WORKLOAD AND POSITION DEPENDENT FORCE OUTPUT AND THE FORCE-CORTICOSPINAL EXCITABILITY RELATIONSHIP DURING ARM CYCLING

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Abstract

The neural control of human locomotion is commonly investigated by measuring supraspinal and spinal (collectively: corticospinal) excitability during arm cycling. Arm cycling has proven to be an efficient addition to both exercise and rehabilitation regimes, specifically for persons experiencing paraplegia due to a spinal cord injury, or other neural impairments which affect mobility and limb function. Importantly, assessing corticospinal excitability to multiple muscles across phases of cycling and at various intensities has provided a broader understanding of how the central nervous system produces locomotor outputs. One aspect of arm cycling that has yet to be widely assessed is the mechanical component; namely force output. Muscular strength (a determinant of the ability to produce force) is necessary for many activities of daily living, as well as for athletic performance and overall musculoskeletal health. Examining both corticospinal excitability and force output across phases and intensities of arm cycling may improve knowledge translation related to training and rehabilitation that incorporate this exercise modality (i.e., promote a neuromechanical approach).

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I would like to dedicate this thesis to my nephew, Noah, and my niece, Lilly.

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List of Abbreviations

%MSO – percent of maximal stimulator output

μs – microseconds

CMEP – cervicomedullary motor evoked potential

CPG – central pattern generator

EMG – electromyography (bEMG – background EMG, iEMG – integrated EMG)

kg – kilogram

mA – milliamp

MEP – motor evoked potential

M_{max} – maximum M-wave

ms – milliseconds

mV – millivolts

MVC – maximal voluntary contraction

M-wave – compound muscle action potential

PPO – peak power output

RPM – revolutions per minute

SD – standard deviation

SE – standard error

TMES – transmastoid electrical stimulation

TMS – transcranial magnetic stimulation

W - Watts

W_{max} – maximum power output (wattage)

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Chapter 1 Introduction

Overview

In recent years, progress has been made in understanding how the central nervous system controls motor output in humans. Specifically, research comparing neural responsiveness during rhythmic and alternating motor outputs such as arm cycling to isometric contractions has provided a means of understanding how patterns of locomotion are produced (Forman et al., 2014; Weavil et al., 2015). The corticospinal pathway, originating in the motor cortex and synapsing with motoneurones in the spinal cord, is one of the primary descending neural networks involved in voluntary motor output. It is therefore useful to measure the responsiveness of this tract at both a "cortical" and a spinal level during motor outputs to compare the neural effort between different muscles, tasks (isometric vs. dynamic), intensities (cadence or workload), phases (flexion vs. extension), and other parameters of movement.

Using arm cycling as a model of locomotor output, we have previously investigated many of the above-mentioned comparisons and found that corticospinal excitability is muscle, phase, and intensity dependent (Lockyer et al., 2019; Spence et al., 2016). Likewise, a more recent study from our lab has shown that EMG activity during arm cycling is muscle, phase, and intensity-dependent (Chaytor et al., 2020). Importantly, there appears to be a linear relationship between EMG and intensity for all muscles studied, including the biceps and triceps brachii. According to an integral neuromuscular principle, the size principle, it would be expected that as muscle activity increases, so too does force output.

Force production (a measure of strength) is an important aspect of functional mobility and can be a determinant of overall musculoskeletal health, as well as athletic performance (Maestroni et al., 2020). Since the 1970s, the relationship between force output and isometric

contraction intensity has been extensively studied, and as a result, is now well-defined for many different muscles (Lippold, 1952; Woods & Bigland Ritchie, 1983). On the contrary, measuring EMG during dynamic contractions has proven to be more challenging in the past due to factors such as lower electrode stability (for an extensive review, see Farina, 2006). Additionally, force output during locomotor output is multidirectional and bilateral, and thus also more challenging to measure. At the time of writing, only one known study examining force produced during arm cycling with stimulations exists (Klimstra et al., 2011). Given the potential implications of understanding the relationship between force and the neural control of locomotion from a neurorehabilitation standpoint, it is therefore important to assess both variables and to explore whether relationships exist that can be used to expand our understanding of human locomotion. Furthermore, the current research is highly exploratory with an aim to improve the available knowledge surrounding force output during dynamic contractions and the neuromechanical outcomes of locomotor output.

Purpose

The purpose of this study was to characterize force output during arm cycling at workloads of 25, 50, and 100 W and across flexion and extension phases of cycling. A secondary purpose of this study was to assess the relationship between background EMG (bEMG), force output, and corticospinal excitability at the above-mentioned workloads.

Research Hypotheses

The two main hypotheses of this study were as follows:

1. Vector force output will be workload-dependent and increase with workload (*25 < 50 < 100 W*) and position-dependent with greater force during the flexion phase (at/approaching 6 o'clock).

2. There will be a positive correlation between vector force output, bEMG, and corticospinal excitability at increasing workloads.

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Chapter 2 Review of Literature

Introduction

Movement, in apparently healthy humans, is often taken for granted for its complexity and preciseness. It occurs fluently and without conscious effort for those of us privileged to live free of mobility impairments. The freedom of independent movement, however, is not unthreatened by the possibility of neurological injury or disease. What able-bodied persons really take for granted when it comes to their ability to self-locomote- whether by walking, running, skipping, crawling, or cycling- is truly a functioning and healthy nervous system. Thus, although movement and locomotion in particular seem to be unconscious outputs, truly they require detailed and precise activity of the central nervous system.

Since the late 1800s, it has been known that motoneurones were the source of electrical activity which enabled movement. In the early 1900s, Sir Charles Sherrington referred to the motoneurone as the "final common path", indicating the cumulative effects of the preceding nervous system activity ultimately acted on the motoneurone in the production of movement (Freeman & Sherrington, 1907). It was then discovered that contraction of the limbs in a rhythmic, alternating fashion could exist in the absence of descending or sensory input, thus suggesting a central spinal mechanism (Graham Brown, 1911). Grillner (1981) coined these spinal circuits central pattern generators, or CPGs. CPGs are sufficient to produce movement in non-human animals, including cats or rats, even when connections to the brain have been lesioned and sensory feedback removed (Duysens & Van de Crommert, 1998; Rossignol, 2011). Indirect evidence of CPGs has been discovered in humans pertaining to stepping (Calancie et al., 1994; Selionov et al., 2009), leg cycling (Zehr et al., 2001), and arm cycling (Solopova et al., 2016; Zehr et al., 2004). However, in humans, it seems as if supraspinal input has a greater importance in the initiation and

control of CPG-mediated outputs (Barthelemy & Nielsen, 2010; Forman et al., 2014; Sidhu et al., 2012), therefore it is integral to assess both supraspinal and spinal pathways when assessing motor production in humans.

Today, much research investigating the neural control of human locomotion involves studying the responsiveness of the corticospinal tract, a major descending neural pathway which carries signals from the brain to the spinal cord where motoneurones are activated causing skeletal muscles to contract. As part of the somatic nervous system, our corticospinal tract allows us to voluntarily produce movement. However, upon examining its responsiveness during movement, a measure known as corticospinal excitability, we can observe patterns of neural activity that characterize movement and locomotion in particular.

In recent years, our lab has researched numerous conditions which influence corticospinal excitability during arm cycling, a model of locomotor output. Arm cycling is a useful model of locomotion given that it allows for greater head and trunk stability compared to other forms of rhythmic motor output such as walking or leg cycling. Additionally, arm cycling has become a commonly implemented tool in rehabilitation and exercise (Behrman & Harkema, 2000), and thus results of our research may be applicable to neurological populations undergoing movement rehabilitation therapy or working on modifying neural pathways, known as neuroplasticity. Although we have extensively researched corticospinal excitability, we have yet to examine the mechanical output generated by arm cycling. In actuality, there has been limited work regarding force production during arm cycling at the time of writing this review. Incorporating neural and mechanical outputs of locomotion may better our understanding of the efficiency of the central nervous system at producing locomotion, and therefore contribute to solving the puzzle that is how human locomotion is generated.

The following review of literature will overview existing knowledge on trends in corticospinal excitability pertaining to different locomotor outputs, muscles, phases of locomotion, and intensity. Methodology used to examine corticospinal excitability at various power outputs will be included. Additionally, a brief summary of force production during arm cycling will follow in order to detail methods of measuring forces during arm cycling. Importantly, there is currently no existing literature assessing the relationship between corticospinal excitability and force production. To conclude, methods of examining the ratio of neural activity to mechanical output will be discussed. A summary of research and future research considerations are presented in closing.

