MUSCULAR ACTIVATION AND CORTICOSPINAL EXCITABILITY ADAPTATIONS TO SPLIT CRANK CYCLING

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ABSTRACT

Introduction – Foot drop is a common motor impairment of the lower limb caused by Acquired Brain Injury (ABI) that can limit mobility and increase risk of falls. Split Crank (SC) cycling is proposed here as a novel paradigm to evoke functional neural plasticity and beneficial muscular adaptations to treat foot drop.

Methods – Healthy participants were randomly assigned to SC or FC conditions for a 5 day intervention. Transcranial magnetic stimulation (TMS) evoked stimulus-response curves (SRCs) for tibialis anterior (TA) and muscle kinematic activation patterns for TA, soleus (SOL), biceps femoris (BF) and vastus lateralis (VL) during cycling were recorded before and after the first and last training sessions.

Results – SRCs revealed no beneficial TA corticospinal excitability adaptations to training but significant increases in duration of TA and BF activity were reported for TA and BF during SC cycling ($p < .05$). This occurred as an immediate response on initial exposure to the task.

Discussion – The strength of evidence for implementing SC cycling with ABI patients in the treatment of foot drop was weaker than hoped. However, increased duration of TA activation shows promise as beneficial for foot drop sufferers. Completion of the study provided new information on an unexplored exercise therapy and useful observations for facilitating clinical translation in the future.
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LIST OF KEY ABBREVIATIONS

**ABI/TBI** – Acquired Brain Injury, Traumatic Brain Injury

**TMS** – Transcranial Magnetic Stimulation

**CSE** – Corticospinal Excitability

**AP/SRC/BSS** – Activation Pattern, Stimulus-Response Curve, Borg Scale Score

**CIMT/LNUS** – Constraint-Induced Movement Therapy, Learned Non-Use Syndrome

**SC/FC** – Split Crank, Fixed Crank

**rpm** – Revolutions per Minute

**TDC/BDC** – Top Dead Centre, Bottom Dead Centre

**TA/SOL/BF/VL** – Tibialis Anterior, Soleus, Biceps Femoris, Vastus Lateralis

**RMSE** – Root Mean Squared Error

**RCV/ICPD/KPE** – Right Crank Variability, Inter-Crank Position Difference, Knee Position

Trace Exclusion
CHAPTER 1 - INTRODUCTION

1.1 – INTRODUCTION PURPOSE

This chapter is aimed at establishing our current understanding of corticospinal excitability (CSE) in animals and humans and how the non-invasive techniques such as transcranial magnetic stimulation (TMS) are used to measure its changes has revealed the capacity to of the nervous system to adapt plastically in response to certain training paradigms. The novel concept of split crank (SC) cycling is introduced and how it may be advantageous for acquired brain injury (ABI) patients in rehabilitation from mobility impairments, focusing specifically on foot drop, over other currently recognised therapies. Finally, since research into this novel therapy is scarce, aspects of the design which need to be established in healthy individuals first are discussed and how they will facilitate progression into a clinical rehabilitation setting in the future.

1.2 – CURRENT UNDERSTANDING OF CORTICOSPINAL PLASTICITY

Historically, the motor cortex was thought of as a static model of muscular representation with little or no capacity for adaptation\(^1\). In addition to this, it was thought that the somatotopical organisation of the motor cortex was discrete for specific body parts where each part occupied a non-overlapping cortical space\(^2\). More recently, the idea of a motor cortex with dynamically changing regions of muscular representation is accepted where sensorimotor reorganization occurs on a day to day basis throughout life\(^3\), contributing the development of the nervous system in early childhood\(^3\) and as an adaptation to environmental changes\(^4\). There is also evidence to support neural plasticity at a spinal level in response to specific conditioning in animals\(^5\) and humans\(^6\) and is why neural adaptations
to training paradigms are often referred to as adaptations of the corticospinal tract in terms of CSE or plasticity.

1.2.1 – Evidence of Corticospinal Plasticity in Animals

To demonstrate these neuroplastic effects, there has been a number of studies in animals which has enabled the use of invasive techniques assessing corticospinal plasticity\(^7\)\(^9\) that would be otherwise unattainable in humans. One study by Kleim et al.\(^7\) looked at changes in rat limb motor cortex representation before and after training with a forelimb reaching task by electrophysiological mapping of the cortex with microelectrodes. Greater forelimb and wrist representations were found for rats in the skilled reaching than unskilled reaching paradigm, displaying an apparent functional plasticity to improve task performance. In a similar experiment by Nudo et al.\(^8\), squirrel monkeys were given either a grasping task targeting digit activity or a key locking task which targeted forearm activity. The grasping task caused expansion of the motor cortex region associated with digits and contraction of the forearm region whilst the key-locking task showed the opposite; expansion of the forearm and contraction of the digit regions. The results seen in both studies were concurrent with an increased success rate of task performance suggesting that the observed nervous plasticity may have been functionally significant and contributed to the observed improvements.

1.2.2 – Measuring Corticospinal Plasticity with Transcranial Magnetic Stimulation

These animal studies allow the use of invasive techniques not possible in humans to give a more detailed picture of the mechanisms driving plasticity. However, their physiology can be quite different from humans which can limit the generalisation of findings. Luckily, there have been recent technological advancements in neuroimaging and non-invasive stimulation techniques that have made looking at similar neuroplastic changes in humans a
possibility\(^{(10,11)}\). In particular, the use of transcranial magnetic stimulation (TMS) has allowed direct assessment of motor cortex representation in humans and the efficacy of the corticospinal tract with relative ease. TMS uses a rapidly changing magnetic field to produce electrical excitation of motor cortical neurons which evokes an electrical response at the muscle they subserve known as a motor evoked potential (MEP)\(^{(12-14)}\). In neurorehabilitative research, TMS evoked MEPs are commonly used to assess changes in CSE for a target muscle via the generation of stimulus-response curves (SRCs)\(^{(12,13,15,16)}\) and cortical maps (CMs)\(^{(10,11,17,18)}\). SRCs are the product of plotting a range of TMS stimulus intensities (ranging from 0 to 100% maximum stimulus output or MSO) which are delivered to a single point on the motor cortex against their corresponding MEP magnitudes to produce a scatter graph. A sigmoidal shaped curve can then be fitted to this scatter where specific changes in its profile following training or rehabilitation can be indicative of changes to CSE, and neuroplastic adaptations by extension, for the muscle of interest\(^{(13,14,16)}\) (Figure 1). CMs rely on a slightly different utilization of MEPs...
whereby a series of stimulations are delivered randomly to multiple scalp sites across a set
grid on the motor cortex at a predefined intensity\textsuperscript{(11)}. The resultant MEP magnitudes can then
be used to construct a muscles motor representation map similar to the one shown in Figure 2
where changes in map volume and area act as the indicators for changes in CSE and motor
cortical re-organisation. In rehabilitation research these measures are considered highly
advantageous due to their high degree of sensitivity which is often not achieved with the use
of graded scales of functional motor recovery such as the Fugl-Meyer Motor Assessment
(FMA) and Brunnstrom Motor Recovery Stage (BRS) assessments. In these cases, small
improvements in neural recovery, which are likely to precede apparent functional motor
progression, may go unseen and experimental or indeed conventional methods of
rehabilitation may be deemed ineffective for the patient’s recovery. As such, the application
of TMS as described above is becoming more widely used (where possible) in a rehabilitation
setting and additionally during cases of experiments involving healthy participants where the
measures are still sensitive enough to detect even the slightest excitability changes and
thereby provide a basis for the application of the proposed therapy or training to patients.
Although the two TMS applications discussed here differ in methodology, they share a
common outcome measure in the quantification of changes in CSE and have both been
assessed as equally effective in successfully achieving this in humans\textsuperscript{(16)}.

1.2.3 – Evidence of Corticospinal Plasticity in Humans

Using TMS to measure plasticity in some of the ways described here, including additional
methods too, has led to a wealth of research documenting how humans also can adapt
corticospinal excitability in response to specific training. Classen et al.\textsuperscript{(19)} used TMS to evoke
twitch responses of the thumb before and after a unidirectional movement training paradigm,
observing how the training altered kinematics of the TMS-evoked movement. It was found
that after the training, the acceleration vector of TMS evoked responses was modulated
towards the trained direction which lasted for around 15-20mins, meaning the training altered
the directional preference of the TMS evoked responses. This effect demonstrates short term
or acute reorganization of
the neural networks
controlling thumb
movement kinematics\textsuperscript{19}
as a neuroplastic response
to the training. In a
different study with a more skilled training exercise, Pascual-Leone et al.\textsuperscript{20} used TMS to map
regions of the motor cortex which represented finger flexors and extensors during 5 weeks of
a 5 finger piano training paradigm. Concurrent with a reduction in number of sequence errors,
the trained hand showed marked map expansion compared to the untrained hand (Figure 3)
attributed to a two stage process of plasticity\textsuperscript{4}. The first stage includes an acute stage of
rapid map size modulation between Monday and Friday representing adaptation of existing
neural pathways, with the slower more discrete changes occurring between Mondays, (with
the weekend for wash-out) illustrating long term cortical structural changes as the skills
become automatic and overlearned\textsuperscript{4}. Following this, it seems that there is the potential for
motor learning to cause lasting neural adaptations contributing to improved task performance,
something which is well demonstrated in similar studies where performance improvements
have been retained following the cessation of training\textsuperscript{21, 22}.

In addition to the majority of this research which is conducted in the upper limb, there is also
evidence to show that repetitive practice based learning can evoke functional neuroplastic
changes in the lower limb as well, though in far fewer numbers. One such example includes
the ‘up’ and ‘down’ conditioning of spinal h-reflexes using or goal orientated feedback\(^{(6)}\).

Thompson et al.\(^{(6)}\) asked participants to stand freely and maintain a level of background soleus activity before a h-reflex was elicited, with its magnitude being visually displayed immediately for the participant to see whether it was inside or out of a ‘up’ (above their average control h-reflex) or ‘down’ (below their average control h-reflex) conditioned range. Participants were able to successfully adapt the size of their h-reflexes to the operant conditioning within early sessions showing task-dependent adaptation, but also over a longer time period, illustrated by changes to their control h-reflexes which became apparent in later conditioning sessions, suggesting a longer term supraspinal influence on adaptation. This suggests a complimentary role of the brain and spine in influencing plasticity in response to task requirements within the nervous system\(^{(6)}\) and shows the lower limb has a similar neuroplastic capacity as the upper limb. In another lower limb study, Perez et al.\(^{(12)}\) used a tracking task controlled by ankle plantar and dorsiflexion to examine plastic changes in neural excitability of the tibialis anterior (TA) using TMS. It was found that TMS motor evoked responses (MEPs) were significantly greater following 32 mins of skilled training, with no significant changes seen in the non-skilled (voluntary ankle dorsi/plantar flexion) and passive training (assisted voluntary ankle dorsi/plantar flexion) groups. This too, shows that in addition to upper limb learning, motor skill training can evoke plasticity affecting lower limb excitability as well.
1.3 – UTILIZING CORTICOSPINAL PLASTICITY IN REHABILITATION

1.3.1 – Acquired Brain Injury and its Associated Motor Impairments

The term Acquired Brain Injury (ABI) is commonly used in rehabilitation research studies but one which is also loosely defined. Following this, many studies are quite vague with their inclusion criteria and often have varied subject populations as a result\(^{(23)}\). However, a comprehensive definition used presently comes from The Toronto Acquired Brain Injury Network, where ABI can be seen as “damage to the brain that occurs after birth and which is not related to congenital disorders, developmental disabilities, or processes that progressively damage the brain”\(^{(23, 24)}\). This definition outlines how ABI can occur through both traumatic and non-traumatic damage to the brain\(^{(24)}\) which is an important factor often overlooked by experiments with ABI patients.

Two of the most common forms of ABI are Stroke and Traumatic Brain Injury (TBI). Stroke is a non-traumatic form of ABI and accounts for a reported 5.5 million deaths per year globally\(^{(25)}\) with an estimated 205,000 cases a year in the UK alone\(^{(26)}\). Stroke often causes motor dysfunction in muscles contralateral to the lesion site causing a sudden neurologic deficit which reduces cortical drive for desired movements\(^{(27)}\), and whilst the loss of upper limb motor function can reduce the ability to perform activities of daily living, stroke can commonly cause lower limb dysfunction as well with subsequent mobility issues being one of the highest reported post-injury health problems\(^{(28)}\).

Similarly, with an incidence of 300 per 100,000 population, TBI is a commonly reported injury in the UK where roughly 83-93% of cases are reported as mild and only around 3% as severe\(^{(29)}\). One of the greatest sources of TBI is via road traffic accidents, accounting for 40% of all TBIs with around 30% of severe cases involving the consumption of alcohol\(^{(29)}\). In cases
of TBI, the most common subject of rehabilitation research is concerning cognitive and behavioural impairments which can be associated with both mild and severe injuries\(^{(30)}\).

Physical deficits of TBI are typically associated with severe cases alone\(^{(30)}\) and are often only mentioned briefly with little focus on novel rehabilitation strategies. However, common examples of TBI physical impairments include loss of balance, altered coordination, postural instability and temporal asymmetry\(^{(31-33)}\) which can affect the generation and execution of rhythmic patterns of muscular activity such as walking.

In addition to stroke and TBI, less common forms of ABI also include meningitis\(^{(34)}\), cancerous brain tumours\(^{(35)}\) and hypoxic injuries\(^{(36, 37)}\) all of which inflict damage to the brain which can contribute to motor impairments too. Typical examples of these impairments include ataxia\(^{(38)}\) and loss of coordination and dizziness whilst walking\(^{(34)}\) both of which may affect the ability to carry out activities of daily living and general quality of life.

### 1.3.2 – Optimising Functional Plasticity in ABI Rehabilitation

The prospect of a human nervous system which has the ability to dynamically adapt to environmental changes is very appealing when considering recovery from damage imposed by a neurological injury such as an ABI. A loss of cortical neurons devoted to a particular motor performance or muscle as a result of ABI can cause impairment, but by tailoring rehabilitation therapies to train the impaired muscle we can elicit functional reorganisation of motor cortical and spinal neurons to compensate, thereby promoting recovery. In these instances the aim is to evoke plasticity which can cause a beneficial or desired outcome, sometimes termed functional plasticity. Evidence of beneficial or functional plasticity following ABI has been made apparent in both animal and human studies. One of the more simplistic examples of this is the use of Constraint-Induced Movement Therapy (CIMT) where use of the affected limb is encouraged during motor training by constraining the
unaffected limb\(^{(39,18)}\). The basis for this concept comes from the proposal of a phenomenon known as learned non-use syndrome (LNUS) (Figure 4) which is considered to be a major hurdle to overcome during ABI motor rehabilitation. Liepert et al.\(^{(18)}\) looked at how 2 weeks of CIMT affected motor cortical representation of the abductor pollicis brevis (APB) muscle in the hand in recovering stroke patients using TMS. It was found that the therapy increased map size of the affected APB indicating an apparent recovery of the cortical neurons lost to the ABI through functional plasticity\(^{(18)}\). Other studies investigating CIMT in humans have found similar findings with varying effect strengths\(^{(40,41)}\) and is something which has been well demonstrated in monkeys as well\(^{(8)}\). From these studies it appears that by neglecting to use an already weakened limb, the region of the motor cortex devoted to its activation will shrink and further exacerbate the impairment, but by engaging the limb in a functional manner this process can be deterred and even reversed with map expansion\(^{(9)}\).

