörgensen and Stapleton, 2012; Norrbrink et al., 2012). Other authors have also commented on the ability of exercise to improve personal perceptions on their abilities (Taub, Blinde and Greer, 1999; Blinde and McClung, 1997), which supports our findings. This improved perception of function could come as a result of improved confidence in their abilities as well as an improved psychological state.

4.9 Feasibility and further improvements

This study was designed to decipher whether a six week arm cycling exercise intervention is a feasible rehabilitation programme. During the focus group, the participants had the general consensus that this programme was indeed feasible. They commented on the ease of task completion and the convenience of independent utilisation of the arm cycle. This is a significant finding as a lack of equipment is often identified as a barrier for exercise in SCI (Nightingale et al., 2018; Williams, Smith and Papathomas, 2014; Fekete and Rauch, 2012; Stephens, Neil and Smith, 2012). The exercise intervention also resulted in psychological and perceived physical improvements, demonstrating the ability to improve QOL and confidence. This exercise intervention also resulted in functional and physiological improvements which is in agreement other arm-cycling interventions in which there were improvements in static balance (Williams et al., 2020). Other research has also documented the ability of upper-limb exercise to improve postural control (Bjerkefors, Carpenter and Thorstensson, 2007; Grigorenko et al., 2004; Tsang et al., 2015). We were also able to demonstrate that our participants were complainant and adhered to the study protocol safely.

During the focus group, participants identified a slight difficulty with implementing the arm cycle initially at home, for example, not being able to find a suitable surface or the correct height to place the ergometer. Other difficulties included, not knowing whether there seating arrangement was appropriate. It could therefore be beneficial in future rehabilitation studies to include a home visit to assist in the first set up of the arm cycle. The participants also highlighted that they believed there would have been increased, measurable differences with an increased rehabilitation duration. It could therefore be useful to extend the programme for a longer amount of time, or implement a follow-up visit three months after an independent, home exercise programme.

4.10 Limitations

We did encounter difficulties and limitations when conducting the research, namely the biggest limitation being COVID-19. COVID-19 meant that research was suspended after less than half of the desired amount of data was collected. This lead to difficulties when identifying trends in data and identifying outliers. It is acceptable to assume with increased data sets, we would have been able to see stronger and possibly significant trends. Following COVID-19, we could not retrieve data from the University or access specific data analysis software's, again leading to difficulty when processing data. It also lead to reduced availability and accessibility to academic resources and facilities.

A further limitation was the study duration; It is likely that a six week period is not long enough to elicit functional improvements. As our study design did not involve a follow-up assessment beyond six weeks, it is unknown what the longer-term effects may be. It would be beneficial in future studies to include a three month

follow up assessment day to monitor and track further changes. Due to variables such as movement artefacts and signal noise, it was challenging analysing and drawing conclusions from our HDEMG data, further data collection is needed to further develop our findings. Although HDEMG allows for more reliable recordings, the reliability specifically in trunk muscles is yet to be established. Further data collection with increased participants is needed to draw accurate trends and conclusions from all aspects of this study. Some difficulties that arouse during the TMS data collection was the need for high intensities to evoke MEPs, this sometimes limited the amount of repetitions and length of time the participants could tolerate the testing. Other difficulties included large movement artefacts seen in the HDEMG analysis which could be a result of noise or muscle spasticity. A further difficulty in the participants was their varied abilities to complete the tasks, for some participants independent sitting was a challenge, therefore the quality of movement during the tasks and a possible factor of fatigue should be considered further in future studies.

4.11 Indications for future study

Our pilot study found trends towards improved postural control and corticospinal excitability following an arm cycling exercise intervention in SCI participants. Further research, utilising the fundamentals of this study, need to be conducted to investigate whether these trends continue to significance in a larger participant population. Correlation analysis also needs to be conducted to establish any trends between improved corticospinal excitability and postural control in the motion and HDEMG analyses. Future studies could also include an eyes closed condition during the perturbation task, a timed-up and go test for ambulatory patients and a self-reported QOL questionnaire. Another factor which could be investigated in the future

is the use of the lower limbs during our tasks. Future studies should consider expanding recruitment partners, as this study utilised a single site for recruitment. A follow up video call session could also be considered to assist with the arm-cycling set up at home. This study should be tested on a larger scale to further investigate trends and significant differences in the data with focus on corticospinal facilitation, reaction times during rapid shoulder flexion and trunk control during multidirectional reaching.