Assessing Corticospinal Excitability

As mentioned above, our lab primarily investigates the change, or modulation, of corticospinal excitability during arm cycling. To do so, we utilize techniques that allow us to measure the responsiveness of the corticospinal tract when stimulations are delivered to the brain and the descending tracts (i.e., the spinal cord). Given that said measures are obtained via surface electromyography (EMG) recorded from muscles involved in motor output, a third measure of peripheral nerve excitability, the muscle compound action potential (M-wave) is taken to ensure that fluctuation in excitability is not due to changes in peripheral nerve propagation that occur with fatigue (Butler et al., 2003; Taylor, 2006; Woods et al., 1987). Methods of assessing corticospinal and spinal excitability will now be discussed.

Transcranial Magnetic Stimulation

The motor cortex is the most superior component of the corticospinal tract- at least anatomically speaking. To stimulate cortical neurons and corresponding descending spinal axons, we use transcranial magnetic stimulation (TMS) (Rossini et al., 2015). The resultant measurable

signal is deemed a motor-evoked potential, or MEP, which is measured via EMG at the intended muscle(s). Therefore, MEPs are used as indicators of corticospinal excitability as a whole, with MEPs larger in amplitude indicating an increased response and therefore heightened activation of the corticospinal tract (Rossini et al., 2015).

TMS is performed using a wire coil and a linked electrical capacitance (Rossini et al., 2015). The shape of the coil affects the depth of brain stimulation and/or the necessary stimulation intensity (Rossini et al., 2015). In our lab, a circular coil, which generally induces a circular current over a larger albeit more superficial brain region, is used. An electric current is generated by the capacitor and briefly creates a magnetic field in the coil. When the coil is held perpendicular to the head, this magnetic field passes non-invasively through the skull and stimulates brain tissue upon firing the stimulation or "triggering" TMS. Depending on where the coil is positioned, a different network of neurons can be activated. For example, in our lab, the center of the coil is held atop a participant's head at vertex (the intersection between naison to inion and tragus to tragus). Additionally, the direction of current flow from the coil must be taken into account in order to activate either the left or right motor cortex preferentially. Experiments in our lab and others often stimulate the dominant motor cortex in order to measure MEPs in the dominant limb.

Transmastoid Electrical Stimulation

Taking into account the activity of the CPGs during locomotion, it is pertinent to also assess spinal excitability independent of cortical input (McNeil et al., 2013). To do so, we utilize transmastoid electrical stimulation (TMES). TMES involves directly stimulating descending axons at the level of the pyramidal decussation, the cervicomedullary junction (Taylor, 2006). In doing so, excitability of the corticospinal tract is assessed in the absence of synaptic cortical activation (Taylor, 2006). TMES is delivered as an electrical pulse (25 – 100 μs duration) via leads attached

to surface electrodes placed just inferior to the mastoid processes at the back of the neck (Taylor, 2006). The resultant measurable signal is a cervicomedullary-evoked potential, or CMEP, which is recorded from the muscle(s) of interest. Incorporating both TMS and TMES in experimental protocols allows for specific observation of whether the brain or spinal cord primarily influences changes in motoneurone excitability during locomotor outputs.

Peripheral Nerve Stimulation

In order to make claims regarding corticospinal and spinal excitability, we also examine peripheral nerve excitability throughout experimental protocols as neuromuscular fatigue can affect motoneurone excitability (Taylor, 2006). During arm cycling experiments investigating upper limb muscles, we stimulate the brachial plexus to elicit a M-wave in the nerve root of interest. This is done via leads placed at Erb's point, with the cathode placed in the supraclavicular fossa and the anode at the acromion. Stimulations of increasing intensity are then delivered until a plateau in the amplitude of the M-wave is observed, namely, the maximal M-wave (M_{max}). MEPs and CMEPs are then normalized to this value to ensure that changes in peripheral nerve propagation due to fatigue at the neuromuscular junction or muscle do not affect results (Taylor, 2006).

Characterizing Muscle Activity During Locomotor Outputs

Background EMG Considerations

As discussed above, the output of the motoneurone pool is an important consideration related to measures of neural responsiveness. Additionally, during locomotor outputs, fluctuation in motoneurone output occurs due to ongoing, alternative activation of the motoneurone pools. For example, the biceps brachii is most active during the flexion phase of arm cycling, thus the motoneurone pool exhibits greater activity throughout this phase compared to extension (more on

this in later sections). In studies assessing corticospinal excitability, motoneurone pool output in the absence of stimulation is often referred to as background EMG (bEMG). Importantly, we assess bEMG when studying neural excitability to understand how the underlying activity of motoneurones influences excitability. In studies examining corticospinal excitability, bEMG is often measured milliseconds (ms) prior to stimulations eliciting MEPs and CMEPs. We refer to this parameter as pre-stimulus EMG and typically measure the amplitude 50 ms prior to stimulation. This allows us to: 1. observe the difference in muscle activity caused specifically by the stimulation and 2. to compare bEMG within trials to ensure that any observed differences in evoked potentials are not due to differences in motoneurone pool output.

Modulation of EMG with Intensity During Arm Cycling

With regards to tonic contractions, the EMG-contraction intensity relationship has been well-documented (Lippold, 1952; Woods & Bigland Ritchie, 1983). Measuring muscle activity during these contractions can be accomplished rather easily when compared to dynamic contractions given the stability of the limb and resultant EMG signal. This EMG-intensity relationship tends to be curvilinear during isometric contractions: at intensities less than 50% maximum contraction intensity, the relationship is linear, above this intensity, there is an exponential increase in EMG followed by a plateau at an intensity of roughly 80% maximum voluntary contraction (MVC) (Konrad, 2005).

Until recently, there was a need to characterize muscle activity of various arm muscles involved in cycling. Given the difficulties associated with recording EMG during dynamic contractions, such as the movement of electrodes, signal non-stationarity, and change in tissue conductivity (Farina, 2006), this area of research has been slowly developing. However, as discussed above, understanding the changes in bEMG during locomotor outputs has significant

implications to furthering our understanding of neural excitability and how the central nervous system produces locomotion.

In an extensive study of muscle activity, Chaytor et al. (2020) characterized EMG (i.e. bEMG) patterns of six upper arm muscles during arm cycling at intensities ranging from 5 – 50% peak power output (PPO). The authors examined phase- and muscle-dependent differences for each intensity and successfully provided for the first time, to my knowledge, a picture of muscle activity during arm cycling. EMG amplitude (normalized to muscle-specific maximal EMG) was analyzed by calculating integrated EMG across a full revolution of cycling and for individual flexion and extension phases. Among the muscles included were the biceps and triceps brachii – two muscles commonly studied in excitability research done in our lab. The authors found that, like isometric contractions, there appeared to be a linear relationship between EMG and intensity for all muscles studied. Likewise, there appeared to be a plateau in EMG at the highest intensity observed (50% PPO). Interestingly, the triceps brachii did not exhibit phase-dependent activity with intensity, as no significant differences between EMG during extension and flexion phases were observed. The elbow flexors (biceps brachii and brachioradialis) on the other hand, were phase dependent as EMG was greater during the flexion phase at all intensities. An overview of EMG patterns for all muscles, intensities, and lengths studied is shown in Figure 1.

This study is a valuable addition to the existing literature surrounding muscle activity and dynamic contractions. In particular, it will assist in research such as the present study which aims to characterize mechanical and neural outputs during arm cycling at various intensities.

Task-dependent Modulation of Corticospinal Excitability

Related to the above-discussed differences between tonic and dynamic measurement of EMG is the idea that corticospinal excitability undoubtably is modulated differently during

locomotor outputs compared to tonic contractions. Specifically, considering the activation of CPGs during locomotor outputs, the spinal component of corticospinal excitability should differ to spinal excitability observed during isometric contractions. In order to make comparisons between isometric contractions and dynamic contractions occurring during locomotor output, it is necessary to match bEMG in the muscle(s) from which MEPs and CMEPs are recorded (Power et al., 2018). This allows comparisons to be made based on contraction intensity, as well as muscle length (e.g., joint angle or muscle length). Corticospinal excitability is then referred to as task-dependent if findings differ during locomotor outputs compared to tonic contractions. In this section, I will present findings from the available research which investigate task-dependent modulation of corticospinal excitability in both the upper and lower limb. The following studies investigate task-dependent differences by measuring corticospinal excitability at equal intensities and muscle positions for both tasks.

Lower Limb Findings

Sidhu et al. (2012) were the first to measure both corticospinal and spinal excitability to a lower limb prime mover during locomotor output and compare the results to an isometric contraction. Using leg cycling as a model of locomotion, subthreshold MEPs were evoked in the knee extensor vastus lateralis when EMG was near peak amplitude, and again during a five-second knee extension contraction. The isometric contraction was done at a position and intensity equivalent to that at which MEPs were elicited during cycling. Additionally, MEPs and CMEPs were elicited during cycling to determine potential phase-dependent modulation of corticospinal and spinal excitability. Subthreshold TMS was included to determine whether activation of cortical inhibitory interneurons projecting to pyramidal neurons resulted in suppression of EMG. This

phenomenon, where present, indicates cortical drive plays a role in activating motoneurones to the muscle of interest during the task at hand (Kujirai et al., 1993).