Although the evidence presented here has established that functional neuroplasticity can occur by simply engaging the affected limb in a broad sense following ABI, it is important to establish which characteristics of these training paradigms are most important for inducing this effect so that rehabilitation can be tailored to optimise motor recovery. For example, in addition to simply engaging the affected limb it is believed that the activity should be skilled.
or novel to maximise behavioural demand and subsequent plasticity during training\(^9, 12, 17, 39, 42, 43\). This has been made apparent in a study by Lundbye-Jensen et al.\(^{42}\) where training involving 4 weeks of either a skilled visuomotor tracking or resistive strength training of the right biceps brachii (BB). Changes in the profile of TMS stimulus-response curves revealed an apparent increase in the corticospinal excitability of the BB muscle with skill training which was not apparent in the strength or control groups. This finding has emerged from similar studies in the human lower limb comparing skilled tracking using dorsiflexion of the ankle with passive movement alone\(^{12}\), in animal studies with monkeys trained to retrieve food pellets from wells of differing size\(^9, 17\) and with simple strength training in rats\(^{44}\). This suggests that the skill acquisition or behavioural demand specifically was driving the plasticity in a functional manner and that the repetition or physical load of the unskilled tasks were not sufficient to evoke plasticity alone i.e. training induced functional neuroplasticity does not simply act in a use or load-dependent manner\(^{43}\). These observations could be consistent with the notion that human motor cortex is concerned more with the organisation of complex motor patterns than executing contractions of specific muscles alone\(^{44}\) which suggests that training aimed at driving neuroplasticity should also be functionally relevant to the specific movements defined as outcome goals of the rehabilitation.

Given the evidence presented here it seems that the parameters of the training needed to evoke the greatest extent of functional plasticity include some level of repetition and a high or increasing skill aspect which requires a degree of learning. Making the training functionally relevant and beginning as early as possible following ABI so as to reduce the effects of LNUS may also prove beneficial in optimising motor rehabilitation therapy. It is important to note however, that no single element of training has been isolated as the most important in inducing functional plasticity\(^{43}\) so each parameter should be considered with equal weight.
1.4 – ABI RELATED FOOT DROP AND ITS CURRENT TREATMENTS

1.4.1 – ABI Related Foot Drop

Whilst upper limb motor impairments associated with ABI can cause disruptions in the performance of daily tasks, lower limb dysfunction can be seen as particularly debilitating as it limits mobility and subsequent independence. One common lower limb impairment which significantly affects mobility, and is often targeted in rehabilitation as a result, is foot drop.

Foot drop limits a person’s ability to produce normal gait from reduced ability to dorsiflex the ankle during the swing phase of walking\(^{(45-47)}\), which can cause limited, to no toe clearance and can result in the stepping foot dragging on the floor\(^{(48, 49)}\). This problem is believed to be caused by partial or total paresis of the ankle dorsiflexor muscles which can result from altered neural transmissions supplying the muscle, or an inherent weakness of the muscle itself\(^{(45-47, 50)}\). People suffering from foot drop often adopt compensated gait strategies to overcome the impairment which can include hitching or excessive bending of the leg at the hip\(^{(47, 48)}\). Over time these maladaptive compensation strategies can cause secondary complications which can lead to deterioration of balance, increased risk of falls, reduced confidence and decreased endurance\(^{(47, 49)}\).

1.4.2 – Treating Foot Drop

1.4.2.1 – Ankle Foot Orthosis (AFO)

An AFO is a mechanical brace which splints the lower limb and foot to keep the ankle in a neutral position during walking which aids toe clearance during the swing phase and promotes heel strike to produce increased stability during gait\(^{(46, 51-53)}\) (Figure 5). Being relatively inexpensive, easy to use and providing continuous ankle stability during walking the AFO is one of the most frequently used treatments for foot drop\(^{(54)}\). Although use of the
AFO has been reported to have beneficial effects on postural stability in early stroke recovery\textsuperscript{(55)} and improve VL activity contributing to more balanced gait\textsuperscript{(56)}, the AFO has several drawbacks as well. A common problem with AFOs is that although they aid toe clearance during swing they do not provide free ankle motion during stance which may lead to abnormal gait patterns\textsuperscript{(57)}. In addition to this they have also been reported as uncomfortable and awkward to use\textsuperscript{(46)} which may explain why patients can be non-compliant with their application\textsuperscript{(58)}. Another disadvantage of AFOs is that by immobilizing the ankle in a neutral position, the TA becomes inactive during walking. This promotes its disuse and potentially accelerates the effects of LNUS\textsuperscript{(39)} through contraction of the motor cortical representation of the TA to further delay recovery\textsuperscript{(59)}. To address some of the criticisms discussed here, there have been several novel AFO designs proposed which include the development of a ‘power-harvesting’ AFO which allows free ankle movement whilst still aiding toe clearance in swing\textsuperscript{(57)} and an ‘active’ AFO with variable joint stiffness aiming to achieve a similar outcome\textsuperscript{(52)}, though these are yet to be commonly used in clinical practice.

1.4.2.2 – Functional Electrical Stimulation (FES)

An alternative to the AFO for the treatment of foot drop is the use of FES. FES is essentially electrical stimulation of a muscle or nerve subserving a muscle that elicits a specific functional movement which, in the case of treating foot drop, is dorsiflexion of the ankle and is usually achieved by targeting the TA. The idea of using electrical stimulation to activate weakened muscles was first tested on stroke patients by Liberson et al.\textsuperscript{(60)} who used a
triggered switch plate in the heel to stimulate TA contraction during walking and promote normal gait. The device was successful in reducing the effects of foot drop and, interestingly, also helped participants recover near normal gait patterns when the device was removed, displaying an apparent therapeutic effect. Since these devices are more discrete and often more comfortable than the AFO alternative, patient reports have indicated a preference towards them\textsuperscript{(53, 54)}, even in cases where the AFO was reported as having greater orthotic effects on ambulation than FES\textsuperscript{(61)}. In addition to patient preferences, training with FES devices has shown beneficial orthotic effects by increased walking speed and reduced physiological cost index (PCI) of walking\textsuperscript{(62-65)}. With direct comparison to the AFO there has also been reports of greater improvements in walking speed, obstacle avoidance and balance\textsuperscript{(51, 54, 62)} suggesting patient preference is met with greater benefits as well. Some studies have also reported a therapeutic effect of training with the stimulators indicating some form of functional plasticity\textsuperscript{(63-65, 66, 67)} (Figure 6), however the effects are often seen in only a select few patients and with such high between subject variability, it may be the case that the benefits can only be experienced by a certain subset of people, potentially of a specific biological predisposition\textsuperscript{(51, 64)}. Although FES seems like a good alternative to the AFO, it is more expensive and there have been reported

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure6.png}
\caption{-- TMS evoked cortical maps of a single stroke participants TA A, prior to use of the WalkAide foot drop stimulator and B, following 6 months of training with the stimulator. Clear increases in MEP strength following the intervention show the power of the therapeutic effect in this individual (Adapted from Everaert\textsuperscript{(67)})}
\end{figure}
problems arising from the use of surface-based FES devices, including cutaneous pain or discomfort from stimulation, mechanical failure, difficulty replicating electrode placement and achieving isolated or deep muscular contractions\(^\text{64, 68, 69}\). As such there is continued research into the feasibility of other alternative therapies.

1.5 – SPLIT CRANK CYCLING AS AN ALTERNATIVE FOOT DROP TREATMENT

As mentioned, the AFO and FES are not without their limitations and have warranted continued research into alternative therapies as a result. One example of this is exercise-based therapies which are often employed as a supplement to conventional rehabilitation to try and accelerate recovery from gait impairments like foot drop. But whilst walking would be the most functionally relevant exercise regime for these patients, muscular weakness and uncoordinated movements make this type of training dangerous without heavy assistance, which can be time consuming and tiring for both the patient and therapist\(^\text{70}\).

With this in mind, lower limb cycling is often employed as an alternative to walking based exercise therapies as it offers body weight support whilst still providing rhythmic, reciprocal muscular activity that may mimic walking\(^\text{71}\). It also reduces the risk of falls where balance control is impaired, and can include progressively increasing resistance to improve

![Diagram A](image1.png)

**Figure 7.** – A. Fixed crank cycling; both pedals are fixed apart at 180°, application of downward force at pedal 1 during the downstroke (DS) results in no simultaneous force application needed upward at pedal 2 during the upstroke (US). B. Split crank cycling; both pedals are decoupled and allowed to move independently of one another, now force application is required both downward and upward during the DS and US respectively.
muscular strength which may lead to the ability for patients to eventually support their own body weight, making the more functionally relevant walking exercise a possibility in the future\(^{(72)}\).

In addition to conventional cycling regimes several novel cycling therapies have been developed to optimise gait recovery for ABI patients specifically\(^{(73,74,70)}\). One novel cycling paradigm which hasn’t received a great deal of attention in a clinical environment is split crank (SC) cycling where the two cranks arms of the bike work independently of one another. This requires the cyclist to apply continuous force to the crank arm throughout the entire crank cycle without assistance from the contralateral foot during the pedalling upstroke (explained further in Figure 7). This cycling paradigm has the potential to provide unique benefits to ABI patients suffering gait impairments like foot drop but there is very little research which has tested this explicitly. In addition to this, the evidence from conventional cycling fixed crank (FC) studies with ABI patients has provided contrasting results regarding the feasibility of this novel cycle training to induce these beneficial effects. Here, this evidence is discussed and areas of the literature which are lacking in this field are highlighted.

1.5.1 – Improving Aerobic Fitness

As mentioned, the use of exercise-based therapies for ABI patients may help to improve aerobic capacity and promote faster motor recovery as a result, but few studies have tested this by using both aerobic fitness and functional gait improvements as primary outcome measures together or, in the instances where they have, measured concurrent increases in them both\(^{(72,75-77)}\). However, there is some evidence provided from a stroke patient case study by Holt et al.\(^{(78)}\) who completed 8 weeks of static cycle training. The patient showed improvements in walking speed and other functional mobility measures which were coupled with improved performance of an incremented aerobic fitness test. Similarly, a review by
Pang et al.\textsuperscript{(79)} concluded that aerobic training can improve general aerobic fitness and functional mobility factors such as walking velocity and endurance for stroke patients. However, it should be noted that these review studies involved aerobic training programmes outside of cycling, such as body weight support treadmill training\textsuperscript{(80)} and water-based endurance exercise\textsuperscript{(81)} and as such, does not provide support for conventional cycle therapy specifically. Following this it seems there is a call for more extensive research assessing both aerobic fitness and functional mobility parameters with conventional cycle training in ABI patients.

With the absence of contralateral limb assistance during the upstroke, SC cycling should require more effort to perform and as such, may provide additional aerobic fitness benefits over FC paradigms. But in contrast to these conventional cycling studies, there is no experimental evidence documenting the aerobic benefits of SC cycling in ABI patients. However, there is one study by Luttrell et al.\textsuperscript{(82)} who compared cardiovascular elements of fitness before and after training with either FCs or SCs in healthy participants. It was found that training with SCs significantly reduced heart rate and VO$_2$ Max compared to pre-training, with the reductions in heart rate reported as significantly greater than those training with normal cranks alone. This suggests that there may be potential aerobic fitness benefits of SC cycling for ABI patients too although it is important to take care when generalising the results of this single study of healthy participants to such a neurologically and physically differing population. The extent of these beneficial effects on functional outcome measures of gait performance are also unknown and as such, may be an interesting research venture in the future.
1.5.2 – Correcting Lower Limb Strength Imbalances

Since cycling with SCs means that both legs have to work at independent intensities and contralateral leg contribution during the upstroke phase of the crank cycle is eliminated\(^{(83)}\), one proposed benefit of training with them is that they may correct strength imbalances between lower limbs. ABI related motor deficits are often concentrated to one side of the body which makes these imbalances quite common and since lower limb muscular strength has been shown as an indicator of post-ABI gait speed and cadence\(^{(84)}\), this asymmetry in strength may contribute to abnormal gait. Correcting this issue could therefore be highly beneficial for rehabilitation of lower limb mobility impairments.

Although research regarding this effect is scarce, one patient’s case report describes personal experience and beneficial effects of using SC training as extended rehabilitation\(^{(85)}\). The 50 year old patient had been instructed by a neurologist to try and participate in some repetitive exercises to ‘retrain the brain’ but with some very basic home rehabilitation exercises he had seen little improvements in gait recovery. Following some advice from a personal trainer about single leg cycling and with the neurologist comments in mind, he started training with SCs and found improvements in gait after several weeks which stretched as far as regaining the ability to run. A similar case involved a patient with cerebral palsy describing how the training helped him correct a self-reported 80/20 strength imbalance in lower limbs to 51/49 in just over a years worth of training\(^{(85)}\). Although these reports are only of isolated cases with patient reports serving as measures of the training, they provide some evidence for the potential of SCs to help correct lower limb strength imbalances contributing the irregular gait.
1.5.3 – Adaptations to Muscular Activation

1.5.3.1 – Correction of Abnormal Activation

Aside from the aerobic fitness and strength factors which may contribute to improved gait following ABI, there have been a number of studies investigating how muscular activation can change in response to conventional cycling exercise. Abnormal muscle activity during gait is something which is well documented in patients suffering from ABI, from diminished magnitude and inappropriate on and offset activity in the ankle plantar and dorsiflexors\(^{(86, 87)}\) to similar deficits in the knee flexor and extensors as well\(^{(87, 88)}\). Rhythmic, reciprocal movements associated with cycling have been proposed to correct these abnormal patterns of activity which may contribute to mobility deficits\(^{(87, 89, 90)}\). However, some of the research supporting this notion is mixed. There is some evidence that ABI patients may be able to adapt both the magnitude and duration of muscular EMG responses during cycling in response to increased load\(^{(100)}\) and speed\(^{(101)}\) respectively but this only shows the ability to modify muscular activation in a ‘scaled’ manner and doesn’t elucidate whether inappropriate on and offset of muscular activity can be modified in response to training too.

Schindler-Ivens et al.\(^{(89)}\) showed that stroke patients have a diminished ability to adapt patterns of muscular activity (on and offsets during the 360 degree crank cycle) between forward and backward cycling as compared to neurologically intact controls. This suggests that the capability to adapt the occurrence of innappropriately timed bursts of muscular activation during locomotor activity is impaired in ABI patients. However, Alibiglou et al.\(^{(93, 94)}\) conducted some experiments using a decoupled ergometer with 12 different relative angular crank positions, established as 30 degree increments from 0 degrees (in phase cycling) through 180 degrees (normal anti-phase cycling) to 330 degrees and found that stroke patients were able to adapt the timing of muscular activation bursts in a similar
fashion to controls, somewhat conflicting with observations of Schindler-Ivens et al.\textsuperscript{(89)}. It is important to mention, however, that these results are from single session experiments and none of these studies investigated the capacity of ABI patients to adapt their abnormal muscular activation with longer term training protocols such as those commonly seen with exercise-based rehabilitation therapies. It is therefore difficult to determine whether a novel cycle therapy such as SC cycling will have the effect of correcting, or even exacerbating, the abnormal muscular activation patterns exhibited by ABI patients that may contribute to impaired gait. Using healthy participants to develop the understanding of training adaptations with SCs will therefore be important to establish feasibility of safe translation to patient groups in the future.