5. Conclusions

We observed improvement in functional reach and postural control in individuals with SCI after six weeks of home-based arm cycling exercise. We also found improvement in neuromuscular function of the back extensors during some functional tasks, including increased muscle activity, and improved muscle homogeneity. Furthermore, there was a tendency of increased excitability of corticospinal tract projections to the ES muscle after six weeks of the arm cycling exercise. Moreover, patients reported high adherence and compliance with the exercise and no serious related adverse event. Our findings suggest that six weeks of home-based, unsupervised arm cycling exercise is a feasible rehabilitation intervention for patients with chronic, incomplete SCI to improve trunk control. Further research with larger sample size and control groups is required to determine the effects of the arm cycling exercise on trunk control after SCI.

Appendix 1: Participant information

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The University of Birmingham
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United Kingdom

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Effects of arm cycling on trunk motor function after spinal cord injury

Research Participant Information Sheet

Version 2 02/04/2019

Invitation

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the study?

A significant proportion of people with spinal cord injury (SCI) have difficulties controlling the muscles of their torso/trunk which results in problems with sitting upright and stabilizing the upper body. The detrimental effects of this include limiting the use of the arms to aid with a number of activities of daily living such as feeding, dressing, weight-shifting, transferring between wheelchairs and bed/toilet and using wheelchairs.

We know that muscles of the trunk become active with almost any movement of the body and our research in healthy people has shown that movements of the arms can "excite" the brain pathways involved in controlling the trunk muscles. These movements can be as simple as bending the elbow, or moving the arms rhythmically.

In this study we want to know:

Can a 6-week arm cycling exercise improve function of the trunk muscles in people with SCI?

Why have I been chosen?

You are someone who has a stable, incomplete cervical or mid-thoracic spinal cord injury, can voluntarily contract selected arm muscles as well as have some residual trunk muscle function.

Do I have to take part?

No. It is entirely up to you. If you would like to take part, you will be asked to sign a consent form. Even after you have signed this consent form and agreed to take part in the study, you are free to withdraw from the study at any time.

Once you have decided to take part in this research, a member of our research team will discuss the study with you and answer any questions you may have by telephone or by email.

What will happen to me if I take part?

If you are happy to take part, you will be invited to the neurophysiological laboratory, located in University of Birmingham, at a convenient time where the full informed consent process will be undertaken and you are invited to take part in the assessments.

We will first assess your trunk muscle function by carrying out a number of short tests.

We will then use brain stimulation and recording of muscle activity to assess how excitable the pathways controlling the trunk muscles are. To do this we will use an investigative procedure called transcranial magnetic stimulation (TMS). This is used to activate the nerves in your brain which control your trunk muscles and involves placing a plastic coil in a specific position over your head, this is connected to a machine which delivers a small magnetic stimulus to the nerves in the brain, this is

not painful and does not involve any needles. We will record the electrical activity from the muscles under study in response to these stimuli using sticky self-adhesive electrodes (like those used to record ECGs) stuck to the skin overlying the muscles. There are two parts in this study and you can take part in either one or both of them.

Part 1. You will be carrying out arm cycling for 30 minutes while having two square electrodes over your head on two different occasions in our lab at University of Birmingham. You can take breaks every 10 minutes or when needed. You might feel a slight tingling initially due to the electrical currents over your head; this should wear off in a minute or so. After the cycling, we will repeat the same neural assessment every 10 minutes for up to 30 minutes. This will allow us to see if any effects outlast a short session of exercise-based repetition. Two visits in total in this part.

Part 2. We will ask you to perform repetitive arm cycling for 30 minutes (no electrical stimulation over your head). You can take breaks every 10 minutes or when needed. After the cycling, we will repeat the same neural assessment every 10 minutes for up to 30 minutes.

An arm bike will be given you so you can do the exercise at home. We will show you how to install the arm bike and explain to you the exercise protocol, which is 30 minutes per day, 5 consecutive days per week, and 6 weeks in total.

To monitor the effects of the exercise, you will need to have the same neural and balance assessments in our labs at 2 and 4 weeks into the exercise. Once the 6-week exercise programme is complete, a final assessment will be performed.

The results will be analysed by computer. We will then see if both neural and balance functions can be progressively improved along the course of the exercise programme.

In total we anticipate that you would come to the laboratory for 4 times, 1.5 hours per time.

You may be invited to attend a focus group where you will be sharing your experience of taking part in this study and discussing your views regarding future applications of the study with other participants and the research team. This will help us to understand what is the need of research in trunk rehabilitation after SCI from patients perspectives. It will be an informal discussion and all conversation will be anonymized. Discussions will be recorded and transcribed by a transcript company; however, no personal identity will be revealed in any way. The conversation will focus on your own experience of undertaking the intervention, feasibility of the intervention and support.