Although no significant differences were reported between subthreshold MEPs of isometric and locomotor tasks, the average amount of EMG suppression was greater during isometric contractions. This suggests that cortical input to the knee extensors was heightened during isometric contractions compared to locomotor output (Sidhu et al., 2012). The authors concluded that the motor cortex excitability contributed to both tasks given that MEP amplitudes decreased with lower TMS (i.e., higher subthreshold) intensities. As for phase-dependent modulation of corticospinal excitability during cycling, MEPs and CMEPs followed similar patterns of change, indicating that changes were likely driven by spinal excitability (Sidhu et al., 2012).

Weavil and colleagues (2015) also compared corticospinal excitability to the knee extensors (vastus lateralis and rectus femoris) during both locomotor output and a tonic contraction. Intensity- and task-dependent modulation was assessed in this study by incorporating various power outputs for cycling and contraction strengths for isometric contractions. Cycling was completed at 30 – 160% W_{peak} while knee extensions were done at 10 – 100% MVC force. Corticospinal excitability to the vastus lateralis increased with contraction intensity until a plateau was reached at 75% MVC and W_{peak} for isometric and locomotor tasks, respectively. In the rectus femoris, both MEPs and CMEPs increased by approximately 110% with intensity without plateauing, regardless of task. Thus, intermuscular differences in corticospinal excitability were observed and potential mechanisms were discussed. Additionally, given that similar increases in MEP and CMEP amplitudes were observed with increasing intensity/bEMG for both tasks,

corticospinal excitability appeared to be primarily influenced by spinal mechanisms during isometric contractions and cycling.

Upper Limb Findings

Corticospinal excitability to the biceps brachii during arm cycling was first assessed in our lab by Forman and colleagues (2014). This study followed research done by Carroll et al., (2006) which revealed MEPs recorded from the flexor carpi radialis to be lesser during arm cycling compared to position and intensity matched tonic contractions. In other words, corticospinal excitability to the wrist flexor was reduced during rhythmic motor output in comparison to an isometric contraction (Carroll et al., 2006). Forman et al., (2014) chose to investigate the same parameters, but in the biceps brachii, given that it is a key muscle in producing arm cycling.

To determine task-differences in corticospinal excitability to the biceps brachii, MEP and CMEP amplitudes evoked during cycling were compared to intensity and position matched tonic contractions. Phase-dependent changes in corticospinal excitability during cycling were examined via MEPs and CMEPs elicited at three different positions: the onset of elbow flexion (3 o'clock), mid-flexion (6 o'clock), and mid-extension (12 o'clock) (Forman et al., 2014). Average pre-stimulus bEMG during cycling was used as an indicator of contraction intensity and isometric contractions were held at this level of EMG. Comparisons of corticospinal excitability between tasks revealed that *supraspinal excitability* was significantly *greater* at 3 and 6 o'clock and spinal excitability was significantly greater at 3 o'clock during arm cycling compared to isometric contraction. Therefore, differences between tasks were primarily due to supraspinal input being enhanced during the flexion phase of arm cycling, with spinal input to the biceps brachii being heightened at the onset of flexion. In summary, this research demonstrated that corticospinal

excitability the biceps brachii is higher during arm cycling than during an intensity-matched tonic contraction and was thus characterized as task-dependent.

Phase-dependent Modulation of Corticospinal Excitability During Locomotor Outputs

Methodology

When considering locomotor outputs, it is integral to take into account the position of the limb when EMG data is assessed, especially when we aim to make claims regarding corticospinal excitability. Unlike isometric or isotonic contractions during which one muscle group contracts, locomotion involves alternating concentric and eccentric contractions of flexor and extensor muscles. A number of challenges associated with EMG collection and analysis of dynamically contracting muscles must be taken into account when interpreting data during locomotor outputs (for review, see Farina, 2006). Thus, partially to alleviate some of said difficulty, it is helpful to examine EMG in a phase-specific manner (i.e., during flexion and extension of the limb, separately).

By investigating corticospinal excitability according to the phase of movement, we also take into account activity of the motoneurone pool in the muscle of interest with respect to the muscle's role in the phase of movement. For example, during arm cycling, EMG is often recorded from the biceps brachii, which acts as an agonist during the elbow flexion phase. By examining the phase of arm cycling throughout which elbow flexion occurs, we can then investigate if heightened corticospinal excitability to the biceps brachii is specific to this phase of movement, when the activation of motoneurones innervating the biceps brachii is higher. Conversely, if we consider the phase of cycling throughout which elbow extension occurs, we can investigate whether corticospinal excitability to the biceps brachii is lesser or greater compared to the flexion phase.

For simplicity, our lab denotes phases of arm cycling in reference to a clock face (Forman et al., 2014). Imagining the elbow position when the cycling hand is at the top-most, centered position as 12 o'clock position, cycling in a clockwise direction, the arm passes from 12 to 3 to 6 o'clock (bottom dead center), and back to 12, constituting one complete revolution. Elbow flexion begins at 3 o'clock, when the arm is fully extended in front of the participant, and ends at 9 o'clock, when the elbow is fully flexed. Conversely, elbow extension begins at 9 o'clock and ends at 3 o'clock. For simplicity, we often elicit MEPs and CMEPs measured from the biceps and/or triceps brachii at mid-flexion (6 o'clock) and mid-extension (12 o'clock). Stimulations are automatically triggered via magnetic sensors placed at said positions.

Upper Limb Findings

Our lab has examined phase-dependent modulation of corticospinal excitability on multiple occasions to date (Spence et al., 2016; Lockyer et al., 2018). The consensus of these studies has been as follows: biceps brachii, the prime elbow flexor, exhibits phase-dependent modulation of corticospinal excitability while triceps brachii, the prime elbow extensor does not. In the biceps brachii, MEPs and CMEPs were larger at mid-flexion (when the muscle is most active) compared to mid-extension (Spence et al., 2016; Lockyer et al., 2018). Interestingly, there was no difference in MEP amplitudes measured from the triceps brachii at flexion and extension, and CMEPs were greater when the muscle was *less* active, at mid-flexion (Spence et al., 2016; Lockyer et al., 2018). The latter finding is evidence that spinal excitability to the elbow extensor, triceps brachii, is heightened during the flexion phase of arm cycling while supraspinal excitability is reduced. Further examination of phase-dependent modulation with respect to cycling intensity will be provided in the following section.

Intensity-Dependent Modulation of Corticospinal Excitability

Corticospinal Excitability to the Biceps Brachii During Isometric Contractions

Corticospinal excitability during isometric contractions has been shown to be intensity dependent (Pearcey et al., 2014). In other words, muscle contraction strength has an effect on the size of MEP and CMEP amplitudes, indicating that changes in corticospinal excitability are associated with the amount of muscle activation. Given that bEMG provides a general indication of the degree of motoneurone output, a high degree of force output typically coincides with high bEMG (i.e. greater motoneurone activity) during submaximal isometric contractions (Konrad, 2005). The force-corticospinal excitability relationship can therefore be assessed during isometric contractions by assessing the size of evoked-responses when bEMG is gradually increased (Pearcey et al., 2014).

Corticospinal and spinal excitability to the biceps brachii during isometric elbow flexion contractions was assessed by Pearcey and colleagues (2014) in a sample consisting of chronic resistance trained (RT) and non-RT individuals. TMS and TMES were used to assess changes in corticospinal and spinal excitability, respectively. For all participants, contractions were completed at a range of intensities from 10 – 100% of MVC force. Muscle activation was deemed low or high at contraction strengths below and above 50% MVC force, respectively. MEPs in the chronic-RT group were found to be smaller at high contraction strengths compared to the non-RT group. On the contrary, there were no differences in CMEP amplitudes between groups for all contraction strengths. The authors concluded that chronic resistance training resulted in decreased supraspinal excitability to the biceps brachii during isometric elbow flexion at force outputs greater than 50% MVC. Regardless of group, at high contraction intensities, corticospinal excitability was primarily influenced by spinal mechanisms. This is shown via a similar change in MEPs and

CMEPs at > 50% MVC force output. At low contraction strengths (10 – 40% MVC), MEP amplitudes show greater increases than CMEP amplitudes, indicating supraspinal factors mediate corticospinal excitability. In summary, corticospinal excitability to the biceps brachii during isometric contraction appears to be primarily mediated by supraspinal input at low force outputs and by spinal factors at high force outputs.

Workload-Dependent Corticospinal Excitability During Arm Cycling

Several studies assessing corticospinal excitability at different contraction intensities during arm cycling have been completed by our lab. Intensity of a locomotor task can be manipulated by cadence (speed) or power output (workload). For the purpose of this review, studies that have defined intensity as power output will be discussed.