1.5.3.2 – Increased Activation of Muscles Related to Foot Drop

Although correcting abnormal muscular activation with cycle training may need further investigation with ABI patients, there is some experiments using SCs and novel instructions with conventional cycling in healthy participants which suggest that SC cycling may increase activation (both in terms of duration and magnitude) of muscles contributing to gait impairments and foot drop. One study by Fernandez et al.\textsuperscript{(95)} describes quasi-significant increases in the magnitude of biceps femoris (BF) and TA EMG activity following 2 weeks of training with SCs. Since the TA and BF are used to dorsiflex the toe and flex the knee respectively, it is likely that the additional effort required to pull up on the pedal (see figure 7) with SC cycling has contributed to training these muscles. This notion is supported by another study which used a ‘pull-up’ conventional cycling condition where participants were instructed to actively pull-up their foot in during the upstroke of the pedalling motion, somewhat simulating the effects expected of SC cycling\textsuperscript{(96)}. Significant increases in magnitude of BF EMG activity and earlier onset of TA activity (and increased duration of activity by
extension) were found, most likely as a result of the increased effort during the cycling upstroke. Considering that the TA is a key muscle involved in rehabilitation of foot drop, increasing the duration and magnitude of its activity during training with SCs could help accelerate the recovery of its function and help to eradicate the effects of this mobility impairment. Similarly, training the BF in this way may help to improve toe clearance during walking by improving flexion of the leg at the knee, all of which suggests beneficial outcomes of training with SCs for these patients. It is important to note, however, that these studies involved the use of healthy participants and using these training paradigms with ABI patients suffering altered and abnormal muscular activation patterns may not induce the same effect. As such, this novel cycling therapy warrants more research before its feasibility with this population can be accurately assessed.

1.5.4 – Corticospinal Plasticity of Muscles Related to Foot Drop

Following the idea that SC cycling may more actively engage the TA than with conventional cycling it may be the case that corticospinal excitability is increased as a result of the training too. This follows from evidence provided in Section 1.3.2 where repetitive, skilled training of a specific action may induce neural plasticity of the muscles it involves\(^{9, 12, 17, 39, 42, 43}\). Since SC cycling is a unique type of exercise it is possible that it will require some aspect of learning to improve performance with training and as such, may fit the criteria to induce these effects. In addition to this, the rhythmical patterns of lower limb motor activity make it quite functionally relevant to walking, with toe lift playing an integral role in performing the exercise, suggesting there could be some functional plasticity to combat foot drop that accompanies the other benefits outlined here.
1.6 – PRESENT STUDY

Since there is very little research investigating the effects of SC training on healthy participants, and none to the author’s knowledge with ABI patients, any potentially adverse effects of the exercise are not well documented. In addition to this, specific parameters of the training such as cycling cadence need to be established for safe implementation with patients and piloting the training protocol may also reveal additional adaptations to methodology which may improve safety and quality of data recorded. Likewise, there is no data regarding adaptations of corticospinal excitability changes which may accompany training of the TA with SC cycling and evidence for any muscular activation adaptations it may induce is scarce. As such the present study is aimed at implementing a SC cycling training protocol with healthy participants, measuring adaptations of lower limb muscular activation and TA corticospinal excitability. The hope is that this will develop our understanding of the kinds of training adaptations SC cycling may evoke and give indication of how feasible such a therapy may be in the rehabilitation from ABI-related foot drop. Although the use of healthy participants makes generalization of results to the target population of ABI patients quite limited, the severe lack of research with SCs has warranted this pilot study to increase our understanding of its effects to provide a stronger basis for potential clinical applications in the future. Similarly, since the target of the study is to try and use a clinically translatable protocol, the exercise intensity used is unlikely to induce any kind of aerobic or strength benefits for the healthy participants and as such, will not be included as experimental measures.
1.6.1 – Hypotheses

1. Corticospinal excitability as assessed by stimulus-response curves will be increased in the TA following 5 days of SC, but not FC, cycle training. This will indicate the skill demand of this muscle necessary to perform the task.

   a. Improvements in SC cycling performance will also accompany this effect to demonstrate skill acquisition with training.

2. Prolonged duration of TA activity throughout one full crank cycle (0-360°) will be seen in the TA following 5 days of SC, but not FC, cycle training. This will indicate learning of its additional activation necessary to perform the task.

3. Prolonged duration of BF activity throughout one full crank cycle (0-360°) will be seen in the TA following 5 days of SC, but not FC, cycle training. This will indicate learning of its additional activation necessary to perform the task.
CHAPTER 2 – METHODS

This chapter provides basic methodological information regarding measures and procedures for both the pilot study and the primary investigation. Aspects of the pilot study findings are discussed and used to optimise the protocol for the primary investigation which is also described in detail.

2.1 – PARTICIPANTS, EQUIPMENT AND PROCEDURES

2.1.1 – Participants

A convenience sample of healthy university students were recruited for participation in both the pilot and primary investigations. All participants were screened using a TMS safety form and gave their consent to participate in the study. Similarly, participants were screened to ensure they did not compete in sports deemed to incur high TA activation (semi-professional football, ballet) or more than 6 hours of cycling per week. Basic demographic data and number of hours of exercise participated in per week were also recorded.

2.1.1.1 – Pilot Study Participants

Four participants (male n=3, female n=1) with a mean age of 21.5 (±0.6) and BMI of 23.7 (±1.5) completed the pilot study protocol. The average number of hours spent exercising per week by the participants was 8.8 (±2.2) for sports including gymnastics, basketball, rugby and resistance exercise.

2.1.1.2 – Primary Investigation Participants

Nineteen participants (male n=18, female n=1) with a mean age of 23.2 (±3.0) and BMI of 23.6 (±2.3) completed the primary investigation protocol. The average number of hours spent exercising per week by the participants was 6.6 (±3.7) for a range of sports, most frequently reported was resistance exercise (n=12) followed by football (n=6).
2.1.2 – The Split Crank Cycle Ergometer

The cycle ergometer is an adapted Monark 824E static bicycle ergometer which has full 360° triggering capabilities (Figure 8) and works with a flywheel (50 cm diameter) system of adjustable resistance by means of additional weight discs (Figure 9). The crank arms were adapted to work independently of each other for split crank (SC) cycling but with the capability of fixing them 180° apart for normal, fixed crank (FC) cycling too (Figure 9). It includes clipless pedals and an adjustable saddle height ranging from 88cm (floor to saddle base) to 110cm in 2cm increments.

Saddle height was adjusted so that there was a slight bend in the knee when sat with the crank arm at bottom dead centre (BDC) and so that the participant was comfortable during cycling.

Figure 8. – Crank arm trigger box with 4 separate trigger capabilities for the left and right cranks of the cycle ergometer. Black dials could be adjusted to trigger at any point in the 360° cycle. Green LED indicates active trigger

Figure 9. – A. The adapted cycle ergometer with the red circle where weight could be added to increase resistance. The resistance used here was 1kg B. The fixed crank set-up with pedals fixed 180° apart (left), achieved using the metal plate depicted (right, red arrow) C. The split crank set-up with pedals unfixed and independent (left), achieved by removing the metal plate (right, red arrow)
2.1.3 – Electromyography (EMG) and Biomechanical Recordings

In both the pilot and primary investigation participants were instrumented with ankle and knee Biometrics twin-axis goniometers placed over the respective joints as shown in Figure 10 to record joint position changes during cycling. These signals were filtered and amplified at a bandwidth of 20-450Hz and gain of 1k using a Biometrics subject unit and K800 Amplifier system (Biometrics Ltd., Cwmfelinfach, Gwent, Wales, UK). Skin preparation prior to EMG electrode placement in both studies involved light abrasion of the target region to remove any impeding dead skin and all EMG signals were grounded using a rubber reference electrode (8.5cm x 4.5cm) placed mid-way along the tibia. Additional AP signals recorded during cycling included the square-wave trigger pulse emitted by the trigger box at top dead centre (TDC) (this served as the trigger for all AP recordings) and both left and right crank arm positions during cycling. SRC recordings were triggered by the automated magnetic stimuli and electrophysiological responses were triggered by a manually operated push-button that also triggered electrical stimuli. All recorded AP and electrophysiological signals were visualised in real-time using Mr. Kick© software (Center for Sensory-Motor Interaction [SMI], Aalborg University) and all SRC signals were visualised in real-time using an automated code in Matlab® (Version 2012a, Mathworks Inc., Cambridge, UK). Following acquisition all data was stored electronically for future offline analysis. All recordings were taken from the participant’s right leg.
2.1.3.1 – Pilot Study Electromyography Recordings

Since pilot EMG measures consisted of only TA muscle APs during cycling. These signals were recorded using Biometrics EMG sensors (Type NOS. SX230, Biometrics Ltd., Cwmfelinfach, Gwent, Wales, UK) placed over the belly of the muscle (for electrode position see Figure 11). The procedure for electrode placement was taken from SENIAM guidelines\(^7\) and ensured accuracy of replicable positioning between trials. This was in accordance with the SENIAM and guidelines which The recorded signals were filtered and amplified at a bandwidth of 20-450Hz and gain of 1k using a Biometrics subject unit and K800 Amplifier system (Biometrics Ltd., Cwmfelinfach, Gwent, Wales, UK). The pre-processed and amplified signal was then passed through a National Instruments (NI)© BNC board (Model USB-6229) and through a USB connection onto a PC. Signals were recorded at a 2kHz sampling frequency and sweep length recordings were defined according to the cadence being used (30, 40, 50 or 60 revolutions per minute [rpm]) with an additional 0.05 second pre-trigger and 0.4 second cushion to allow for timing and rhythm errors in metronome pacing. Since there were only single muscle recordings being used in the protocol, the use of simple and more portable EMG system was employed.

2.1.3.2 – Primary Investigation Electromyography Recordings

Muscle EMG recordings for the primary investigation included responses of TA, SOL, VL and BF for APs and TA alone for SRCs and electrophysiological recordings. Signals were
recorded using Ambu® Blue Sensor N electrodes in a bipolar montage placed over the belly of the respective muscle (Figure 11). Again, the procedure for electrode placement was taken from SENIAM guidelines\(^{(97)}\). The placement of SOL was modified to measure the more lateral aspect of the muscle in accordance with previous studies in our laboratory. In this case, the SENIAM guidelines were used but the electrode was placed on the lateral rather than the medial aspect of the leg. Following these guidelines ensured the accuracy of replicable positioning between trials. The raw EMG signals were band pass filtered at 20Hz-1kHz and with a 50Hz notch filter before being amplified by a gain of 5k using a Digitimer D360 isolated patient amplifier system. Processed signals were then passed through a NI BNC board (model 2090) and USB mass transfer onto a PC in a similar fashion to the pilot data. AP sweep lengths were 1.95 sec with a 0.05 sec pre-trigger and SRC sweep lengths were 0.45 sec with a pre-trigger of 0.15 sec. Both sets of data were recorded at a 2kHz sampling frequency. Electrophysiological responses from TA were processed and recorded using the same Digitimer set-up but with a gain of only 1k, using a 0.12 sec sweep length with a 0.05 sec pre-trigger. A more robust and sophisticated EMG recording system was used for this protocol since there were multiple muscle recordings during cycling and measures involving responses to TMS.

2.1.3.3 – Activation Pattern Electromyography Signal Processing

Gain and filtering settings were adjusted to maximise the signal without exceeding the A/D card voltage window (i.e. clipping) and maximise the signal to noise ratio respectively. Similarly, a 50Hz analogue notch filter (Digitimer Ltd) was used in the primary investigation to reduce ambient line noise in the signal (this was unavailable when using the Biometrics system in the pilot study). After recording and storage of AP EMG data, signals were full wave rectified and digitally low-pass filtered at 10Hz. This created a linear envelope of the
signal, smoothing the trace enough to detect points in the crank cycle where muscles became active (onset) and inactive (offset). Mean signals for each participants AP were also normalised to the peak EMG activity of that trace before they were group averaged, making comparison between participants easier to visualise when the traces were presented in the Results chapter.

2.1.4 – Peripheral Nerve Stimulation

All electrical stimuli were delivered using a Digitimer constant current stimulator (model DS7A). The device was set to stimulate at 300V_{MAX} with a 0.2 ms pulse width, using a bipolar stimulation probe to stimulate the common peroneal nerve just below the fibula head to elicit a response in the TA. Details regarding recordings of EMG responses are provided in the previous section.

2.1.5 – Transcranial Magnetic Stimulation

All magnetic stimuli were generated using a Magstim Rapid2 magnetic stimulator (Magstim Ltd., Whitland, Wales, UK) and delivered transcranially using a custom built saddle coil (Serial no. SP15526, Magstim Ltd., Whitland, Wales, UK) ranging from 0 to 100% of the maximum stimulator output or %MSO.
2.2 – DATA ACQUISITION PROCEDURES

2.2.1 – Stimulus-Response Curves

2.2.1.1 – Infrared Tracking and Brainsight

Participants were seated in an adapted recumbent chair before placing an infrared sphere marked elastic headband on their heads (Figure 12). The reflective spheres were tracked by a Northern Digital Inc.© (NDI) Polaris® Vicra® infrared camera and Brainsight™ 2 (software version 2.0.8, Rogue Research Inc., Montreal, Canada) software (Figure 13) making it possible to track the participants head movements in real time. Specific landmarks on the participants head and face were then registered with Brainsight™ in reference to the marked elastic headband using an infrared sphere marked ‘wand’ (Figure 12). This allowed the TMS coil, also marked with infrared spheres, to be accurately tracked in real time over the scalp in reference to the participants head position in 3D space (Figure 13). Having this capability meant that deviation away from the target stimulation site on the participants motor cortex could also be monitored during SRC acquisition and regulated by the participants themselves using Brainsight’s™ Bullseye target system as shown in Figure (14). The headband and facial landmark registration process also meant that specific stimulation sites on the participant’s motor cortex could be stored in Brainsight™ and accurately reproduced in subsequent sessions.
2.2.1.2 – Locating the Stimulation Site

Once participant tracking and registration set-up was complete, the site of stimulation to use in the SRCs was located. An intensity of 60-70% MSO was chosen dependent on the participant’s resting motor threshold (stimulus intensity needed to evoke 50µV response in 5 out of 10 successive stimuli) before single stimulations were delivered to a small area of the motor cortex (roughly 10cm x 10cm) close to the midline, slightly contralateral to the side of the recording site. The coil was moved around this region of the motor cortex until the site which produced the greatest MEP magnitude from the TA was found. MEP magnitude was calculated as the peak to peak value of the MEP trace which was visualised in real time using Mr. Kick© software. The position of the coil on the participants head was recorded with every individual stimulus by Brainsight™ software. This meant that once the optimal

![Figure 13. – Brainsight Polaris output view. Left shows the infrared sphere marked objects which are being tracked (in this case the headband and the coil) which is made apparent by the green dots in the camera field of vision on the right.](image)

![Figure 14. – Brainsight Bullseye view. By making small movements with their head, the participant can correctly adjust the position of the coil so that it sits directly over the stimulation site. This is achieved when the red dot and circle sit in the middle of the purple crosshairs](image)
MEP stimulation site was located, the coils position on the motor cortex could be stored and used with the Bullseye target system during the following SRCs.