What are the side effects of any treatment received when taking part?

The assessment techniques are safe and non-invasive and there are minimal risks from having these test performed under strict safety guidelines which include stringent exclusion criteria. All tests will be performed within your limits of tolerance and you will be given as must rest as you need between tests.

You may experience mild muscle soreness following the arm cycling exercise. The discomfort can be managed by taking pain killers or hot/cold packs.

What are the possible benefits of taking part?

The function of your trunk muscles may improve after the exercise programme.

Will my taking part in this study be kept confidential?

In order to carry out the research project described above, we will need to collect information about you, and some of this information will be your personal data. Under data protection law, we have to provide you with very specific information about what we do with your data and about your rights. We have summarized the key information you need to know about how we will use your personal data on a separate page attached with the information sheet (Appendix 1).

More information on how the University processes personal data can be found on the University's website on the page called 'Data Protection - How the University Uses Your Data' (https://www.birmingham.ac.uk/privacy/index.aspx).

What if something goes wrong?

In the extremely unlikely event that anything goes wrong while you are taking part, local hospital facilities are available (A&E department), as well as an emergency assistance telephone 44444. You should call 999 if there is a medical emergency when undertaking the study at home.

University of Birmingham holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that University of Birmingham is at fault. This does not affect your legal rights to seek compensation.
If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Dr Chloe Chiou,
The normal National Health Service complaints mechanisms are also available to you.

What will happen to the results of the research study?
The results of the study will be analysed by the research team and presented at neuroscience, neurological and other health care conferences and published in scientific journals. No individual subject will be identified in any report or presentation arising from the research.

Who is organising and funding the research?

The study will be run by a research team based at University of Birmingham and funded by University of Birmingham.

Will I be paid for taking part in the study?

You will not be paid for your participation in the study, but we will pay for your travel expenses to and from University of Birmingham. Please keep the receipts for your journey as these will be required for your reimbursement.

Who has reviewed the study?

This study has been approved by HSC REC B.

Contact for further information about this study.

If you would like to consider this study further before you make your decision, please take your time to do so. You may ask for further information by telephoning 0121 414 2555. The person to speak to is the chief investigator, Dr Chloe Chiou. Alternatively, you may also send an email to s.chiou@bham.ac.uk to request further information.

Inclusion:

You are eligible to take part in this study if you:

1) Have a stable, incomplete cervical or thoracic spinal cord injury and are able to voluntarily move arms as well as sit still without support.
2) Are aged 18 years or over.

Exclusion:

You CANNOT take part in this study if you:

1) Have had injuries to the brain and/or brain surgery.
2) Are pregnant, breast feeding, or have any chance that you could be pregnant.
3) Have a history of epilepsy (fits or seizures) or a family history of epilepsy.
4) Have any metal (other than in your spine) or a medical device inside your body.
5) Are currently taking antidepressants drugs.

Appendix.

Who is the Data Controller?

The University of Birmingham, Edgbaston, Birmingham B15 2TT is the data controller for the personal data that we process in relation to you.

What data are we processing and for what purpose will we use it?

We will collect and process your personal data to conduct the research project, as explained in the Participant Information Sheet.

What is our legal basis for processing your data?

The legal justification we have under data protection law for processing your personal data is that it is necessary for our research, which is a task we carry out in the public interest. These data will not be used to make decisions about you.

Who will my personal data be shared with?

We will not share your data with any third party.

Sometimes, external organisations assist us with processing your information, for example, in providing IT support and transcription service. These organisations act on our behalf in accordance with our instructions and do not process your data for any purpose over and above what we have asked them to do. We make sure we have appropriate contracts in place with them to protect and safeguard your data. If your personal data are transferred outside the European Union (for example, if one of our partners is based outside the EU or we use a cloud-based app with servers based outside the EU), we make sure that appropriate safeguards are in place to ensure the confidentiality and security of your personal data.

How will my personal data be kept secure?
The University takes great care to ensure that personal data is handled, stored and disposed of confidentially and securely. Our staff receive regular data protection training, and the University has put in place organisational and technical measures so that personal data is processed in accordance with the data protection principles set out in data protection law.

The University has an Information Security Management System based on ISO27001 with a range of controls covering the protection of personal information. Annual security awareness training is mandatory for staff and the University is accredited under the NHS Information Governance Toolkit, the Payment Card Industry Data Security Standard and is in the process of gaining Cyber Essentials Plus for defined services.