Spence et al. (2016) measured corticospinal excitability from the biceps and triceps brachii at 6 and 12 o'clock to determine whether differences existed between antagonistic muscles and to characterize workload-dependent changes by phase. Using relative workloads of 5 and 15% peak power output (PPO), MEPs were found to be workload-dependent for both muscles, and CMEPs were workload dependent in the triceps only (15% > 5% PPO). Spinal mechanisms appeared to contribute to higher excitability with workload given that MEPs and CMEPs changed in a similar fashion in both the biceps and triceps brachii. Importantly, this demonstrates that corticospinal excitability during arm cycling is muscle-dependent when power output is manipulated and varies for antagonistic muscles.

In a study comparing the effects of cadence and power output on corticospinal excitability, Lockyer et al. (2018) further investigated phase- and muscle- specific changes to supraspinal and spinal excitability during arm cycling. Using relative workloads of 20, 40, and 60% W_{max} and cadences of 60 and 90 rpm, power output and cadence were shown to differently modulate

corticospinal excitability. During the less active phase for each muscle (i.e., 12 o'clock for biceps brachii, 6 o'clock for triceps brachii), increasing power output had no significant effect on spinal excitability (i.e., CMEPs). More so, in the biceps brachii, MEP amplitudes increased between higher power outputs (60% > 40% W_{peak}). MEPs in the triceps brachii at 6 o'clock were significantly different between the greatest and least power outputs (60% > 20% W_{peak}). These results suggest that supraspinal excitability is enhanced with power output during the less active phase of cycling for the biceps and triceps brachii. Increasing power input enhanced corticospinal excitability during flexion more than extension biceps brachii and similarly for both phases in the triceps brachii.

In a follow-up study, Lockyer and colleagues (2019) assessed corticospinal excitability to the biceps brachii at six contraction intensities ranging from 25 – 250 W. Unlike the above-mentioned research, power output was not relative to each participant (i.e., absolute power output was used). Evoked responses were measured from the dominant biceps brachii at mid-flexion, when the muscle was most active. Additionally, two stimulation intensities were used to assess whether modulation of corticospinal excitability with increased power output was influenced by the use of weak (10% M_{max}) or strong (40% M_{max}) stimulations. The authors hypothesized that corticospinal excitability would increase with power output using the weak stimulation without reaching a plateau but would plateau and decrease near maximal power output when a strong stimulation was used. Contrary to this hypothesis, plateaus were observed for both weak and strong stimulation intensities, however MEP and CMEP amplitudes reached a plateau at lower cycling intensities when strong stimulation was used compared to weak. Importantly, MEP amplitudes were larger than CMEPs at greater power outputs, regardless of stimulation intensity. This study was essential in demonstrating changes in corticospinal excitability to the biceps brachii over a

wide range of workloads during cycling. It also confirmed our lab's previous findings that supraspinal factors attributed to changes in corticospinal excitability with increasing power output during arm cycling.

Force Output Measurements

Force-EMG Relationship During Isometric Contractions

Similar to the above-mentioned relationship between isometric contraction intensity and EMG, force output during isometric contractions has been well-documented and provide insight as how force is correlated to muscle activity (Lippold, 1952; Woods & Bigland-Richie, 1983). Given that for isometric contractions, intensity is often measured as a percentage of MVC force - the latter of which is measurable via a strain gauge - the curvilinear relationship between force and EMG holds true for most muscles, including the biceps and triceps brachii (Konrad, 2005). The straight-forward ability to measure force output during isometric contractions enables comparisons of force and surface EMG (such as in tests of corticospinal excitability) to be completed with ease.

Measuring Force During Arm Cycling: Methodology

Part of the difficulty with measuring force output during rhythmic motor output is that force is generated in several planes of movement. For example, arm cycling requires force output in the horizontal and vertical directions to propel the limb through each revolution. To date, only one assessment of force output during arm cycling has been done (Klimstra et al., 2011). The authors measured force at the right handle of the cycle ergometer using a 6-axis force transducer. The orientation of the transducer remained constant throughout each revolution, enabling forces to be measured in the horizontal (X) and vertical (Y) directions consistently at all elbow positions. A resultant vector (Z) force was calculated via the addition of X and Y vector forces across phases of arm cycling. In this study, the relationship between force output and cutaneous nerve reflexes

across a complete revolution was examined. Participants cycled at a cadence of 60 rpm while the superficial radial nerve was stimulated every two to four seconds. The authors found that stimulation elicited significant negative X forces (i.e., backwards) while cycling at the 1 to 4 o'clock positions. Additionally, a significant positive Z force (i.e., lateral) was observed upon stimulation at all positions except 6 to 8 'clock (Klimstra et al., 2011). These results are depicted in Figure 2. Though this study examined mechanical responses to cutaneous nerve stimulation, these results may contribute to the construction of a biomechanical model of arm cycling, which is in part the goal of the current research.

Using the above-mentioned methods of measuring force at the handles, our intention is to characterize X, Y, and Z forces in relation to corticospinal excitability measured from the biceps brachii during arm cycling. By obtaining said measures at three different cycling intensities, we may furthermore characterize potential relationships between the modulation of corticospinal excitability and force output during a locomotor output.

Neuromuscular Efficiency

Jones, Power, & Herzog (2016) introduced "neuromuscular efficiency" as a way to assess force output per muscle activity (i.e. force/EMG) - in other words, a measure of how proficient the motoneurone pool was in producing a certain amount of force. A higher force/EMG ratio indicates a more "efficient" contraction given less motoneurone activity equates a higher force output. For example, surface EMG has been shown to be lower during eccentric maximal voluntary contractions compared to maximal concentric and isometric contractions (Duchateau & Baudry, 2013). Thus, it might be expected that neuromuscular efficiency would be greater during eccentric contractions compared to concentric and isometric contractions. In actuality, Jones et al., (2016) found that among contractions of the adductor pollicis muscle at submaximal intensity,

neuromuscular efficiency was significantly greater for concentric contractions and lesser for eccentric contractions compared to the isometric reference contraction. It should be noted that in this study, measures of force and EMG were recorded following lengthening and shortening contractions, as opposed to during.

In the present research, we aim to investigate neuromuscular efficiency across phases of arm cycling and at varying intensities. Thus, factors to take into account are: 1. phase-specificity (i.e., eccentric versus concentric contractions of the muscle of interest), 2. the force-EMG relationship across increasing dynamic contraction intensities. Incorporating this measure into this study may further the current understanding of the production of locomotor outputs at various intensities and uncover a link between muscle activity (i.e., the neural component) and force (i.e., the muscular component) during said outputs.

Conclusion

The available literature highlighting measures of corticospinal excitability during isometric and locomotor motor outputs provides a basis of understanding task-specific modulation of neural control. Importantly, using both TMS and TMES allows researchers to deduce whether changes in excitability are attributable to supraspinal or spinal mechanisms. Arm cycling studies – such as those done by our lab – have allowed investigation of changes in corticospinal excitability to the biceps and triceps brachii (the upper limb prime movers) in phase- and intensity- dependent manners. A consensus amongst the research is that corticospinal excitability to the biceps brachii is phase-dependent and is raised by increasing power output at submaximal intensities. Likewise, corticospinal excitability to the triceps brachii is raised with increasing power output, seemingly due to supraspinal mechanisms.

There is currently a lack of research surrounding neuromechanical outcomes during arm cycling with no study having assessed mechanical correlates of corticospinal excitability to date. The proposed research will therefore be the first to examine intensity-dependent modulation of corticospinal excitability along with force outputs during arm cycling, and to my knowledge, any locomotor task. Given that there is currently a lack of knowledge surrounding neuromechanical outcomes related to movement production, results of this research may help to clarify how central nervous system output modulates biomechanical components of movement. One potential discovery that may prove highly beneficial is whether neuromuscular efficiency is observed between cycling intensities. This might suggest that neural activity can be "reserved", or that less corticospinal excitability can produce a certain force output. A neuromechanical model of arm cycling can therefore potentially contribute to improving neurorehabilitation by allowing clinicians to manipulate mechanical outputs such as force based on an underlying understanding of neuromuscular efficiency.

Figure Legend

Figure 1. Integrated EMG (iEMG) of six upper-limb muscles shown during flexion (dark grey background) and extension (light grey background) phases of arm cycling. iEMG is shown for relative intensities (10, 20, 30, 40, and 50% peak power output) and at an absolute workload of 25 W.