2.2.1.3 – Automated SRC Acquisition

With the stimulation site established, the coil was then fixed at this location on the participants scalp with a monitor displaying the Bullseye target to them for position regulation during SRC acquisition (Figure 14). A train of 70-100 stimuli were then delivered at pseudo-random intensities to the motor cortex at 0.5Hz through an automated program designed and developed in Matlab® (Version 2012a, Mathworks Inc., Cambridge, UK). The code allowed real-time visualisation of MEP traces and the plotting of their peak-to-peak magnitude (non-normalised) against magnetic stimulus intensity to study the data spread as it developed (Figure 15). Upper and lower boundaries of stimulus intensity could be manipulated during stimulation to ensure that a well distributed spread of MEPs could be

![Graph](image_url)

*Figure 15.* – Matlab dialogue window during SRC acquisition. Peak-to-peak (PTP) value of the MEP is recorded and plotted in real time against its corresponding stimulus intensity. Upper and lower boundaries could be manipulated during acquisition (red box) to provide a well distributed spread of data
achieved on the real-time plot (Figure 15). The train of stimuli could also be paused if the participant significantly deviated away from the target coil position and needed to recover or if stimulation became uncomfortable which occasionally occurred with trains of consecutively high intensities.

2.2.1.4 – MEP Magnitude Normalisation (Mmax)

So that SRCs could be normalised across all participants, the maximal electromyographical response of the TA was recorded for each participant which was elicited using electrical stimuli delivered to the common peroneal nerve. The current (mA) of the electrical stimuli was steadily increased from 0 until there was an apparent plateau in the peak-to-peak value of the M-wave on the EMG trace (Figure 16). Once the plateau was reached, the resultant value was recorded as the Mmax and MEPs in later analysis were expressed as a proportion of this value to appropriately normalise results between participants.

![Figure 16. – Example EMG trace showing how peak-to-peak value of M-wave (between red lines) is recorded. The current is gradually increased until this value reaches a plateau (3 consecutive traces within 0.05mV of each other) and is recorded as the Mmax](image)
2.2.2 – Activation Patterns and Borg Scale Scores

Before AP recordings began, participants were allowed a short amount of time to get up to the appropriate speed and instructed to emulate 180° interlimb phase differences, as in normal FC cycling, as closely as possible (this sometimes took a few minutes in cases where SC cycling was found particularly difficult). A single AP sweep consists of EMG muscle and biomechanical recordings corresponding to one full 360° movement of the bicycle crank for the participant’s right leg. A full or completed AP consists of a total of 60 individual sweeps of activity whose acquisition time is dependent on the cycling cadence. Sweep recordings were triggered according to a pre-defined crank arm position of 0° (TDC) but had the capability of being set as any point between 0 and 360° of the crank arms range of motion using a dial on a custom built triggering box (Figure 8). To avoid inducing fatigue during cycling, it was also decided to have participants report their level of exertion during cycling. This was done using the Borg scale of perceived exertion (Figure 17) and limited to a reported level of 8 at which point the exercise was stopped.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Adapted from Borg (99)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Nothing at all</td>
<td>(Just Noticeable)</td>
</tr>
<tr>
<td>0.5</td>
<td>Very, Very Weak</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Very Weak</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Weak</td>
<td>(Light)</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Somewhat Strong</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Strong</td>
<td>(Heavy)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Very Strong</td>
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<td>8</td>
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<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Very, Very Strong</td>
<td>(Almost Max)</td>
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<tr>
<td>-</td>
<td>Maximal</td>
<td></td>
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</table>

Figure 17. – The Borg Scale of Perceived Exertion (adapted from Borg (99)). Participants reported their increasing physical exertion from 0 to 10 during cycling.
2.3 – PILOT STUDY

2.3.1 – Background and Purpose

Before testing can begin there are two key factors of the training which need to be established; the cycling intensity and the training session duration. Since we are using healthy participants in the present study, it is important that the chosen training parameters are realistically translatable to use with recovering ABI patients too. It is also important that the training parameters are not too exhausting for the present participants as fatigue could affect normal patterns of muscular activity\(^{(100)}\).

Cycling intensity has been defined using a number of different measures in studies where the exercise is employed as a rehabilitation therapy. Parameters such as systolic blood pressure\(^{(75)}\), heart rate\(^{(72)}\), work rate as a percentage of VO2 Max\(^{(75)}\) and scales of perceived exertion\(^{(72)}\) have all been used both individually and in combination to achieve a target cycling intensity. Pedalling cadence is another common measure which regulates the speed at which the participant cycles, offering similar absolute physical exercise intensity between subjects. Pedalling cadence ranges in studies of this nature from 40-70 rpm\(^{(70, 72, 76, 101, 102)}\) using both motor\(^{(72, 101)}\) and non-motor\(^{(70, 76, 102)}\) aided cycle ergometers. As such, a reasonable range of cadences chosen to pilot test here were 30, 40, 50 and 60 rpm.

In the interest of making the training applicable to ABI patients who may find it difficult to exercise for long periods of time, a maximum of 20 minutes worth of continuous cycling was set as an upper limit for training sessions. Borg scale scores of perceived exertion (BSSs) also served as stop criteria for testing. It should also be noted that all pilot testing was performed with the SC as this is the exercise paradigm whose effects are known the least about. Since the continuous force application of both legs during the performance of SC cycling is most
likely more physically demanding than the reciprocal action associated with normal FC cycling, it can be assumed that conclusions based on factors such as fatigue measures in these tests will hold true for both paradigms.

2.3.2 – Pilot Design

To determine the unknown factors discussed previously, participants were asked to come into the lab and cycle for 20 min or until they reached a BSS of 8 which was self-reported at 2 min intervals. Each cadence was maintained by coordinating the motion of the right crank arm through 0° or TDC with a corresponding metronome tone. Participants had TA APs recorded from their right leg at each cadence before completing the training which was followed by a minimum of 20 min washout period prior to testing the new cadence. Order of cadence completion was randomised to try and counterbalance carry-over effects between testing sessions. For an overview of the protocol design, refer to Figure 18 with details of specific procedures described in the sub-sections which follow. For full details of procedures refer back to Sections 2.1 and 2.2.

Figure 18. – Flow diagram of the pilot training protocol (BSS = Borg Scale Score, AP = TA Activation Pattern)
2.3.3 – Pilot Results

A raw TA EMG trace from the 30 rpm cycling cadence is shown for one participant in Figure 19 with group average traces rectified and low-pass filtered at 10Hz shown in Figure 20. Biomechanical knee and ankle group averages are also shown in Figure 21. The profiles of the TA traces are discussed in more detail in the section which follows (Section 2.3.4.1).

![Figure 19](image1.png)

**Figure 19.** – Raw TA EMG data from a single sweep taken from 1 participant cycling at 30 rpm

![Figure 20](image2.png)

**Figure 20.** – Group mean TA EMG traces for all cadences, rectified and low pass filtered at 10Hz. All data was normalised to peak EMG amplitude (labelled as Max EMG on y-axis)
Figure 21. – Mean ankle (top) and knee (bottom) biomechanical joint position traces for all of the 4 cadences

Figure 22. – Bar chart displaying the time each participant was able to cycle for until exhaustion (Borg scale rating of 8) for each of the 4 cadences. If exhaustion was not reached the exercise was halted at 20 mins.
Results of the cycling durations are displayed in Figure 22 with all participants reaching the upper time limit of 20 min for 30 rpm and a general trend of reduced cycling time with increasing cadence. No statistical analysis was carried out for this data due to the low number of participants.

2.3.4 – Pilot Discussion and Implications for Primary Investigation

Below is a summary of the findings for the different aspects of the experiment. The implications of these findings for the methodology of the primary investigation are discussed.

2.3.4.1 – Implications of Pilot Activation Patterns

The profiles of the EMG traces show some variation between cadences with a common pattern of a steeper activation gradient for both the 50 and 60 rpm cadences, whilst the 30 and 40 rpm cadences show a more gradual rise to peak activation (Figure 20). Ankle and knee position traces appear to show little variation between cadences, perhaps with a slight tendency of reduced plantar flexion of the ankle around the middle of the crank cycle (180°) with faster cadences (Figure 21). Based on the AP data alone it seems that a faster cadence of 50 or 60 rpm may be the most appropriate choice for the primary investigation since it provides greater magnitude of TA activation for a larger proportion of the crank cycle than the lower 30 and 40 rpm cadences. From a rehabilitation perspective, this could help to maximise the extent of training benefits for the TA and provide accelerated recovery of foot drop symptoms. However, the more physically challenging aspect of the faster cadence may prove to be too exhausting for a high enough dosage of the training and is likely to induce the confounding variable of fatigue. This was examined by the duration testing.
2.3.4.2 – Implications of Cycling Durations

The cycling duration results have shown a typical trend of a negative correlation between cycling cadence and the duration it could be maintained for. In the case of the higher cadences, the healthy participants were reporting a BSS of 8 after only 6.5 (±1.9) and 5.5 (±1.0) min for 50 and 60 rpm respectively and as such, it seems unlikely that recovering ABI patients would be able to safely replicate these intensities for a fraction of that time or even at all. Since the intensity was so rapidly exhausting for the healthy subjects, it may also prove dangerous for application to ABI patients in that it may exacerbate their existing medical conditions and indeed prove detrimental to recovery. Although both and 50 and 60 rpm have been successfully used in other rehabilitation studies, it may be the case here that the additional physical demand of SC cycling specifically has made the exercise more challenging and more difficult to maintain. At the other end of the spectrum, the upper time limit of 20 min was comfortably reached by all participants during cycling with the lowest cadence of 30 rpm. This cadence was also the one which participants found most difficult to maintain during testing due to the large gaps between metronome tones. The remaining cadence of 40 rpm appeared to be challenging but not exhausting since the average duration fell under the limit by a relatively small margin (7.5 min) and being easier to maintain pace as well, seemed the most suitable choice for the primary experiment. It was also decided that an upper time limit of 15 min would be used instead of 20 to decrease the likelihood of participants reaching relative exhaustion on consecutive days of training in the main experiment, thus reducing the chances of measures made on the final day being affected as a result.

2.3.4.3 – Additional Observations

The Borg scale of perceived exertion was chosen for this experiment because it is a simple, validated measure of perceived exertion. Its use proved generally quite effective in this sense
and also in accurately assessing the participant’s level of exertion during cycling. However, with self-reports of exertion only being requested every 2 min, the exact point of fatigue was often overlooked and resulted in participants overworking themselves to the next 2 min interval. The revised methodology will therefore include the request of an exertion rating every 1 min instead of 2. This should help to resolve this issue of oversights and provide a more reflective means of assessing when the subject reaches the point of fatigue.

In addition to this, EMG recordings of knee extensor and flexor muscles vastus lateralis (VL) and biceps femoris (BF) and the ankle plantar flexor muscle soleus (SOL) will be made in the primary investigation. These measures, along with the TA EMG activity and biomechanical data of knee and ankle joint positions during cycling should give a more global understanding of how entire leg APs may be altered with training. Although additional muscle recordings will be made in the primary investigation, it is important to note that the greatest adaptations to activation with SC cycling are still expected to be seen in the TA.

Another observation is that participants often found it difficult to maintain cycling pace with the metronome when trying to correspond only the right crank arm through TDC with the metronome tone. With some participants who found it particularly difficult, the metronome pace was multiplied by 2 so that there was a tone corresponding with both the right and left crank arms crossing TDC alternatively. Since this proved so effective in improving the ability to maintain the desired pace, it was decided that this technique would be solely used in the primary investigation protocol, disregarding the previous method entirely.

2.3.5 – Pilot Study Conclusions

The primary finding from the pilot study was that the most appropriate cycling cadence to use as a compromise between optimal TA activation and appropriate physical demand is
40 rpm. In addition to this, a reduced training session duration of 15 min and BSS reports every 1 min should help to both reduce the likelihood of fatigue occurring but also to more accurately identify its point of occurrence if it does. Finally, by including SOL, VL and BF recordings in APs a more global understanding of lower limb adaptations to SC cycling may also be made possible in the primary investigation.

2.4 – PRIMARY INVESTIGATION

2.4.1 – Design

To effectively test whether SC cycling can increase the CSE of the TA and alter muscle APs, randomised, controlled, between-subjects 5 day training protocol was established. Participants were assigned to either the split crank (SC) or fixed crank (FC) condition using randomly permuted blocks generated by an online randomization scheme using a web-based procedure (http://www.randomization.com). This design ensured that both groups were kept balanced during random allocation. Participants completed 5 consecutive days of either SC (experimental group) or normal FC (control group) cycling at 40 rpm for 15 min or until they reached a BSS of 8 which was reported every minute during the session. Metronome pace was set to 80 bpm (twice the cycling cadence) so that each tone corresponded with alternating left and right crank arms crossing their respective TDCs, assisting the participant in maintaining the cadence. On days 1 and 5 APs and SRCs were acquired from the participant’s right leg before and after the 15 min training session to measure changes in muscular patterns of activity and CSE of the TA respectively. These assessment times were selected to investigate short term or transient adaptations to the task (initial exposure) and how this response changed after 4 days training, but also to examine any persistent adaptations which would be apparent prior to day 5 following 24 hours of washout post-exercise. These time points reflect a similar methodology employed by Pascual-Leone et al. (4) (Figure 3) who were interested in
both the rapid and gradual neuroplasticity induced with 5 finger piano sequence training. The complete training protocol design is displayed in Figure 23 and for details regarding the basic procedures and measures which were made refer back Sections 2.1 and 2.2.

*Figure 23.* Flow diagram of the primary investigation protocol Key = SRC - stimulus-response curve recorded, AP - Four muscle activation pattern recorded, Mmax - TA Mmax recorded, S1 Pre/Post – recording time point before and after first training session, S5 Pre/Post – recording time point before and after last training session
2.5 – PRIMARY INVESTIGATION DATA ANALYSIS

2.5.1 – Activation Pattern Trace Selection and Exclusion Criteria

To account for participant errors in maintaining the metronome pace, a program was written in Matlab® to retrieve the section of EMG or biomechanical data which corresponded with the minimum and maximum of the right crank position trace representing 0 and 360 degrees respectively (Figure 24). Additionally, the program expressed the data with a crank position-base instead of a time-base which meant that onset and offset analysis could be normalised between traces and participants. If a mean muscle EMG trace did not show distinct patterns of activity and inactivity they were excluded from analysis, as were the traces of the same muscle for measures made at other time points too. Also, with individual crank arm independence, limb position is slightly less constrained in SC than FC cycling and as such, can cause the direction of pedalling to reverse for brief periods of time during task...
performance. The expectation was that this effect would be diminished with training as performance improved, meaning that group mean trace averages would be skewed more heavily in session 1 than session 5 by these reversals. Since this skewing may lead to false detection of significant changes in muscular activation timing between sessions these reversal traces and their associated muscular activity were excluded from analysis. This was achieved by visual inspection of the knee position traces where these periods of reversal were easy to detect and remove. This is illustrated in Figure 25, where the traces with a reversal are indicated by red arrows.

2.5.2 – Detecting Activation Pattern Muscle EMG Onset/Offset of Activity

Once the traces were filtered and normalised, the time in the crank cycle where each muscle became active and inactive was identified using a bespoke script written and developed in Matlab®. The script used a dual cursor configuration set to a 70ms time window and was

![Figure 25](image)

**Figure 25.** – Diagram showing all 60 knee position traces superimposed for one participant and 3 traces which were excluded due to pedal direction reversal (indicated by red crosses and arrows)

![Figure 26](image)

**Figure 26.** – Matlab dialogue window showing A. how dual cursors set to 70ms time window were used to select region of background EMG activity, B. how 180ms window is used to indentify detection region for onset and C. the onset point detected, shown as a blue cross
placed by visual inspection around the flat area of EMG that preceded the onset. The root-mean-square of the electromyogram within this window was defined as the background EMG and can be seen in Panel A of Figure 26. The mean value and standard deviation of the background EMG was used to define the onset and offset of muscle activity. Onset was the point in the trace between the dual cursors where EMG activity exceeded the mean plus 3 standard deviations of the threshold activity, and was identified by visual inspection of a 180ms dual cursor window (Panel B, Figure 26.). Offset was defined as the point where the EMG activity fell below this value and was identified using dual cursor time window of the same length. From both onset and offset of muscle activity, total duration of activity was also calculated in degrees.