In relation to this project, all participants will be allocated a study ID at point of consent. The Consent forms will be stored in a secure cabinet by the research team at the prospective sites. Anonymized data will be stored on University computers.
Personal data required to contact patients will be stored on the secure University server (i.e. Bear RDS) that is password protected and the meets University of Birmingham criteria for storing personal data. This information will be kept for 10 years as per University of Birmingham policy.
Data generated by this study will be kept for 10 years as per University of Birmingham guidelines including the patient consent forms. This data will be appropriately destroyed after 10 years.
Only members of the research team will have access to the information and data collected. The Chief investigator will be the custodian of the data, which will be stored in a password-protected computer at University of Birmingham.
The subjects will be anonymised with regards to any future publications relating to this study.

How long will my personal data be kept?
Your data will be retained for 10 years after the publication of the research outcomes. If you withdraw from the project, we will keep the information we have already obtained but, to safeguard your rights, we will use the minimum personally-identifiable information possible.

Your rights in relation to your data
You may have the following rights in respect of your personal data:

- The right to access to your data (often referred to as a Subject Access Request).
- The right to rectification of inaccuracies in your data.
- The right to erasure of your data (in certain circumstances).
- The right to restrict processing of your data (in certain circumstances).
- The right to object to the processing of your data (in certain circumstances).
- The right to ask for your personal data to be transferred electronically to a third party.

However, your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the project, we will keep the information we have already obtained but, to safeguard your rights, we will use the minimum personally-identifiable information possible.

If you would like more information on your rights, would like to exercise any right or have any queries relating to our processing of your personal data, please contact:

The Information Compliance Manager, Legal Services, The University of Birmingham, Edgbaston, Birmingham B15 2TT

Email: dataprotection@contacts.bham.ac.uk Telephone: +44 (0)121 414 3916

If you wish to make a complaint about how your data is being or has been processed, please contact our Data Protection Officer.

Mrs Carolyn Pike, OBE, The Data Protection Officer, Legal Services, The University of Birmingham, Edgbaston, Birmingham B15 2TT

Email: dataprotection@contacts.bham.ac.uk Telephone: +44 (0)121 414 3916

You also have a right to complain to the Information Commissioner's Office (ICO) about the way in which we process your personal data. You can make a complaint using the ICO's website.

1-10 Borg rating of perceived exertion scale	
0	Rest
1	Really easy
2	Easy
3	Moderate
4	Somewhat hard
5	Hard
6	
7	Really hard
8	
9	Extremely hard
10	Maximal effort

Appendix 3: Exercise diary

UNIVERSITY OF BIRMINGHAM

The University of Birmingham
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Exercise Diary for the research study: Effects of arm cycling on trunk motor function after spinal cord injury

Day	Exercise		Is the exercise complete?	Notes (e.g. reasons that the exercise is not complete, exercise-related discomfort, etc)
1	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
2	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
3	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
4	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
5	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
6	Rest Day			
7	Rest Day			
	Duration:	RPM:	Yes	

8	Rotations	Breaks (how many times):	No	
9	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
10	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
11	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	
12	Duration:	RPM:	Yes	
	Rotations	Breaks (how many times):	No	

Congratulations! You have completed 10 sessions of exercise. It is time to see how much you have improved.

Assessment appointment date:

Appendix 4: Exercise instructions

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Exercise instructions for the research study: Effects of arm cycling on trunk motor function after spinal cord injury

PROTOCOL: 30 MINUTES/DAY, 5 CONSECUTIVE DAYS/WEEK, 6 WEEKS

- Please ensure that the arm bike is secured firmly on a table.
- The height of the table needs to be adjusted according to the height of the seat you use for the arm cycling. An appropriate setting should allow you to comfortably perform the arm cycling for at least 30 minutes.
- Try to sit upright without leaning on the back rest of your chair during the cycling so the exercise can challenge your balance control.
- Try to keep the same rhythm for cycling. We recommend a speed of 60rpm.
- Use your phone/watch or a timer to time the duration of your exercise.
- Take a short break to remind you the time. Try to keep the length as minimum as possible. You can use the back rest during the break.
- Record the amount of exercise you have complete today.
    - Workout time
    - Distance
    - Total rotations

You can find the information from the displayed screen of the bike.

If you have any questions, please contact the research team. Contact details of the Chief Investigator can be found on the top left corner.

Happy Exercise! ☺

Assessment appointment date:

Initial assessment:
2 weeks:
4 weeks:
Final assessment:

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