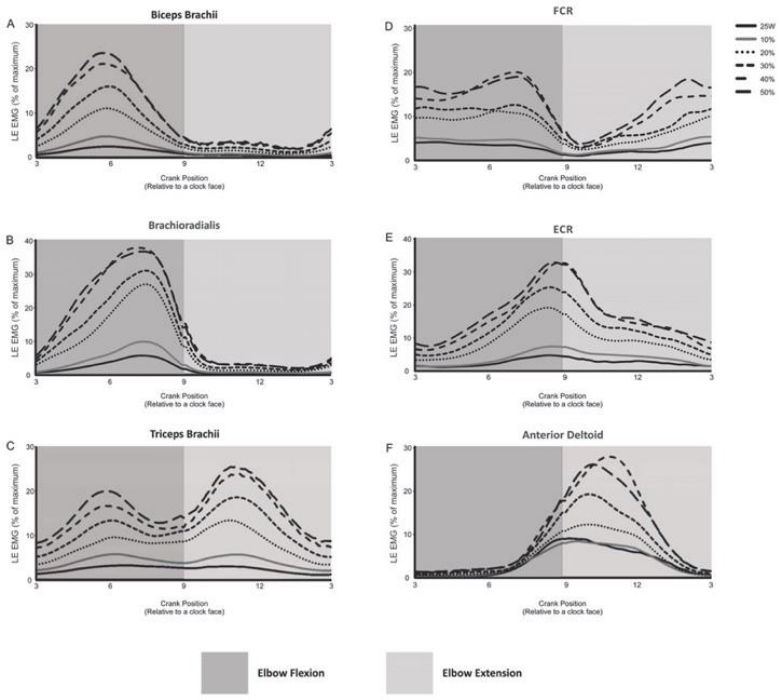

Figure 1. iEMG of six upper-limb muscles while arm cycling at different intensities. From "Changes in muscle activity during the flexion and extension phases of arm cycling as an effect of power output are muscle specific", by C. P. Chaytor et al., 2020, *PeerJ, 8,* https://doi.org/10.7717/peerj.9759.

Figure 2. Average force outputs in the horizontal (X), vertical (Y), and vector (Y) directions during unstimulated arm cycling (black dots) and when cutaneous stimulation of the superficial radial nerve was delivered during arm cycling (white dots). Significant differences ($p < .05$) are denoted via the presence of asterisks.

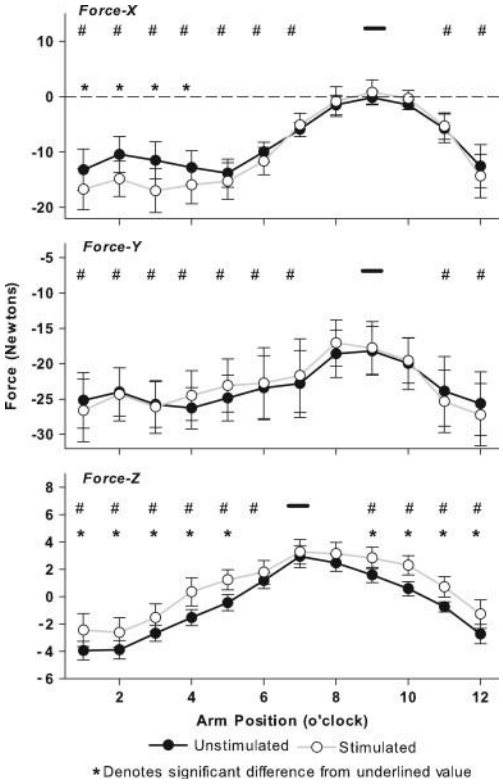

Figure 2. Kinetics during stimulated and unstimulated trials in relation to the movement cycle. From "Biomechanical outcomes and neural correlates of cutaneous reflexes evoked during rhythmic arm cycling", by M. D. Klimstra et al., *Journal of Biomechanics, 44*(5), https://doi.org/10.1016/j.jbiomech.2010.12.017.

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Chapter 3 Workload and position dependent force output and the force-corticospinal excitability relationship during arm cycling

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Running head: Force and corticospinal excitability during arm cycling

Key words: intensity, workload, force, transcranial, transmastoid, MEP, CMEP, EMG

3.0 ABSTRACT

This is the first study to examine workload-dependent force output and corticospinal excitability to the biceps and triceps brachii during arm cycling. Supraspinal and spinal excitability were assessed using transcranial magnetic stimulation and transmastoid electrical stimulation, respectively. Motor-evoked potentials (MEPs) and cervicomedullary-evoked potentials (CMEPs) were measured from the dominant arm biceps and triceps brachii at mid-flexion (i.e., the 6 o'clock position relative to a clock face). Force output was measured throughout cycling at 12 clock positions in the horizontal and vertical directions from both handles of the arm cycle ergometer via a six-axis force transducer and were used to calculate a vector force. Arm cycling was completed at three workloads (25, 50, and 100 W). Dominant arm vector force output increased with workload ($p < 0.01$), was greatest during the flexion or "pulling" phase of cycling at 5 o'clock ($p < .05$) and lowest during the extension or "pushing" phase at 8 and 9 o'clock ($p < .05$). There was a moderate positive correlation ($r = 0.53$) between force and MEP amplitude to the biceps and triceps brachii, and force and CMEP amplitude ($r = 0.53$) to the triceps brachii. There were moderate positive correlations ($r = 0.53$) between force and MEP amplitude of the biceps and triceps brachii, and between force and CMEP amplitude ($r = 0.53$) to the triceps brachii and a weak positive correlation between force and CMEP amplitude ($r = 0.37$) to the biceps brachii. There were moderate positive correlations between force and pre-stimulus EMG of the triceps brachii prior to MEPs and CMEPs ($r = 0.42$ and 0.43, respectively), and of the biceps brachii prior to MEPs ($r = 0.54$) and a weak positive correlation between force and pre-stimulus EMG prior to CMEPs of the biceps brachii ($r = 0.37$). This work demonstrates that force output during arm cycling is workload and position dependent. It also demonstrates that force and corticospinal excitability to the biceps and triceps brachii and spinal

excitability to the biceps brachii are moderately and weakly correlated, respectively, across increasing workloads.

3.1 INTRODUCTION

Arm cycling, like other models of locomotor output (e.g., running, leg cycling), is a complex, bilateral task involving many muscles. Such tasks are under the control of a central pattern generator (CPG) located in the spinal cord which activates spinal motoneurones ultimately producing flexion and extension of the involved muscles (Grillner, 1981). One method of studying the neural control of motor output is by measuring the responsiveness of the corticospinal pathway by means of transcranial magnetic stimulation (TMS) and transmastoid electrical stimulation (TMES). The resultant amplitude of motor evoked potentials (MEPs) and cervicomedullary evoked potentials (CMEPs) provides insight as to whether supraspinal or spinal factors primarily contribute to motor output. Corticospinal excitability during upper limb CPG-mediated activity has been shown to be dependent on the phase (flexion or extension; Spence et al., 2016) and intensity (Spence et al., 2016; Lockyer et al., 2018, 2019) of movement. For upper body cycling, phase has been defined according to positions of a clock face, with 3 to 9 o'clock being flexion and 9 to 3 o'clock being extension (Forman et al., 2014). It is also important to note that intensity of locomotor output may be manipulated by cadence, workload (power output), or a combination thereof (Lockyer et al., 2018).

A higher voluntary contraction intensity leads to an increase in muscle activity, making the motoneurone pool from which corticospinal excitability is measured more excitable (Taylor, 2006). This is an important consideration when comparing different motor tasks such as tonic and dynamic contractions, as unmatched muscle activation prevents valid comparisons in measured corticospinal excitability (Carroll et al., 2006; Forman et al., 2014; Power et al., 2018). Furthermore, given rhythmic motor outputs consist of alternating shortening and lengthening (i.e., dynamic) contractions, there is a heightened importance of measuring EMG across phases

of movement; an effort which is made more challenging by factors innate to dynamic output, for example, decreased electrode stability (Farina, 2006).

Chaytor and colleagues (2020) recently characterized the activity of six different muscles of the upper limb- including the biceps and triceps brachii- across phases of arm cycling over a range of intensities. There was a linear relationship between intensity (workload) and EMG for all muscles, as well as a greater EMG during the flexion phase for the biceps brachii. No difference in EMG was observed for the triceps brachii between phases; a finding previously demonstrated by Spence et al. (2016), albeit at lower intensities.

The relationship between corticospinal excitability and contraction intensity has been well-documented during isometric contractions (Pearcey et al., 2014), as well as locomotor outputs (Weavil et al., 2015; Spence et al., 2016; Lockyer et al., 2018, 2019). There appears to be task, muscle, and phase dependent alterations in corticospinal excitability. Likewise, the relationship between muscle activity and force output has been well-documented and shown to be both linear (Lippold, 1952; Woods & Bigland Ritchie, 1983) and non-linear (Woods & Bigland Ritchie, 1983) during isometric contractions. Several studies have demonstrated a linear relationship between force output and EMG in lower limb locomotor outputs, such as leg cycling (Sargeant & Davies, 1977; Sanderson et al., 2000). However, there is a lack of available knowledge regarding the mechanical outcomes of arm cycling, with the sole study examining force output across phases of arm cycling being that of Klimstra and colleagues (2011). Their study investigated the effect of cutaneous nerve stimulation on force output while cycling at a constant workload. The relationship between corticospinal excitability and force output has yet to be assessed during arm cycling.