2.5.3 – Split Crank Performance Indices

So that the extent of learning could be quantitatively measured, 3 measures of task performance were devised to assess both the consistency of the pedalling motion and the extent to which normal FC cycling was emulated.

2.5.3.1 – Right Crank Variability (RCV)

The first performance measure assessed the error or variability of each crank cycle for the right leg as compared to a normal FC counterpart, providing an index of how smoothly and
consistently the participants could cycle with SCs. To do this, a linear regression between the minimum and maximum points in the crank position trace was calculated and used as a model of ideal pedalling motion to compare the actual recorded trace against (Figure 27). The root mean squared error (RMSE) was then calculated at each data point before it was averaged for each individual sweep and then across the entire 60 sweeps to produce a value indicative of right crank position variability for each recorded AP. All calculations were automated using a predefined code in Matlab® with resultant values being exported and stored for statistical analysis.

2.5.3.2 – Inter-Crank Position Difference (ICPD)

Additionally, the extent to which participants could accurately maintain a 180° separation between the left and right cranks was measured. This performance index allowed assessment of improvements in pedal control and the ability to emulate normal FC cycling; something which was heavily encouraged throughout training sessions. To do this, the average distance in degrees between each crank was calculated for each individual sweep and used to obtain and average for each AP which was measured. All calculations were made using a predefined code in Matlab® with resultant values being exported and stored for statistical analysis.

2.5.3.3 – Knee Position Trace Exclusions (KPE)

With training, the expectation is that the consistency of smooth, continuous cycling and the adoption of appropriate strategies will improve and as such, there would be a decrease in the number of traces excluded for containing periods of pedal direction reversal. Since knee position traces were used to identify the occurrence of these reversals, the number of knee position traces that were excluded were used as a performance index for training with SCs.
2.5.4 – Stimulus-Response Curve Analysis

Matlab® software was used to select the appropriate section of the EMG trace and identify the peak-to-peak magnitude of the MEP. TMS misfires and traces with a root mean squared (RMS) value which was greater than 3 standard deviations away from the 60 sweep mean RMS value were also excluded at this stage as well. This controlled for confounding traces and unwanted background activity respectively. Following exclusions, a set of analysed MEPs was obtained and a sigmoid curve was fitted around their scatter according to the equation below\(^{13}\) where MEP magnitude at any given stimulus intensity \((i)\) is given as \(\text{MEP}_i\).

\[
\text{MEP}_i = \text{MEP}_{\text{Min}} + \frac{\text{MEP}_{\text{Max}} - \text{MEP}_{\text{Min}}}{1 + e^{(i50-i/S)}}
\]

The four parameters of the curves are the MEP minimum or base offset \((\text{MEP}_{\text{Min}})\), MEP maximum or curve plateau \((\text{MEP}_{\text{Max}})\), the stimulus intensity at the point of inflection \((i50)\) and the slope at the point of inflection \((S)\) where the inverse of the slope \((1/S)\) is directly proportional to the maximum steepness of the curve\(^{13}\). Outlying MEPs were defined as those which lay outside of the predefined prediction interval and were also excluded from the curve fitting. In addition to the 4 parameters, the correlation coefficient \((r^2)\) of each curve was calculated to measure how well the curve fitted the data set. Curves with an \(r^2 < 0.7\) were excluded as a quality control measure with subsequent and previous curves for that participant being excluded from group data as well so as not to skew the mean. Similarly, participants whose curves did not reach a relative upper plateau (usually due to high TMS thresholds) were also excluded from analysis. This procedure follows from a previous study in our laboratory\(^{98}\). Figure 28 shows an example SRC which is superimposed over the data scatter including a raw MEPs translation from analysis to the plot.
2.5.5 – Statistical Analysis

2.5.5.1 – Muscle Onset/Offsets, Performance Indices and Borg Scale Scores

The effect of training on muscle onset, muscle offset and activity duration were tested with a mixed design repeated measures analysis of variance (rmANOVA) with factors time point (S1 Pre, S1 Post, S5 Pre, S5 Post) × crank type (SC and FC). For SC performance indices, rmANOVAs were used to test RCV RMSE, ICPD and KPE with time point factors alone. BSSs were measured during each of the 5 training sessions so were tested using a rmANOVA with factors session number (S1, S2, S3, S4, S5) x crank type (SC and FC). These statistical tests were aimed at investigating both the adaptations to training over time and global differences between SC and FC cycling strategies as a whole.

2.5.5.2 – Stimulus-Response Curve Parameters

To assess changes in the profile of SRCs, statistical analyses were carried out on the different parameters of the curves sigmoid equation. All four parameters were tested using mixed design rmANOVAs (time point and crank type factors as stated in the previous section) where increases in MEP_{Max}, MEP_{Min} and Slope would be indicative of increased CSE for the TA, likewise a reduction in i50 as described in Figure 29.
Figure 29. — Example of shift in stimulus response curve representing an increase in corticospinal excitability for the TA which might be seen following training with split cranks.
3.1 – BASELINE CHARACTERISTICS AND EXCLUSIONS

All participants which were recruited successfully completed the training protocol without any dropouts or incomplete sessions due to over-exertion. However, there were a number of exclusions during analysis which are detailed here and summarised in Figure 30.

For the SC group, one participant was excluded from all AP analysis (including performance indices) since failed goniometers meant inappropriate knee position traces could not be removed as with other participants. Similarly, cross-talk on the BNC board led to exclusion of 4 sets of SOL and 2 sets of VL data for AP analysis. The BF data for one participant was also excluded here due to highly contrasting patterns of activity to the mean of others, deeming it an outlier (this is explored more in Chapter 4). Electrical malfunctions of the bike also meant that left crank position data was not recorded for 3 participants in the SC group, meaning that the ICPD performance index could not be measured. For SRCs, there were 3 participants who showed highly variable responses to TMS and recorded curves with an $r^2$ of less than 0.7 and had all curves excluded for their data set as a result.

In the FC group 1 participant was excluded from all AP analysis due to absence of right and left crank position data which was needed to determine EMG activity at specific points in the crank cycle (electrical malfunction). Loss of data due to an unexpected computer shutdown also excluded another participant from all AP analysis. Cross-talk of the BNC board excluded SOL activity data for 3 participants and an additional 2 for TA. Only one participant showed varied TMS responses to give curves with an $r^2$ of less than 0.7 and another whose high threshold meant that the curve plateau was not found. Both sets of curves were excluded accordingly.
Figure 30. – Flow diagram of exclusions and dropouts during the trial based on CONSORT Statement framework. All participants were able to successfully complete the protocol, predominant attrition of data was due to equipment failures.
A table of participant’s baseline characteristics following random allocation into the experimental (SC) or control (FC) conditions are shown in Table 1.

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<thead>
<tr>
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<th>Split Crank</th>
<th>Fixed Crank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>24.2 ± 4.5</td>
<td>22.1 ± 1.5</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.8 ± 0.1</td>
<td>1.8 ± 0.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77.8 ± 10.8</td>
<td>76.4 ± 6.9</td>
</tr>
<tr>
<td>BMI (kg m²)</td>
<td>24.3 ± 2.3</td>
<td>22.8 ± 2.2</td>
</tr>
<tr>
<td>Avg. Hrs. of Ex. P/W</td>
<td>6.9 ± 5.1</td>
<td>6.3 ± 2.3</td>
</tr>
</tbody>
</table>

Table 1. – Baseline characteristics of participants in the Split and Fixed crank conditions

3.2 – STIMULUS-RESPONSE CURVE RESULTS

After all exclusion criteria were enforced a total of 14 participants were included for analysis (SC n= 7, FC n = 7). SRCs acquired from both SC and FC had minimal MEP exclusions following analysis (8.3 ± 1.2 and 9.1 ± 5.2 respectively). Unlike the AP analysis, significant differences in curve parameter values between crank types will be disregarded here as TMS evoked muscular excitability is inherently variable from person to person and was not normalised or controlled between groups prior to testing. Using the averaged SRC parameters, a group average set of SRCs could be constructed which is shown in Figure 31. Statistical analysis of the group averaged parameters revealed that there was only one significantly measurable difference between time points which was actually a reduction in MEP_max with SC training between S1 Pre and S5 Post sessions ($F_{3,12} = 6.91, p < .05$) (Figure 40). Similar to the ICPD results, the small sample size has produced a large standard deviation in SRC parameters and they have not been plotted as error bars on the MEP_max interaction plot to avoid masking the main effect (Figure 32). A summary of all results including standard deviations is provided in Table 2. Reasons for this unpredicted effect are explored more in Chapter 4, though generally results suggest little TA CSE changes for either training type.
Figure 31. — Group averaged stimulus-response curves measured at 4 different time points for Split and Fixed Crank cycling groups, MEP magnitude given as a percentage of Mmax. %MSO = Percentage of maximal stimulator output. Key = * - MEP, significantly different from Split Crank S1 Pre ($p < .05$)
Figure 32. – Interaction plot for MEP_{\text{Max}} stimulus-response curve parameter measured at 4 different time points for both Split and Fixed Crank. MEP_{\text{Max}} magnitude given as a percentage of Mmax. Error bars are not depicted for the same reasons as previously described for ICPD results (Section 5.1.2.2). Key = * - significantly different from Split Crank S1 Pre (p < .05)

<table>
<thead>
<tr>
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<th>S1 Pre</th>
<th>S1 Post</th>
<th>S5 Pre</th>
<th>S5 Post</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Split Crank (n=7)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEP_{\text{Min}} (x 10^{-3})</td>
<td>0.08 ± 0.22</td>
<td>2.22 x 10^{-1} ± 2.00 x 10^{-15}</td>
<td>0.25 ± 0.60</td>
<td>0.27 ± 0.44</td>
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<tr>
<td>MEP_{\text{Max}}</td>
<td>0.20 ± 0.07</td>
<td>0.17 ± 0.07</td>
<td>0.18 ± 0.09</td>
<td>0.13* ± 0.07</td>
</tr>
<tr>
<td>i50</td>
<td>64.13 ± 10.33</td>
<td>63.56 ± 6.69</td>
<td>65.25 ± 10.57</td>
<td>65.17 ± 9.04</td>
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<tr>
<td>Slope</td>
<td>7.74 ± 2.97</td>
<td>7.13 ± 2.39</td>
<td>6.33 ± 3.37</td>
<td>5.12 ± 1.98</td>
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<table>
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<th>S1 Post</th>
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<th>S5 Post</th>
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<td><strong>Fixed Crank (n=7)</strong></td>
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<tr>
<td>MEP_{\text{Min}} (x 10^{-3})</td>
<td>1.09 ± 1.26</td>
<td>0.57 ± 0.86</td>
<td>0.89 ± 1.24</td>
<td>0.75 ± 0.93</td>
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<td>MEP_{\text{Max}}</td>
<td>0.22 ± 0.18</td>
<td>0.17 ± 0.15</td>
<td>0.17 ± 0.15</td>
<td>0.18 ± 0.15</td>
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<tr>
<td>i50</td>
<td>74.80 ± 12.30</td>
<td>74.90 ± 11.76</td>
<td>75.53 ± 10.24</td>
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<td>Slope</td>
<td>6.42 ± 1.49</td>
<td>6.62 ± 2.72</td>
<td>6.69 ± 1.37</td>
<td>7.35 ± 1.90</td>
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</tbody>
</table>

Table 2. – Results summary for the 4 different stimulus-response curve parameters. Results measured at 4 different time points for both Split and Fixed Crank groups. Key = * - significantly different from Split Crank S1 Pre (p < .05)
3.3 – ACTIVATION PATTERN RESULTS

3.3.1 – Onsets, Offsets and Active Durations Results

A summary of the results for the onsets of offsets of muscular activity are shown in Table 3. No significant differences in muscle onset or offset were found between time points with

<table>
<thead>
<tr>
<th>Split Crank</th>
<th>TA</th>
<th>SOL</th>
<th>VL</th>
<th>BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 Pre Onset</td>
<td>159.3 ± 40.7</td>
<td>17.3 ± 16.2</td>
<td>246.2 ± 39.8</td>
<td>69.2 ± 21.1</td>
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<tr>
<td>S1 Pre Offset</td>
<td>76.2 ± 21.2</td>
<td>304.6 ± 42.3</td>
<td>183.5 ± 59.2</td>
<td>335.3 ± 3.2</td>
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<tr>
<td>S1 Post Onset</td>
<td>156.5 ± 22.0</td>
<td>33.8 ± 13.5</td>
<td>207.9 ± 34.3</td>
<td>75.2 ± 13.4</td>
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<tr>
<td>S1 Post Offset</td>
<td>77.2 ± 14.7</td>
<td>337.4 ± 13.2</td>
<td>160.1 ± 7.2</td>
<td>345.7 ± 6.5</td>
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<td>S5 Pre Onset</td>
<td>158.6 ± 10.0</td>
<td>45.4 ± 11.8</td>
<td>224.8 ± 91.5</td>
<td>78.7 ± 18.2</td>
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<tr>
<td>S5 Pre Offset</td>
<td>62.5 ± 20.2</td>
<td>314.2 ± 58.1</td>
<td>129.1 ± 57.5</td>
<td>341.5 ± 9.9</td>
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<tr>
<td>S5 Post Onset</td>
<td>158.3 ± 9.2</td>
<td>47.2 ± 11.1</td>
<td>245.2 ± 34.2</td>
<td>77.4 ± 13.4</td>
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<td>S5 Post Offset</td>
<td>77.2 ± 24.2</td>
<td>296.3 ± 68.2</td>
<td>150.6 ± 1.2</td>
<td>341.1 ± 10.0</td>
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<tr>
<td>Average Onset</td>
<td>158.2* ± 23.1</td>
<td>35.9* ± 17.3</td>
<td>231.0* ± 54.6</td>
<td>75.1* ± 10.3</td>
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<tr>
<td>Average Offset</td>
<td>73.3 ± 29.5</td>
<td>313.1 ± 48.5</td>
<td>155.8* ± 39.2</td>
<td>342.4* ± 8.4</td>
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<td>S1 Pre Onset</td>
<td>273.2 ± 14.4</td>
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<td>S1 Pre Offset</td>
<td>93.7 ± 65.1</td>
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<td>S1 Post Offset</td>
<td>89.7 ± 59.6</td>
<td>295.3 ± 42.9</td>
<td>198.5 ± 7.9</td>
<td>241.3 ± 16.5</td>
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<td>S5 Pre Onset</td>
<td>276.1 ± 7.4</td>
<td>14.8 ± 14.2</td>
<td>297.2 ± 25.5</td>
<td>22.6 ± 45.4</td>
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<td>S5 Pre Offset</td>
<td>79.2 ± 64.5</td>
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<td>278.8 ± 5.7</td>
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<td>247.5 ± 42.5</td>
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<td>Average Onset</td>
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<td>41.3 ± 41.2</td>
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</tbody>
</table>

Table 3. – Table of results for onsets and offsets of muscular activity. Results measured at 4 different time points. All values are given in degrees. S1/S = training session 1 and 5. Key = * – significantly different from corresponding Fixed Crank average (p < .05)
respect to crank type indicating minimal modifications to cycling strategies with training (Figure 33). However, on average, all 4 SC muscle onsets were significantly different to FC results (TA $F_{1,12} = 192.2, p < .05$; SOL $F_{1,7} = 11.24, p < .05$; VL $F_{1,7} = 6.88, p < .05$; BF $F_{1,12} = 10.85, p < .05$) (Figure 34). Similarly, SC average muscle offsets were significantly different from FC for VL ($F_{1,7} = 9.42, p < .05$) and BF ($F_{1,12} = 80.57, p < .05$). Table 4 shows the results of the active durations for the 4 different muscles with TA ($F_{1,12} = 30.93, p < .05$) and BF ($F_{1,12} = 9.38, p < .05$) reaching significant differences with respect to crank type but none of the muscles reaching statistically significant differences between time points (all presented in Figure 33). The large differences between crank types are clearly presented by the crank activation diagrams in Figure 34 and the processed EMG traces displayed in Figure 35.
Figure 34. – Crank activation diagrams for the average muscle activations of 4 different time points for the split and fixed cranks. Key = * - Onset significantly different from Split Crank, ‡ - Offset significantly different from Split Crank, - Active Duration significantly different from Split Crank (all p < .05)

<table>
<thead>
<tr>
<th></th>
<th>TA</th>
<th>SOL</th>
<th>VL</th>
<th>BF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Split Crank</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1 Pre</td>
<td>276.9 ± 32.9</td>
<td>287.3 ± 51.4</td>
<td>297.3 ± 32.5</td>
<td>269.0 ± 22.9</td>
</tr>
<tr>
<td>S1 Post</td>
<td>280.8 ± 31.5</td>
<td>303.5 ± 13.3</td>
<td>312.2 ± 32.7</td>
<td>273.6 ± 11.8</td>
</tr>
<tr>
<td>S5 Pre</td>
<td>263.9 ± 22.0</td>
<td>268.8 ± 34.2</td>
<td>264.3 ± 34.0</td>
<td>262.8 ± 18.2</td>
</tr>
<tr>
<td>S5 Post</td>
<td>278.9 ± 29.1</td>
<td>249.2 ± 61.6</td>
<td>265.4 ± 53.9</td>
<td>263.7 ± 13.3</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>275.1* ± 28.7</td>
<td>277.2 ± 49.5</td>
<td>284.8 ± 39.6</td>
<td>267.3* ± 16.7</td>
</tr>
<tr>
<td>(n=9)</td>
<td>(n=5)</td>
<td>(n=3)</td>
<td>(n=7)</td>
<td></td>
</tr>
</tbody>
</table>

|                  |        |        |        |        |
| **Fixed Crank**  |        |        |        |        |
| S1 Pre           | 180.5 ± 78.8 | 259.0 ± 20.8 | 269.0 ± 37.0 | 218.8 ± 69.8 |
| S1 Post          | 169.4 ± 62.7 | 255.1 ± 28.5 | 258.1 ± 37.4 | 185.8 ± 53.0 |
| S5 Pre           | 163.2 ± 70.7 | 269.6 ± 32.0 | 255.7 ± 23.3 | 225.5 ± 50.3 |
| S5 Post          | 145.1 ± 41.4 | 290.0 ± 36.9 | 256.5 ± 20.0 | 197.0 ± 70.9 |
| **Average**      | 164.6 ± 61.0 | 283.4 ± 28.3 | 259.8 ± 28.9 | 206.8 ± 60.5 |
| (n=5)            | (n=4)  | (n=6)  | (n=7)  |        |

Table 4. – Table of results for duration of muscular activity. Results measured at 4 different time points. All values are given in degrees. S1/S5 = training session 1 and 5. Key = * – significantly different from corresponding Fixed Crank average (p < .05),
Figure 35. – Processed EMG traces for TA, SOL, VL and BF. Onsets are indicated by the red crosses and offsets by the blue ones. All data was normalised to peak EMG amplitude (labelled as EMG Max on y-axis) Key = * - Onsets or offsets are significantly different from each other (p < .05)
The differences between knee and ankle joint positions between the 2 crank types is displayed in Figure 36 and appear to be quite minimal, perhaps with slightly earlier onset of ankle plantar flexion for SC cycling over FC.

![Figure 36](image)

**Figure 36.** — Biomechanical joint position data for the ankle and knee averaged from all 4 time points (Split and Fixed Crank)

### 3.3.2 – Performance Index Results

#### 3.3.2.1 – Right Crank Variability Results

In general the RMSE of the right crank reduced with training, indicated by significant reductions from S1 to S5 \(F_{3,8} = 11.85, p < .05\) (Figure 37). This demonstrates that participants were able to improve the consistency of their performance with SC training.
Since there were some participants for whom both left and right crank data could be obtained, some participants were excluded from this section of analysis (included n=6). There were no statistically significant changes in the absolute crank position differences between the 4 time

**Figure 37.** Interaction plot for changes in RMSE with Split Crank training. Key = * - significantly different from S1 Pre and S1 Post ($p < .05$)

### 3.3.2.2 – Inter-Crank Position Difference Results

Since there were some participants for whom both left and right crank data could be obtained, some participants were excluded from this section of analysis (included n=6). There were no statistically significant changes in the absolute crank position differences between the 4 time

**Figure 38.** Interaction plot showing changes in inter-crank position differences measured at 4 time points. Dashed line shows the target difference of 180° with the red arrows indicating the deviation from this target. There were no significant differences in results between any of the 4 different time points
points (F3,5 = 0.56, ns) but the data showed a trend towards actually increasing the error (position deviation from the target of 180°) with the training (Figure 38). Possible reasons for this are discussed further in Chapter 4. With such a low sample population, the standard deviations of the inter-crank position differences are quite large and as such would mask the changes seen in Figure 34 if they were plotted as error bars. Accordingly, the standard deviations were plotted on a separate set of axes (Figure 39) where it is apparent that they reduced with training, indicating an improvement in the ability to produce more consistent cycling strategies. It is important to note, however, that none of these reductions achieved statistical significance (F3,5 = 2.21, ns).

![Figure 39.](image)

**Figure 39.** Interaction plot showing changes in the standard deviation of inter-crank position differences measured at 4 time points. There were no significant differences in results between any of the 4 different time points.

### 3.3.2.3 – Knee Position Trace Exclusions Results

The number of KPEs decreased with training with statistically significant reductions from S1 Post to S5 Pre and Post (F3,7 = 6.50, p < .05) (Figure 40), indicating a similar margin of performance improvement to the RCV index. A summary of all performance index results can be seen in Table 5.
3.3.3 – Borg Scale Score Results

BSSs were, on average, significantly greater for SC cycling than FC across all 5 time points \((F_{1,17} = 10.35, p < .05)\) and significant reductions were reported between sessions 1 and 4 for SC cycling \((F_{4,17} = 4.13, p < .05)\) (Figure 41) which could be an indication of improvements in physical fitness or efficiency of cycling strategy with SC training. There was also a significant interaction between crank type and session number during training sessions 1 to 3 \((F_{4,17} = 5.20, p < .05)\). A summary of BSS results can be seen in Table 6. Interestingly there was a slight increase in BSS between S1 and S5 for the SC group, though this difference did not achieve statistical significance.

![Graph showing the number of excluded knee position traces for SC and FC cycling over different time points.](image)

**Figure 40.** – Interaction plot showing changes to the number of excluded knee position traces due to reversed pedalling direction over 4 different time points. Key = * - significantly different from S1 Post \((p < .05)\)

<table>
<thead>
<tr>
<th></th>
<th>S1 Pre</th>
<th>S1 Post</th>
<th>S5 Pre</th>
<th>S5 Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCV (n=9)</td>
<td>0.079 ± 0.032</td>
<td>0.061 ± 0.031</td>
<td>0.024 * ± 0.011</td>
<td>0.027 * ± 0.006</td>
</tr>
<tr>
<td>ICPD (n=6)</td>
<td>175.2 ± 18.1°</td>
<td>174.6 ± 20.4°</td>
<td>170.3 ± 8.7°</td>
<td>171.3 ± 8.6°</td>
</tr>
<tr>
<td>KPE (n=9)</td>
<td>8.6 ± 2.5</td>
<td>10.1 ± 3.1</td>
<td>3.6 † ± 4.1</td>
<td>4.9 † ± 3.7</td>
</tr>
</tbody>
</table>

**Table 5.** – Split Crank performance indices results summary. RCV = Right Crank Variability RMSE, ICPD = Inter-Crank Position Difference (Target was 180°), KPE = Number of Knee Position Trace Exclusions. Key = * - significantly different from RCV S1 Pre and Post, † - significantly different from KPE S1 Post (all \(p < .05\)).
Figure 41. – Interaction plot showing the average Borg Scale Scores for each of the 5 training sessions for both Split and Fixed Crank. S1/2/3/4/5 = training session number. Key = * - significantly different from Fixed Crank in that session, † - significantly different from Split Crank S1 (p < .05)

<table>
<thead>
<tr>
<th></th>
<th>S1</th>
<th>S2</th>
<th>S3</th>
<th>S4</th>
<th>S5</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Split Crank</td>
<td>2.9^* ± 0.6</td>
<td>2.3^* ± 0.7</td>
<td>2.1^* ± 0.7</td>
<td>1.7† ± 0.5</td>
<td>2.1 ± 0.5</td>
<td>2.2^V ± 0.5</td>
</tr>
<tr>
<td>Fixed Crank</td>
<td>1.2 ± 0.4</td>
<td>1.0 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>1.2 ± 0.2</td>
<td>1.4 ± 0.3</td>
<td>1.2 ± 0.1</td>
</tr>
</tbody>
</table>

Table 6. – Results summary for the Borg scale scores of perceived exhaustion. S1/2/3/4/5 = training session number. Key = * - significantly different from Fixed Crank in that session † - significantly different Split Crank S1, ^V - significantly different from Fixed Crank average (all p < .05)
CHAPTER 4 – DISCUSSION

The purpose of this experiment was to implement a split crank (SC) training protocol with healthy participants to develop our understanding of its associated muscular activation and corticospinal plasticity adaptations. The hope was that these findings might provide a basis to pursue SC cycling as a novel rehabilitation therapy to treat the symptoms of foot drop for recovering acquired brain injury (ABI) patients. Despite several equipment failures the protocol was implemented successfully and the implication and significance of the subsequent findings are discussed here.

4.1 – INTERPRETATION OF RESULTS

4.1.1 – Corticospinal Excitability Adaptations – Stimulus-Response Curves

It was hypothesised that corticospinal excitability (CSE) for the tibialis anterior (TA) would increase following novel SC cycle training due to its high skill demand, but not in the low skilled, conventional fixed crank (FC) control group. This prediction was not met since there were no significant increases in any of the stimulus response curve (SRC) parameters with split crank (SC) training, suggesting little or no plasticity adaptations for this target muscle. Since this result was paralleled in the low skilled FC condition, it suggests that the tasks skill demand was not high enough to evoke the neuroplastic adaptation which was expected. Interestingly, there was 1 significant change in MEP$_{\text{Max}}$ with the SC condition but it was actually a decrease between Pre and Post session 5. Since this indicates a reduction in CSE with SC training this comes as somewhat of a surprise as it completely contradicts the predicted outcomes of the intervention. Since SC cycling requires a large contribution of muscular activity from the TA to perform (as shown by activation pattern results, see Section 3.3), it may be that the muscle was fatigued during training which has been shown to decrease
MEP amplitude\(^{(103)}\) and may have contributed to the observed decrease in MEP\(_{\text{Max}}\). However, this would again come as a surprise since the exercise intensity was very low, eliciting an average score of only 2.2 (±0.5) which correlates to a description of only ‘Weak (Light)’ on the Borg scale. Considering the sample population were young healthy participants it also seems unlikely that the training intensity, aimed at recovering ABI patients, would induce any sort of fatigue. As such the basis for this apparent reduction in CSE is difficult to explain yet without a similar finding in the FC control group, it suggests that this may be a trait of the SC training specifically which should be investigated further. Follow up studies using larger sample populations may also help to confirm or oppose this result in the future.

4.1.2 – Muscular Activation Adaptations

The hypotheses for muscular activation adaptations were that both tibialis anterior (TA) and biceps femoris (BF) would exhibit increased periods of activity during SC cycling than with FC cycling reflecting the increased toe lift and knee flexion necessary to perform the cycling upstroke during exercise. Whilst these results were observed, the hypothesis was only partially met in that the adaptation occurred immediately with initial exposure to the task and not as a more gradual response to training (indicating skill acquisition) as was predicted. These results suggest that, at least for this sample population, the skill demand of the task was not high enough to induce a gradual learning response in these muscles. Despite this, the present findings of increased TA and BF activity are somewhat in agreement with work by Fernandez et al.\(^{(95)}\) and Mornieux et al.\(^{(96)}\) who found small increases in magnitude of TA and BF responses with a SC cycling task and active ‘pull-up’ instruction respectively. This is an important similarity as it contributes to our understanding of SC cycle training and its associated muscular activation as a relatively unexplored topic of research.
Interestingly, earlier vastus lateralis (VL) activity onset and delayed soleus (SOL) activity onset were also measured with SC cycling too; a finding which was not hypothesised prior to the experiment. Considering the task demands, it may be that earlier onset of VL activity served to drive the limb forward through top dead centre (TDC) following the cessation of the upstroke and into the downstroke where its primary function of knee extension could be employed\(^{104,105}\). The period of co-contraction between VL and BF might then reflect additional knee and potentially hip stabilisation during the cycling upstroke where lack of contralateral limb assistance may produce a greater extent of variability in joint position. With prolonged muscular activation of TA and BF needed to perform the upstroke, it may be the case that muscular activation associated with the downstroke could be delayed and such, may explain the delayed SOL onset which is typically associated with ankle plantar flexion and the downstroke motion\(^{104,105}\). Since these observations have not been reported previously they may carry significance in establishing a better knowledge base of SC cycling and could be important when assessing future clinical applications too.

### 4.1.3 – Performance Indices and Borg Scale Scores

The indices of SC cycling performance were hypothesised to improve with SC training indicating gradual skill acquisition with the intervention, which was hoped to be accompanied with increases in CSE of the TA and adaptations to TA and BF muscular activity during cycling too. Whilst the gradual adaptations to CSE and muscular activation were not observed, it is interesting that both the right crank variability (RCV) and knee position exclusions (KPEs) showed evidence of gradual improvements throughout the 5 days of training. Contrary to both the muscular activation and CSE results this suggests that there was some aspect of learning or skill acquisition that was required to successfully perform the task. This is supported to some extent by the results of the Borg scale scores (BSS) which showed significant reductions
during the SC training intervention. This apparent reduction in energy expenditure, or effort during cycling, may represent a learning process whereby cycling efficiency is improved, perhaps through improving performance consistency which is indicated by improvements in RCV and KPE during the training too.

Although RCV and KPEs appear to have worked well as SC performance indices, the inter-crank position difference (ICPD) index provided slightly contrasting results in that the position difference actually deviated further from the target of 180° with training. This may be due to the fact that participants were instructed to keep, but never specifically positioned with, pedals 180° apart meaning that they had no awareness of the correct positioning prior to training, only the position which they perceived to be correct.

Since the current methodology simply gave an average ICPD for each sweep, there was no information about at which points in the crank cycle specifically the greatest deviations occurred. In future, a more thorough analysis of inter-crank position during cycling could include an assessment of ICPD on a sample point-to-point basis (Figure 41) which could also be used as participant feedback to help direct attention on how maintain an optimal ICPD during training sessions. Although absolute ICPD values have provided contradictory results to both the predicted outcomes and the other 2 performance indices, reductions in the standard deviations gave some indication of how participants were able to improve the consistency of
pedal strokes. Although it should be mentioned that these differences were not statistically significant and should be interpreted as speculation only.