The purpose of the present research was two-fold: (1) to characterize force output during arm cycling at different phases (i.e., elbow positions) and intensities (i.e., workloads), (2) to determine whether there is a relationship between force output and i. corticospinal excitability and/or ii. background EMG to the dominant arm biceps and triceps brachii during arm cycling. It was hypothesized that: (1) force output would be workload-dependent, and greater at higher workloads, (2) force would be position-dependent and greater during the flexion or "pulling" phase of cycling compared to the extension phase, and (3) there would be a positive correlation between force and both corticospinal excitability and EMG for both the biceps and triceps brachii.

3.2 METHODS

Ethical approval

Prior to partaking in this study, all potential risks were fully disclosed, and participants were given the opportunity to ask questions. All participants then gave written, informed consent before partaking in the study. This study was conducted in accordance with the Helsinki declaration and all protocols were approved by the Interdisciplinary Committee on Ethics in Human Research at Memorial University of Newfoundland (ICEHR No. 20190632-HK).

Participants

Twelve healthy volunteers between the ages of 18 and 30 participated in the current study (one female, one left hand dominant). Participants had no known neurological impairments. Prior to receiving TMS, all participants completed a safety checklist to screen for contraindications to magnetic stimulation (Rossi et al., 2009). A Physical Activity Readiness Questionnaire (PAR-Q+) was completed to screen for contraindications to physical activity (Canadian Society for Exercise Physiology, 2002). Hand dominance was determined using the Edinburg handedness

inventory (Veale, 2014). The data for one participant was discarded as no range of motion (i.e., position) data was recorded. Of the data for the eleven remaining participants, the EMG data for one participant was not included in data analysis due to an error with the EMG signal.

Experimental set-up

Arm cycling was performed using a SCIFIT arm cycle ergometer (model PRO2 Total Body, Tulsa, OK, USA). Cranks of the ergometer were locked 180° out of phase. Seat height and position were adjusted so that the center of the arm crank shaft was aligned to the height of the participant's shoulder and so that the handles were at no more than arm's length when the elbow was fully extended. Participants wore wrist braces to maintain a neutral pronated position while cycling and to limit the influence of reflex connections between the wrist flexors and biceps brachii (Manning & Bawa, 2011). Arm position during cycling was indicated with respect to a clock face, with 3 – 9 o'clock being elbow flexion and 9 – 3 o'clock being elbow extension. Position was monitored throughout cycling via a custom-built potentiometer that tracked range of motion via magnets placed around the handle. All stimulations were triggered when the dominant arm passed 6 o'clock (i.e. mid-flexion), when biceps brachii is most active (Forman et al., 2014). Cycling cadence was set to 60 rpm for all cycling trials. During the experimental protocol, cycling was completed at 25, 50, and 100 W, making a total of three experimental trials per participant.

Electromyography recordings

EMG was recorded from the dominant arm biceps and triceps brachii. Ag-AgCl surface electrodes (MediTraceTM 130 Foam Electrodes with conductive adhesive hydrogel, Covidien IIC, Massachusetts, USA) were placed in a bipolar configuration on the mid-muscle belly of the biceps brachii and the lateral head of triceps brachii (interelectrode distance = 2 cm). A ground

electrode was placed on the lateral epicondyle. Prior to electrode placement, skin was shaved, abraded, and cleaned with an isopropyl alcohol swab to reduce potential electrical impedance which would interfere with the EMG signal. EMG sampling was conducted at 5 KHz using a CED 1401 and Signal 5 software (Cambridge Electronic Design Ltd., Cambridge, UK). Signals were amplified and filtered with a three-pole Butterworth filter (10-1000 Hz).

Stimulation conditions

M-waves, motor-evoked potentials (MEPs), and cervicomedullary-evoked potentials (CMEPs), and were elicited by Erb's point stimulation, TMS, and TMES respectively. All evoked responses were measured from the dominant biceps brachii at the 6 o'clock position via surface EMG. Stimulation intensities were determined while cycling at 60 rpm with a workload of 25 W.

Brachial plexus stimulation

Muscle compound action potentials (M-waves) were elicited via electrical stimulation of the brachial plexus at Erb's point (DS7AH; Digitimer, Welwyn Garden City, Hertfordshire, UK). The cathode was placed in the supraclavicular fossa and the anode over the acromion process. Using a pulse duration of 200 μs and an initial stimulation intensity of 25 mA, biceps brachii M_{max} was determined by gradually increasing stimulation intensity until a plateau in M-wave amplitude was found (i.e., M_{max}). Stimulation intensity was set to 120% that which was used to elicit M_{max} for the experimental protocol to ensure maximum nerve stimulation throughout the study. MEP and CMEP amplitudes were normalized to M_{max} upon analysis to account for changes in peripheral neuromuscular propagation.

Transcranial magnetic stimulation

MEPs were elicited via TMS using a Magstim 200 stimulator (Magstim, Whitland, Dyfed, UK) and a circular coil (13.5 cm diameter). The coil was held at the vertex of participant's skull, which was determined by measuring the mid-points between naison and inion and between tragi and marking the spot at which they intersected (Forman et al., 2014). The coil was held parallel to the floor and oriented so that the direction of current flow preferentially activated either the left or right motor cortex, depending on hand dominance. TMS intensity used throughout the experimental protocol was determined while cycling at 60 rpm and 25 W. Beginning at 25% magnetic stimulator output (MSO), stimulation intensity was gradually increased until MEP amplitude was approximately 15% of M_{max}. At this stimulation intensity, TMS was then delivered for 8 trials. This %MSO was accepted for use throughout the protocol if MEP amplitudes fell between 10 – 20% M_{max} in 4 of 8 trials.

Transmastoid electrical stimulation

CMEPs were elicited via TMES at the cervicomedullary junction. Stimulations were delivered via Ag-AgCl electrodes placed slightly inferior to the mastoid processes and a Digitimer current stimulator (DS7AH, Digitimer Ltd., Welwyn Garden City, Hertfordshire, UK). Using a pulse duration of 200 μs and an initial stimulation intensity of 25 mA, stimulation intensity was gradually increased until CMEP amplitude was approximately 15% M_{max} of (i.e., equal to MEP amplitude). At this stimulation intensity, TMES was then delivered for 8 trials. If CMEP amplitude fell between 10 – 20% M_{max} in 4 of 8 trials, this stimulation intensity was used to elicit CMEPs during the experimental protocol.

Force measurements

Bilateral force output was measured from the arm crank handles of the SCIFIT arm cycle ergometer. Force transducers consisted of 8 x 350 Ω strain gauges (Micro Measurements Model CEA-06-125UW-350) on a mounting plate (10 x 6 mm) that were connected by a Wheatstone bridge. Voltages were converted to force (Newtons) using a pre-calibrated equation and force outputs were collected online. Force in the vector (z) direction was obtained by calculating the square root of the sum of squared horizontal (x) and vertical (y) forces (*equation 1*). Force was displayed during data collection.

Equation 1.

$$Vector_z = \sqrt{(x^2 + y^2)}$$

Experimental protocol

Participants visited the lab on two separate days for this study. The first day consisted of a familiarization session to ensure that participants could cycle at the required workloads (25, 50, and 100 W) and to introduce them to the three stimulation conditions. The second day consisted of the experimental protocol, during which participants completed three cycling trials at each of the aforementioned workloads. The order in which workloads were completed was randomized, and a two-minute rest period was provided between trials. For all trials, cycling was completed at a cadence of 60 rpm and lasted 140 seconds. A total of 8 TMS, 8 TMES, 2 $M_{max,}$ and 2 blank (unstimulated) frames were delivered during each trial. Stimulations were separated by 7 seconds and delivered in randomized order. A one-minute rest period was allotted during each trial after half (10) of the total stimulations were delivered prior to completing the remainder of the trial.

Data analysis

Peak-to-peak amplitudes of MEPs, CMEPs, and M-waves of the dominant arm biceps and triceps brachii at 6 o'clock were assessed using Signal 5.08 data collection software. MEPs and CMEPs were normalized to M_{max} to account for potential changes in peripheral neuromuscular propagation during experimental protocol. It is important to note that for the triceps brachii, the M_{max} was not determined specifically for the triceps brachii. Rather, the maximal elicited M-wave set to the maximal stimulation intensity used to elicit Mmax in the biceps brachii. Pre-stimulus EMG of the biceps and triceps brachii were measured from the rectified virtual channel as the mean of a 50 ms window prior to the stimulus artifact (Forman et al., 2015). All measurements were obtained from the average of all evoked frames per each stimulation (i.e., 8 MEPs, 8 CMEPs, 2 M_{max}, 2 blanks) for each trial. Average force output was measured from the horizontal (x), vertical (y), and vector (z) directions at each of the twelve clock positions.