The SC group showed a slight increase in BSS between sessions 4 and 5 which was slightly surprising considering the general trend of reduction that occurred in the sessions before. Although this difference did not reach statistical significance, it could reflect an aspect of the protocol which is causing some additional physical exertion for the participants and affecting their reported scores. However, since this effect was not seen in the FC control group it seems unlikely that this effect has been caused by the protocol design and may perhaps have been eradicated with the use of a larger sample size than the relatively small one used presently.

4.1.4 – Performance Index and Learning Effect Discrepancies

The results obtained here have provided mixed evidence regarding whether there was some kind of learning or skill acquisition with the SC cycling paradigm. Since the muscular activation adaptations in the TA occurred on initial exposure, it is fair to assume that the task did not provide sufficient skill demand for this muscle during the intervention to evoke any corticospinal plasticity as a training response. This is of course, reflected in the results from the SRCs which showed no CSE improvements between the beginning and end of the trial. The apparent improvements in task performance and reduction in energy expenditure may therefore represent some form of skill acquisition or more gradual training adaptation concentrated to a muscle or muscles which were not measured under the current protocol. Since the evidence provided presently has shown that the main adaptations to muscular activation are induced to overcome the upstroke of SC cycling, we can expect that any additional training effects may be evoked in muscles which could help to achieve this. Muscles associated with hip flexion seem to fit this description well since their activity has been documented as occurring predominantly during the later stages of the crank.
cycle\(^{(104, 105, 106)}\) and is supported by participant reports of muscle ache around the hip during cycling. It could therefore be the case that SC cycling induces increased hip flexor activity in addition to that of TA and BF to help achieve the upstroke of the crank cycle following absence of contralateral limb assistance. This effect may occur more gradually than with muscles that were measured presently and could, to some extent, explain why there were parallel improvements in performance which were measured over a similar timescale. Equipment limitations meant that a maximum of only 4 muscles could be recorded presently to give a fairly broad representation of lower limb muscular activation changes with SC cycling. Similarly, SRC recordings were limited to the TA only as the primary muscle of interest too. Follow up studies may therefore benefit from recording a larger group of muscles, both in terms of EMG activity and SRCs, to better understand some of the training adaptations which SC has the potential to induce. This may also provide a stronger basis of knowledge which may be used to assess feasibility of implementing a clinical SC cycling paradigm in the future.

### 4.2 – STUDY STRENGTHS AND LIMITATIONS

#### 4.2.1 – Strengths

This has been one of very few studies investigating training adaptations associated with SC cycling and as such, has helped to establish a better knowledge base for how this exercise regime may be translated to a clinical setting in the future. Despite the fact that not all of the hypotheses were satisfied, the results revealed new information regarding the timing and duration of lower limb muscular activity with SC cycling that may guide future research and follow up studies of a similar nature. The findings of increased duration of TA and BF during SC cycling are also supported by the research of Fernandez et al.\(^{(95)}\) and Mornieux et al.\(^{(96)}\) and suggests that there may be beneficial training effects for these muscles over conventional
FC cycling which is normally used in a clinical setting. Although such benefits for patients suffering ABI-related foot drop is beyond the scope of this study, these findings may facilitate the transfer of this exercise therapy into a clinical trial in the future where these effects can be tested conclusively. Conducting the study with a healthy population meant that beneficial adaptations to the protocol could also be identified in terms of optimising both quality of data collected and safety of participants if the study was ever to be replicated with ABI patients (these are discussed in Section 4.3). The additional research questions and parameters of training which were raised during the completion of this investigation are discussed here, including the importance of addressing them before clinical trials with patients can commence.

4.2.2 – Limitations

4.2.2.1 – Size and Type of Sample Population

Although the conduction of this experiment with healthy participants has been necessary to develop a firmer knowledge base of SC cycling and its associated training adaptations, it does create a large limitation in generalising the findings to the target population of recovering ABI patients. Absence of a physical activity exclusion criteria for the experiment resulted in recruitment of participants that were quite physically active (average exercise participation of 6.6 [±3.7] hours per week). As such, their experiences of SC cycling are likely to differ from an ABI patient who, in addition to motor impairments, may also have been sedentary for some time. Similarly, the low sample size reduces the power of the statistical tests and makes the generation of definite conclusions more difficult. This means that whilst current findings improve knowledge of this scarcely researched topic, additional studies with larger and more appropriately matched samples of participants are essential to accurately assess the feasibility of this exercise therapy as a clinical rehabilitation strategy.
4.2.2.2 – Knee Position Trace Exclusions Criteria

The use of KPE proved to be a good indicator of performance consistency in that it showed how the occurrence of the brief reversals of pedalling direction was reduced with training. It also removed the chance of recording false muscular adaptations occurring between the first and last sessions of training (see Section 2.5.1). However, whilst the exclusion criteria here was defined as traces which showed visible reversals (found using superimposition of all 60 knee position sweeps; see Figure 25, Section 2.5.1) a more robust exclusion criteria which can be replicated in subsequent experiments should be developed. One potential solution to this could involve using a band of tolerance set at 2 or 3 standard deviations away from the mean trace, creating a more standardized method of excluding knee position traces in similar experiments.

4.2.2.3 – Maintenance of Cycling Cadence

During training some participants had difficulty maintaining the desired cycling cadence. Since the cycle ergometer used a flywheel resistance system, increasing the cycling speed could reduce the resistance of cycling and as such, became a tendency of a several participants in the SC group as a way of alleviating the physical demands of the task. However, this was corrected to some extent by constant verbal instruction from the investigators and this effect was generally alleviated towards the end of the training intervention. Some participants in the SC group also struggled to keep to the 40rpm pace despite the use of the metronome whose tone corresponded with each pedal stroke going through TDC alternately. This effect was particularly apparent in the early training sessions, where a large degree of concentration was devoted to performing the novel task and not to maintaining cycling pace.
An alternative which could have been used is a cycle computer providing a digital read-out of current rpm that gives participants real-time feedback on cycling pace, allowing them to make constant adjustments during training (Figure 42). However, due to the independence of crank arms in SC cycling, individual legs may cycle at varying speeds making adjustments for the participants very difficult and attentionally demanding. Perhaps more importantly, the cadence may also then be more difficult for the investigator to regulate compared to the more widely audible metronome tone. Following this, it seems that helping participants maintain a desired cadence during SC cycling may be difficult to achieve and as such, should be considered both for future studies and when assessing feasibility of translation into a clinical setting too, where arguably the ability to produce rhythmic patterns of motor activity will already be impaired.

4.2.3.4 – Identifying Multiple Cycling Strategies

An additional difficulty which arose during analysis was regarding a muscle trace for one participant, specifically in BF, which displayed a highly contrasting pattern of activity to the remaining participants’ group mean (Figure 43). After some in depth analysis the abnormality could not be attributed to equipment malfunction or any other confounding variables the investigators were aware of and due to the effects that this trace had on group mean analysis, the BF trace and subsequent traces for this participant were excluded as outliers. Since this participant was part of the SC condition and typical patterns of muscular activation are not well established with this task, it is conceivable that such outlying results may have been a result of the utilization of an alternative cycling strategy to the remaining majority of participants. Since there was so much unknown regarding muscular activation with SC training prior to this study it was difficult to have predicted that multiple strategies may have been utilized and additional analysis to deal with this was not employed as a result. In future
experiments it may be interesting to see if more than one strategy exists to perform SC cycling. By analysing APs trace by trace instead of using the mean, separate strategies may be identified within a single AP or muscle and could lead to a better understanding of the way in which participants learn to perform the task. Following this, specific instructions regarding cycling technique may be developed to evoke a strategy which will produce the most beneficial muscular activation for the target population and their rehabilitation needs.

4.2.3.5 – Equipment Failures

One limitation of the current study which led to significant data exclusion was the number of equipment failures during testing. The major contributors of which included electrical bike malfunctions causing loss of performance analysis, and cross-talk between EMG channels causing loss of muscle AP data (see Figure 30). Although these equipment failures were the major cause of data attrition, their occurrence prior to the investigation were unforeseeable, especially since there had been no such issues during pilot testing. Maintenance of the SC ergometer was also made particularly difficult due to its novel design and limited technical assistance with knowledge of its mechanical and electrical properties. Future studies may benefit from using a more commercial SC design such as the equipment available from PowerCranks© (www.powercranks.com) where better support and advice regarding repairs

Figure 43. – The SC group mean trace for BF superimposed over the single participants trace deemed an outlier

![Graph showing EMG magnitude normalized to EMG max vs. crank position in degrees. Red line represents group mean, black line represents an outlying trace.](image.png)
may be available. For other equipment failures which occurred here, simple replacements of faulty apparatus for future experiments should resolve the attrition issues of this investigation.

4.3 – PROTOCOL ADAPTATIONS TO CATER FOR AN ABI POPULATION

As mentioned previously one of the benefits of using a healthy sample population is that adaptations to the protocol can be highlighted which may help to cater to an ABI patient sample population in the future; both in terms of safety and knowledge gained from findings. Whilst there are obvious aspects which will need modifying, such as the cycling resistance, other less obvious training parameters were identified here too. This section describes some of these protocol adaptations and outlines areas of research which should be addressed to facilitate a safe clinical translation of SC cycling.

4.3.1 – Rating Perceived Exertion and Muscle Ache

In the present study the use of the Borg scale provided an effective means of quantifying the additional physical demands of SC cycling and controlling for the effects of aerobic fatigue. The evidence for these additional physical demands has given some insight into the potential benefits of SC cycling on aerobic fitness factors ABI patients may gain over and above conventional FC cycling based interventions as well. However, the scale did not reveal the extent of participant reported muscle ache that occurred with SC cycling; a factor that may limit participation for weaker patient populations. Following this, an effective supplement to the Borg scale may be the use of visual analogue scales (VASs) to rate muscular pain during cycling \(^{(107)}\). Its simplistic nature could make it easy to implement in the future and the findings which stem from its inclusion could be important to consider prior to testing with ABI patients where muscle ache caused by SC cycling could be particularly harmful. Making this adaptation to the protocol is likely to make participation safer for our target population of
participants but also allows the effects of fatigue to be more closely monitored and controlled to reduce the likelihood of excitability or muscular activation measures being affected.

4.3.2 – Saddle Type/Design

One adaptation to the apparatus used which will be necessary for extended this research into the target population will be to change the type of saddle used on the cycle ergometer. Although the healthy participants used presently had very little difficulty co-ordinating movements and maintaining both their balance and position on the saddle, ABI patients experiencing decreased muscular strength and postural control may find it more challenging due to the upright, low body weight supporting saddle. For these reasons, using a similar ergometer could prove dangerous for patients who may be subject to a greater fall risk and subsequent injuries which may exacerbate existing conditions and unnecessarily prolong recovery. To address this issue a number of other experiments used in clinical settings have used a recumbent cycle ergometer\(^{87, 89, 101}\). This variation of conventional cycling caters for ABI patients who have significantly decreased postural or core strength making the ability to maintain an unassisted upright body position exhausting or in some cases impossible.

However, this modification to conventional cycling has been criticised for not accurately representing the upright posture needed to maximise potential for lower limb muscular recovery or that which is maintained during normal walking\(^{70}\). In addition to this, muscular activity during cycling has been shown to be body-position dependent\(^{108}\) which means that maintaining an upright body position during cycling may more closely mimic the muscular activation associated with walking and act as a more task-appropriate, functionally relevant form of rehabilitation. However, it is still unknown whether such body-position dependent modulations of muscle activation would occur in a similar paradigm involving SC cycling. With the likelihood of a recumbent ergometer being needed for the first application of SC
cycling to an ABI population, a pilot experiment of this nature will be important to determine whether the beneficial effects on muscular adaptation are enhanced, or even negated, with altered body position. An alternative to this would be to employ the use of a more body weight supporting saddle like the one proposed by Hancock et al. (70) (Figure 44). This way upright cycling can be performed with minimal injury risks and the added benefit of more accurately mimicking the upright posture needed for walking which may provide greater potential for improvements in lower limb muscular activity (70).

4.3.3 – Aerobic Fitness, Strength and Functional Outcome Measures

Due to the nature of the sample population used presently and the relatively low intensity of the training regime it was decided to not include outcome measures of aerobic fitness and muscular strength. Considering the physically active nature of participants the addition of these the training was not expected to induce adaptations of this nature, making the inclusion of these measures redundant and unnecessarily time consuming. However, one of the aspects of SC training which makes it so attractive is that it appears to require more physical effort than the FC alternative and as such may provide greater aerobic fitness benefits for ABI patients as a result. Similarly, the independent training of lower limbs with SC cycling may help to correct strength imbalances which are common in ABI patients (85, 82) and may contribute to gait impairments. Although these measures were not included presently, the inclusion of BSSs has provided some indication that SC cycling may be more physically
demanding than FC (SC mean BSS = 2.2 ± 0.5, FC mean BSS = 1.2 ± 0.1 mean, significantly
different $p < 0.05$) and as such, it is imperative that these outcome measures are included in
future experiments with participants who are more likely to see these benefits than those used
presently. Similarly, the inclusion of functional outcome measures of walking and mobility
will be a necessary inclusion to establish whether any of the training adaptations that are
measured provide any kind of functional benefits, especially since this is the key outcome of
this training therapy and rehabilitation. If there are no measurable improvements in functional
outcomes with ABI patients the training adaptations will be irrelevant.

4.4 – TRAINING PARAMETERS AFFECTING MUSCULAR ACTIVATION

The use of cycle ergometers during research experiments inherently produces a number of
different factors which need to be controlled to reduce inter and intra-subject variability of
results. Some of these factors are explored in this section including how investigating them
further may reveal methods to optimise activation of target muscles for rehabilitation.

4.4.1 – Saddle Height

The present study used a fairly basic criteria of a visible slight bend in the knee when the
pedal was at BDC to determine participant saddle height which was kept consistent
throughout the training intervention. Although this variable was controlled in the present
study it is interesting to note that there is considerable research demonstrating the ways in
which changing saddle height can modulate muscular activation during cycling\(^{(106,109-111)}\). Sanderson et al.\(^{(110)}\) hypothesised that by inducing changes in knee and ankle kinematics,
increasing the saddle height can modulate the environment in which leg muscles operate and
as such, alter their activation during cycling. Other research has suggested that there is little
modulation of these joint angles when saddle height is altered\(^{(109)}\) and results concerning
alterations to specific muscular activation in this field are often quite mixed\(^{106,109,110}\). One common theme amongst these studies is that any modifications of muscular activity is typically concerning changes in magnitude of integrated EMG activity and not adaptations to onset or offsets which were typically neglected as an outcome measure\(^{106,109,110}\). As such it may be interesting to investigate the effects of modulating saddle height on the timing of muscular activity during both FC and SC cycling too. This could be especially important if a specific cycling position was found to increase the magnitude and duration of activity of muscles targeted in rehabilitation such as the TA with foot drop. This may then contribute to optimising the rehabilitative capacity of a SC therapy if it is ever implemented in a clinical setting in the future.