Statistical analysis

Statistical analysis was completed using IBM's SPSS Statistics version 27 (IBM Corporation, Armonk, New York, USA). The assumption of sphericity was tested for all data using Mauchley's Test and when violated, the appropriate correction was used to correct for degrees of freedom. To test whether there were statistical differences in force output between workloads and positions, a two-way repeated measures ANOVA [Workload (25, 50 and 100 Watts) x Position (12 positions relative to a clock face)] was used. Differences in MEP, CMEP, and pre-stimulus EMG amplitude between workloads were assessed using separate one-way repeated measures (RM) ANOVAs. Sidak post-hoc comparisons were used to determine

differences between groups where significant differences were found. Significance for all tests is set to $p < .05$. Results are reported as mean ± *SD.*

3.3 RESULTS

3.3.0 Biceps brachii

3.3.0.1. Force output and MEPs

MEP amplitude. Group data for MEP amplitudes to the biceps brachii were 22.6%, 39.7%, and 61.5% M_{max} for 25, 50, and 100 W, respectively. There was a significant effect for workload ($F_{(1.193, 10.737} = 28.451$, $p = .000$). Pairwise comparisons revealed there was a significant increase in MEP amplitude with workload (25 W < 50 W < 100 W, $p < .005$ for all comparisons).

Force – MEP amplitude correlations. Figure 3A shows group data for vector force and MEP amplitude. There was a moderate correlation between vector force at the 6 o'clock position and MEP amplitude with increasing workloads (25 W < 50 W < 100 W, $r = 0.53$). There was a very weak correlation between vector force and MEP amplitude at 25 W ($r = 0.13$) and 50 W ($r = 0.15$), and no correlation at 100 W ($r = 0.027$).

Pre-stimulus EMG for MEPs. As a group, pre-stimulus EMG prior to MEPs was 0.126, 0.271, and 0.550 mV at 25, 50, and 100 W, respectively. There was a significant effect for workload ($F_{(1.042, 9.377} = 20.684$, $p = .001$). Pairwise comparisons indicated that pre-stimulus EMG significantly increased prior to MEPs with increasing workload (25 W < 50 W < 100 W, $p < .05$ for all comparisons).

Force – pre-stimulus EMG correlations. Figure 3C shows group data for vector force and pre-stimulus EMG prior to MEPs. There was a moderate correlation between vector force and pre-stimulus EMG with increasing workloads (25 W < 50 W < 100 W, $r = 0.54$). There was a

very weak correlation between vector force and pre-stimulus EMG at 25 W (r = 0.17) and 100 W (r = -0.18), and no correlation at 50 W (r = 0.09).

3.3.0.2. Force output and CMEPs

CMEP amplitude. Group data for CMEP amplitudes to the biceps brachii were 20.2%, 25.1%, and 40.2% M_{max} for 25, 50, and 100 W, respectively. There was a significant effect for workload ($F_{(1.210, 10.892} = 8.621$, $p = .002$). Pairwise comparisons revealed there were significant differences between 25 and 100 W ($p = .046$), and 50 and 100 W ($p = .006$), but not 25 and 50 W ($p = .633$).

Force – CMEP amplitude correlations. Figure 3B shows group data for vector force and CMEP amplitude. There was a weak correlation between vector force at the 6 o'clock position and CMEP amplitude with increasing workloads (r = 0.37). There was a weak correlation between vector force and CMEP amplitude at 25 (r = 0.12), 50 (r = -0.21), and 100 W (r = -0.17).

Pre-stimulus EMG for CMEPs. As a group, pre-stimulus EMG prior to CMEPs was 0.133, 0.258, and 0.588 mV at 25, 50, and 100 W, respectively. There was a significant effect for workload ($F_{(1.071, 9.638} = 19.679$, $p = .001$). Pairwise comparisons indicated that pre-stimulus EMG increased prior to CMEPs with increasing workloads (25 W < 50 W < 100 W, $p < .05$ for all comparisons).

Force – pre-stimulus EMG correlations. Figure 3D shows group data for vector force and pre-stimulus EMG prior to CMEPs. There was a weak correlation between vector force and pre-stimulus EMG with increasing workloads (25 W < 50 W < 100 W, r = 0.37). There was no correlation between vector force and pre-stimulus EMG at 25 (r = -0.01), 50 (r = 0.07), and 100 W (r = -0.00).

3.3.1 Triceps brachii

MEPs and CMEPs to the triceps brachii were normalized to the maximum amplitude of the M-wave in the triceps brachii elicited by evoking M_{max} in the biceps brachii (see *Data Analysis*).

3.3.1.1. Force output and MEPs

MEP amplitude. Group data for MEP amplitudes to the triceps brachii were 11.0%, 24.9%, and 26.5% M_{max} for 25, 50, and 100 W, respectively. There was a significant effect for workload ($F_{(2,18)} = 8.241$, $p = .003$). Pairwise comparisons revealed there was a significant difference in MEP amplitudes between 25 and 100 W ($p = .003$), but not between 25 and 50 W ($p = .54$) or 50 and 100 W ($p = .97$).

Force – MEP amplitude correlations. Figure 4A shows group data for vector force and MEP amplitude. There was a moderate correlation between vector force at the 6 o'clock position and MEP amplitude with increasing workloads (25 W < 50 W < 100 W, $r = 0.53$). There was a very weak correlation between vector force and MEP amplitude at 25 ($r = -0.14$) and a weak correlation at 50 ($r = 0.25$), and 100 W ($r = 0.22$).

Pre-stimulus EMG for MEPs. As a group, pre-stimulus EMG prior to MEPs was 0.0505, 0.0780, and 0.122 mV at 25, 50, and 100 W, respectively. There was a significant main effect for workload ($F_{(1.087, 9.779)} = 16.459$, $p = 0.002$). Pairwise comparisons indicated that pre-stimulus EMG significantly increased prior to MEPs with increasing workload (25 W < 50 W < 100 W, $p < .05$ for all comparisons).

Force – pre-stimulus EMG correlations. Figure 4C shows group data for vector force and pre-stimulus EMG prior to MEPs. There was a moderate correlation between vector force and pre-stimulus EMG with increasing workloads (25 W < 50 W < 100 W, $r = 0.42$). Correlations at

individual workloads were very weak (r = -0.14), weak (r = 0.25), and zero (r = - 0.04) at 25, 50, and 100 W, respectively.

3.3.1.2. Force output and CMEPs

CMEP amplitude. Group data for CMEP amplitudes to the triceps brachii were 15.5%, 20.2%, and 24.6% M_{max} for 25, 50, and 100 W, respectively. There was a significant main effect for workload ($F_{(2, 18)} = 3.849$, $p = 0.041$). Pairwise comparisons revealed there were significant differences between 25 and 100 W (p = .47), but not 25 and 50 W (p = .52) or 50 and 100 W (p = .493).

Force – CMEP amplitude correlations. Figure 4B shows group data for vector force and CMEP amplitude. There was a moderate correlation between vector force at the 6 o'clock position and MEP amplitude with increasing workloads (25 W < 50 W < 100 W, r = 0.53). There was a very weak correlation between vector force and MEP amplitude at 25 (r = -0.18) and 50 W (r = 0.16), and a weak correlation at 100 W (r = 0.37).

Pre-stimulus EMG for CMEPs to the triceps brachii. As a group, pre-stimulus EMG prior to CMEPs was 0.051, 0.075, and 0.132 mV at 25, 50, and 100 W, respectively. There was a significant main effect for workload ($F_{(1.054, 9.487)} = 13.788$, p = .04). Pairwise comparisons indicated that pre-stimulus EMG significantly increased prior to MEPs with increasing workload (25 W < 50 W < 100 W, $p < .05$ for all comparisons).

Force – pre-stimulus EMG correlations. Figure 4D shows group data for vector force and pre-stimulus EMG prior to CMEPs. There was a moderate correlation between vector force and pre-stimulus EMG with increasing workloads (25 W < 50 W < 100 W, r = 0.43). There was a very weak correlation between vector force and pre-stimulus EMG at 25 (r = -0.14), 50 (r = 0.24), and 100 W (r = 0.22).

3.3.2 Force output across workloads and positions

Workload and position (interaction). There was a significant interaction between workload and position for group data ($F_{(22, 198)} = 783.58$, $p = .00$).

Workload (individual positions). Table 1 shows group data for average vector force at all twelve individual positions at 25, 50, and 100 W. Table 2 summarizes the results of the one-way RM ANOVAs (12) used to assess the effect of workload at individual positions. There was a significant main effect for workload at all positions. Pairwise comparisons revealed vector force increased with workload (25 W < 50 W < 100 W, $p = .00$ for all comparisons) at all positions except 8 ($p = .823$) and 9 o'clock ($p = .077$) where there was no significant difference between 25 and 50 W.