4.4.2 – Hand Position

One factor which was not controlled was hand position during cycling (Figure 45). Altering hand position has the effect of altering the hip angle during cycling and has been shown to affect both magnitude and the timing of muscular EMG responses\(^{109,112}\). The latter is of particular importance to the present study which employed muscle onset, offset and active durations as a primary outcome measure, meaning that with participants adopting different hand positions as they pleased, the failure to control this variable may have considerably affected results. For future research this can be easily controlled by picking a single hand position to use across all participants but it may be interesting to investigate the effects of a range of hand positions on muscle kinematics with SC cycling to see how it differs from the existing research concerning
conventional FCs. In a similar fashion to saddle height adaptations, investigating muscular activation adaptations between different hand positions during SC cycling could reveal specific orientations that optimally activate muscles of interest, such as the TA with foot drop rehabilitation. This again, would help to optimise the rehabilitative capacity of SC cycle therapy with patients and could be an important research venture to facilitate the translation of such an intervention into a clinical setting.

4.4.3 – Other Parameters

Investigating both saddle height and hand position variations with SC cycling may reveal optimal parameterization of training for ABI populations but another parameter whose exploration could provide useful information too is adaptations to crank length. Previously proposed by Hancock et al.\(^{70}\), the idea was that this may address the issue of limited participation in exercise stemming from severe hemiparesis by attenuating exercise intensity of the weakened limb specifically. Similarly, adaptations to crank length have also been shown to modulate both muscular activity level and timing with healthy participants on FCs\(^{113}\). Although such variables are typically associated with optimising performance for high level or elite cyclists, their effect on muscle kinematics in SC cycling remain unknown. It may therefore be interesting to pursue such a research opportunity, particularly if the results can reveal a method of grading entry into a SC training regime for patients with particularly severe physical impairments in a similar fashion to the description by Hancock et al.\(^{70}\).
4.5 – IMPLICATION OF RESULTS FOR ABI-RELATED FOOT DROP REHABILITATION

This investigation was conducted with the hope that findings may provide evidence to support future application of a SC cycling training protocol to promote rehabilitation from mobility impairments with special focus on foot drop specifically. Although it appears that the present findings have produced mixed evidence to support this notion, it has raised additional questions to direct future research and hopefully promote translation of the regime into a clinical setting in the future.

One aspect of the present study’s findings which weakens support of such a translation is the lack of CSE adaptation which occurred in the TA. The expectation of increased CSE with training formed a strong basis for the proposition of SC cycling as being beneficial over other foot drop treatments and exercise therapies, so its absence somewhat weakens this argument. However, this result is most likely due to the low skill demand of the task for the healthy population of participants used presently which may differ considerably for the target population of ABI patients. With physical deficits in the lower limb, ABI patients are required to effectively ‘re-learn’ previously habitual patterns of motor activity involved in the use of the impaired muscles in order to recover normal function\(^4\). Simple rhythmic exercises such as walking or cycling therefore become much more difficult to achieve and could require a greater skill demand during participation as a result\(^1\). If this is the case with SC cycling, the skill demand may be much higher and we could expect to see associated plasticity of CSE in the TA, and even additional muscles, as a result of training. Similarly, immediate damage to the motor cortex following an ABI and additional contraction of representation regions from disuse will create an inherently weakened corticospinal connection between the motor cortex and the affected muscle, leaving the potential for training based excitability adaptations.
to be quite high. In the case of the sample of healthy participants used presently, the absence of damage to the motor cortex and weakened corticospinal connections to muscles leaves little room for functional changes to CSE with training in what some may consider to be a ‘ceiling effect’. This means that the expected neuroplastic adaptation may be larger in a sample of ABI patients. If this was to be the case, more gradual adaptations to both muscular activation and CSE would be expected with training and could warrant a longer intervention in order to measure these effects, similar to other studies examining exercise based-therapies in a clinical setting\(^{(72, 75, 77)}\). However, since the present study was only conducted on healthy participants theses comments are only speculative and at this stage determining the feasibility of a clinical application of SC cycling with ABI patients is far beyond the scope of this study.

Although the results for muscular activation did not occur on the same timescale as was predicted, the increased activity duration of TA and BF in SC suggest that these muscles may be trained more extensively than with the common FC alternative. Since strength measures were not used presently and EMG magnitude was not normalised for comparison between sessions 1 and 5, the training benefits of this prolonged activation are unknown. However, with a particular weakness in foot drop, it could be expected that the increased activation of the TA specifically may contribute to accelerating treatment of this impairment over FC alternatives. The additional SC training adaptation which may occur in the hip flexors could also be beneficial for ABI patients by contributing to improved swing phase of walking, making them an additionally beneficial muscular adaptation for the promotion of lower limb motor rehabilitation and correction of abnormal gait\(^{(116)}\). However, it should be stressed that these comments are again speculative and the functional benefits associated with both the measured and predicted muscular adaptations to SC cycling remain unknown.
Since there are many parameters of SC cycling regimes which have remained unexplored, additional studies in healthy participants will be necessary to develop a better understanding of the underlying the mechanisms of SC training adaptations and whether this approach will be beneficial and feasible to conduct with recovering ABI patients.

4.6 – CONCLUSIONS

Whilst the present study has provided new information regarding a relatively unexplored exercise therapy, the results have not supplied the predicted strength of evidence to support SC cycling as a beneficial regime for sufferers of ABI-related foot drop. However, muscular activation data still showed promising effects of such a regime in the training of the TA which is key for the treatment of foot drop and as such, warrants further investigation. The completion of the study has also been effective in directing future research and identifying protocol adaptations to help facilitate the safe translation of this exercise therapy into a clinical setting in the future. The completion of this additional research, however, is imperative for such an occurrence to efficaciously take place.


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Appendix A – Participant TMS Safety and Consent Form

Information Sheet on Transcranial Magnetic Stimulation (TMS)

Transcranial magnetic stimulation (TMS) is a neurophysiological technique that delivers a brief magnetic pulse to the head and induces an electric current in the underlying brain. This technique is painless and involves no risks. The effects of TMS vary depending on the area of the brain stimulated. The TMS protocol used in this study has been approved by the local ethics committee.

For the purpose of this study, TMS is used to assess the response of the brain to a brief magnetic pulse. The effects of TMS are temporary and have no long-term effects. The TMS protocol used in this study has been approved by the local ethics committee.

Information Sheet on Peripheral Nerve Stimulation (PNS)

Peripheral nerve stimulation (PNS) is an electrophysiological technique used to test reflexes. It involves stimulating a nerve via surface electrodes and measuring the response. PNS is a safe and painless technique that has been used in clinical trials.

We will obtain both structural and functional MRI scans to measure changes in brain activity as you perform a behavioral task (e.g., feeding and extending the fingers). You will be in the scanner for 20-30 minutes.

Due to the strong magnetic field in the scanner room, you will be required to remove all metallic objects or objects that can be affected by the magnetic field. This includes: (i) metal anywhere in the head (including magnets, pins, and clips from surgical procedures), (ii) cardiac pacemakers, cochlear implants, and medical devices, (iii) electrodes inside the heart, (iv) electronic devices, (v) increased intracranial pressure, and (vi) a family history of epilepsy. If you have any of these conditions, you must inform the study team.

Information Sheet on Brain Imaging and Functional Magnetic Resonance Imaging (fMRI)

Magnetic resonance imaging (MRI) is a medical imaging technique used to visualize internal structures. The fMRI scanner uses a powerful magnet and radio waves to produce highly detailed images of the brain. Unlike other imaging tests, MRI does not use radiation. The fMRI scanner is noisy, but you will be provided with ear protection.

Cortico spinal Plasticity

Version 1.0

2004/2012

Approval Number Approved by UoB Ethics Committee (Date)

NB: As one would expect there will always be a first available while you are in the laboratory, and you will not be left unsupervised during your visit to us.
Copy to be retained by Participant

Participant Consent

Participant Number: __

Please give full name in capitals _________________________

Information on TMS

I confirm that I have read the consent form and have completed the above questionnaire. The nature, purpose and possible consequences of the procedures have been explained. I understand that I may withdraw from the study at any time. I confirm that I have been through the TMS and MRI screening procedures, and that I am happy to participate in this study.

Name (in CAPITALS) ___________________________________________

Signature ___________________________ Date _________________

Approval Number Approved by UoB Ethics Committee (Date)

<table>
<thead>
<tr>
<th>Have you read the invitation letter/information sheet?</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you had an opportunity to ask questions and discuss this study?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Have you received satisfactory answers to your questions?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Have you received enough information about the study?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Have you completed the screening questionnaire?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

Who have you spoken to?
- Dr Michael J Grey
- Dr François – Xavier Li
- Mr Jonathan Mathias
(Person to be confirmed)

Another person? Name: _________________________________

Do you understand that your are free to leave the study:
- at any time?
- without having to give a reason for leaving?
- and without affecting your medical care?

Yes | No

Please note: All data arising from this study will be held and used in accordance with the Data Protection Act (1984). The results if the study will not be made available in a way which could reveal the identity of individuals.
Neuroplasticity and Neurorehabilitation Laboratory
School of Sport and Exercise Sciences, University of Birmingham
Edgbaston Birmingham B15 2TT
Telephone: +44 (0) 000000
Fax: +44 (0) 000000

Copy to be retained by Experimenter

Participant Consent

Participant Number: ___

Please give full name in capitals __________________________

Information on TMS

I confirm that I have read the consent form and have completed the above questionnaire. The nature, purpose and possible consequences of the procedures have been explained to me and I understand that I may withdraw from the study at any time. I confirm that I have been through the TMS and MRI screening procedures, and that I am happy to participate in this study.

Name (in CAPITALS)_________________________________________

Signature__________________________ Date _________________

Approval Number Approved by UoB Ethics Committee (Date)

Participant Questionnaire Ppt.No ______

Gender: O male O female

Dominant Hand: O left O right

Native English Speaker: O yes O no

Age (please specify) ___ yrs.

Have you read the invitation letter/information sheet? YES NO

Have you had an opportunity to ask questions and discuss this study? YES NO

Have you received satisfactory answers to your questions? YES NO

Have you received enough information about the study? YES NO

Have you completed the screening questionnaire? YES NO

Who have you spoken to?

Dr Michael J Grey
Dr François – Xavier Li
Mr Jonathan Mathias
(Person to be confirmed)

Another person? Name: __________________________

Do you understand that you are free to leave the study:

• at any time?
• without having to give a reason for leaving?
• and without affecting your medical care?

YES NO

Please note: All data arising from this study will be held and used in accordance with the Data Protection Act (1984). The results of the study will not be made available in a way which could reveal the identity of individuals.

Corticospinal Plasticity Version 1.0 20/04/2012
If you agree to take part in this study, please answer the following questions. The information you provide is for screening purposes only and will be kept completely confidential.

### CIRCLE or CROSS OUT

<table>
<thead>
<tr>
<th>Question</th>
<th>YES / NO</th>
<th>Details</th>
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<tbody>
<tr>
<td>Have you ever suffered from any neurological or psychiatric conditions?</td>
<td></td>
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<tr>
<td>If YES please give details (nature of condition, duration, current medication, etc)</td>
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<tr>
<td>Have you ever suffered from epilepsy, febrile convulsions in infancy or had recurrent fainting spells?</td>
<td>YES / NO</td>
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</tr>
<tr>
<td>Does anyone in your immediate or distant family suffer from epilepsy?</td>
<td>YES / NO</td>
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<tr>
<td>If YES please state your relationship to the affected family member.</td>
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<tr>
<td>Do you suffer from migraines?</td>
<td>YES / NO</td>
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<tr>
<td>Have you ever undergone a neurosurgical procedure (including eye surgery)?</td>
<td>YES / NO</td>
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<tr>
<td>If YES please give details.</td>
<td></td>
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<tr>
<td>Do you currently have any of the following fitted to your body?</td>
<td>YES / NO</td>
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<tr>
<td>Heart pacemaker</td>
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<td>Cochlear implant</td>
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<td>Medication pump</td>
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<tr>
<td>Surgical clips</td>
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<tr>
<td>Are you currently taking any prescribed or prescribed medication?</td>
<td>YES / NO</td>
<td></td>
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<tr>
<td>If YES please give details.</td>
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<tr>
<td>Are you currently undergoing anti-malarial treatment?</td>
<td>YES / NO</td>
<td></td>
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<tr>
<td>Have you drunk more than 3 units of alcohol in the last 24 hours?</td>
<td>YES / NO</td>
<td></td>
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<tr>
<td>Have you drunk alcohol already today?</td>
<td>YES / NO</td>
<td></td>
</tr>
<tr>
<td>Have you had more than one cup of coffee, or other sources of caffeine, in the last hour?</td>
<td>YES / NO</td>
<td></td>
</tr>
<tr>
<td>Have you used recreational drugs in the last 24 hours?</td>
<td>YES / NO</td>
<td></td>
</tr>
<tr>
<td>Did you have very little sleep last night?</td>
<td>YES / NO</td>
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</tr>
<tr>
<td>Have you already participated in a TMS experiment today?</td>
<td>YES / NO</td>
<td></td>
</tr>
<tr>
<td>Have you participated in more than one TMS experiment in the past 6 months?</td>
<td>YES / NO</td>
<td></td>
</tr>
<tr>
<td>Are you taking any prescribed drugs (prescribed by your GP or a hospital)?</td>
<td>YES / NO</td>
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<tr>
<td>Is there any chance that you could be pregnant?</td>
<td>YES / NO</td>
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<tr>
<td>Are you left or right handed?</td>
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</tbody>
</table>

Signed: ___________________________ Date: ___________________________

Name (in block letters): ___________________________ Approval Number: ___________________________

Approval Number Approved by UoB Ethics Committee (Date)

Corticospinal Plasticity Version 1.0 20/04/2012
Appendix B – Participant Information Sheet

Participant Information Sheet

We are conducting a study to look at the effect of a novel cycling paradigm known as split crank cycling on corticospinal excitability and activation changes to muscles of the lower limb. Split crank cycling is the same as normal cycling apart from the two pedals work independently of each other, meaning that the downstroke of one pedal cannot assist the upstroke of the other. This means force has to be applied to the pedal throughout the 360 degree movement.

The hope is that we may find evidence to support the use of split cranks in a rehabilitation therapy for patients suffering from lower limb motor impairments associated with acquired brain injuries.

For this experiment you will be required to come into the lab on 5 consecutive days; 1.5 hours on the first and last days and around 20 minutes on the 3 days in between. On 1st entry to the lab we will introduce you to the equipment and ask you to sign some consent forms before attaching pairs of electrodes to 4 muscles on your leg. Following this we will use a painless and non-invasive technique with transcranial magnetic stimulation (TMS) to measure the excitability of 1 of these muscles. This will be followed by a brief recording of muscular activity during cycling on the bike before you will cycle for 15 minutes at 40 rpm (very low cycling cadence) or until you reach a pre-defined score on a reported exertion scale. Once you have finished cycling we will record muscular activity during cycling again followed by another measure of muscular excitability with TMS.

On the 2nd, 3rd and 4th days you will come in and only need to cycle for the 15 mins at 40 rpm with no muscular recordings or TMS measures being taken. Then finally, on the 5th day, you will come in and repeat the same experimental protocol as the first day which will mark the end of the experiment.

I have read the attached Information sheet and discussed the investigation with........................... who has explained the procedures to my satisfaction. I am willing to undergo the investigation but understand that I am free to withdraw at any time without having to give an explanation and that doing so will not affect any treatment or care I may receive. I have also been provided with the relevant contact details for questions that I may have.

Signed: .................................
Witnessed: .................................
Date: .................................

For any further information please contact
Nick Kitchen
Email: .................................
School of Sport and Exercise Sciences, University of Birmingham
Edgbaston, B15 2TT, Birmingham, UK
Appendix C – Ethical Approval

UNIVERSITY OF
BIRMINGHAM