Workload (grouped positions). Figure 1 shows group data for average vector force for all 12 positions combined at 25, 50, and 100 W. There was a significant main effect for workload ($F_{(2, 18)} = 871.36$, $p = .00$). Pairwise comparisons revealed vector force increased with workload (25 W < 50 W < 100 W) ($p = .00$ for all comparisons).

Position (*individual workloads).* Table 2 shows group data for average vector force at 12 positions of a clock face at 25, 50, and 100 W. There was a significant main effect for position at 25 ($F_{(11, 99)} = 49.665$, $p = 0.00$), 50 ($F_{(11, 99)} = 24.229$, $p = .00$), and 100 W ($F_{(11, 99)} = 28.549$, $p = .00$). At 8 o'clock, force was significantly less than all positions 2 – 7 o'clock for each workload ($p < .05$ for all comparisons). At higher intensities, force at the 8 o'clock position was also significant less than at 1, 11, and 12 o'clock (50 and 100 W) and 10 o'clock (100 W) ($p > .05$ for all comparisons).

Position (grouped workloads). Figure 2 shows group data for average vector force collapsed for workload at 12 positions of a clock face. There was a significant main effect for

position ($F_{(11, 99)} = 38.969$, $p = .00$). Pairwise comparisons revealed a significantly lower vector force at positions 8 and 9 o'clock compared to all other positions (i.e., 10 – 7 o'clock) ($p < .05$ for all comparisons). Vector force at 4, 5, and 6 o'clock was significantly greater than all other positions except 11 and 12 o'clock ($p < .05$ for all comparisons), and 6 o'clock was not significantly greater than 3 o'clock ($p = .995$).

3.4 DISCUSSION

This study was the first to: (1) characterize force output during arm cycling at different workloads and (2) assess the relationship between force output and corticospinal excitability during arm cycling. The primary findings of this study were as follows: (1) There is a positive correlation between force output and corticospinal excitability to both the biceps and triceps brachii at increasing workloads of arm cycling, (2) There is a significant increase in vector force at increasing workloads, and (3) Vector force is position-dependent and is greater during the flexion or "pulling" phase of cycling compared to the extension or "pushing" phase

3.40 Positively correlated force and corticospinal excitability at increasing workloads

In both the biceps and triceps brachii, there was a moderate positive correlation between vector force and MEPs and CMEPs (Figures 3A, 3B, 4A and 4B This relationship was observed when workloads were grouped, however at individual workloads, the correlation between variables was weak or did not exist. This indicates that either: (1) there is not enough available data to find a significant correlation between force and corticospinal and/or spinal excitability at individual workloads or (2) the relationship between force and corticospinal excitability is not present at individual workloads. To establish whether either of these proposed explanations are valid, future studies should aim to gather more data, either by increasing the number of evoked potentials per trial and/or by recruiting more participants.

Corticospinal excitability and force output at increasing workloads was previously examined during isometric contractions of the biceps brachii by Pearcey et al., (2014). MEP and CMEP amplitudes, along with force (kg) was recorded during 5 second elbow flexion contractions ranging from 10 – 100% maximum voluntary contraction (MVC) force. In resistance trained participants, the authors observed a plateau in the amplitude of MEPs and CMEPs at roughly 40% and 50% MVC, respectively. Weavil and colleagues (2015) also recorded an increase in corticospinal excitability followed by a plateau at a submaximal intensity (75% MVC) during isometric contractions of the knee extensors. Although neither study directly compared force and corticospinal excitability, Pearcey et al. (2014) used a ratio of absolute force to MEP/CMEP amplitude to normalize between resistance and non-resistance trained (RT) participants. Corticospinal excitability to the biceps brachii per a given force was lower for RT subjects at all intensities. This indicates that the force-corticospinal excitability relationship may vary based on participants' training background, something which was not accounted for in the present study. Additionally, the force to MEP ratio was lower at increasing intensities (Pearcey et al., 2014). In the present study there was an increase in both force and MEP amplitude with workload, however, there was a mere three intensities included compared to ten in the study by Pearcey and colleagues (2014). Another important difference between these studies is that force measurement is more complex during locomotor output compared to isometric contractions as it is multidirectional. Whereas absolute force was obtained by Pearcey et al. (2014), vector force was calculated from vertical and horizontal force and subjected to correlations. In summary, although there is no direct correlational data to observe for tonic contractions, it appears as if the force-corticospinal excitability relationship may be task and muscle dependent.

Intensity-dependent modulation of corticospinal excitability has been previously shown during arm (Lockyer et al., 2018; Lockyer et al., 2019; Spence et al., 2016) and leg cycling (Weavil et al., 2015). Lockyer and colleagues (2019) demonstrated that MEPs and CMEPs to the biceps brachii increased with absolute workload up until 200 and 150 W, respectively. Muscle-dependent differences in corticospinal excitability were recorded during leg cycling by Weavil et al. (2015) who observed a plateau in MEPs and CMEPs to the vastus lateralis at Wpeak, and no plateau (i.e., a continual increase) to the rectus femoris up until roughly 160% Wpeak. As intensity did not exceed 100 W (a relative submaximal intensity) in the current study, it is not surprising that no plateau in evoked-potential amplitudes were observed. Likewise, as higher absolute workloads have been implemented in previous arm cycling studies (Lockyer et al., 2019), it would be expected that force output at 100 W does not typically correspond to participants' maximum possible force produced. The "ceiling" of corticospinal excitability and force production should be considered for future work in this area, as the current study has only provided insight to a relatively low range of intensities.

3.4.1 Positively correlated force and background EMG at increasing workloads

Preceding this work, several studies investigating arm (Bernasconi et al., 2006; Hundza et al., 2012; Spence et al., 2016) and leg cycling (Bigland Ritchie & Woods, 1974; Duchateau et al., 1986; Taylor & Bronks, 1994) have examined the workload-EMG relationship, but none included a measure of mechanical (force) output. Thus, there remains more research to be done to develop a full understanding of the EMG-force relationship during dynamic contractions.

The relationship between EMG and force during isometric contractions has been studied since the 1950's (Lippold, 1952; Bigland Ritchie & Woods, 1977; Woods & Bigland Ritchie, 1983). Woods & Bigland Ritchie (1983) examined iEMG and force during tonic contractions of

the biceps and triceps brachii and found an overall non-linear relationship, with a linear trend at intensities greater than 30% MVC force. In the current study, we found that there were positive correlations between pre-stimulus EMG and force with increasing intensity at the 6 o'clock position for the same muscles (Figures 3 & 4, C, D). This work follows the recent contribution of Chaytor et al. (2020), who have successfully mapped the iEMG of six muscles across phases of arm cycling at various workloads. At the 6 o'clock position, there were significant increases in biceps brachii iEMG at higher workloads. There were also significant increases in triceps brachii iEMG at higher workloads, though there was no difference between the 6 and 12 o'clock positions. In the present study, the correlation coefficient was larger for pre-stimulus EMG prior to MEPs (r = 0.53, Figure 3C) to the biceps brachii than EMG prior to MEPs and CMEPs in the triceps brachii (r = 0.42 and 0.43, respectively, Figure 4 C & D). However, there was a weaker correlation for pre-stimulus EMG prior to CMEPs in the biceps (Figure 3D, r = 0.37) compared to both conditions in the triceps brachii. Although there was a main effect of workload on CMEP amplitude in the present study, Spence et al. (2016) found that spinal excitability was position, but not intensity-dependent to the biceps brachii during arm cycling. In said study, relative workloads of 5 and 15% PPO were used, whereas absolute workloads (25, 50, and 100 W) were included in the present study. There were no significant differences in CMEP amplitude between 25 and 50 W for both muscles. This may have resulted in a weaker correlation across workloads. A stronger correlation between force and CMEPs to the triceps brachii may have been relevant to the method of normalization used, as M_{max} was set to the maximum elicited response in the biceps brachii (see *Stimulation Conditions*).

3.4.2 Workload-dependent changes in force output during arm cycling

As hypothesized, group data for vector force showed that the magnitude of force significantly increased with workload (Figure 1). This refers to the average vector force for all twelve positions combined, indicating that, as a complete revolution, force increased with workload. Of the individual positions examined, there were significant increases in force output at higher intensities (25 < 50 < 100 W, $p = 0.00$) at positions 10 to 7 o'clock. At 8 and 9 o'clock (i.e., the onset of extension), there were significant differences in force output during the 100 W trial compared to 50 and 25 W, but no difference between the two lower workloads. Therefore, it appears as if workload-dependent differences in force output during arm cycling may be specific to elbow position at the time of measurement. As will be discussed in the following section, force output at 8 and 9 o'clock were lower than all other positions. It may be that there was no effect of workload on force output between lower intensities at these positions due to the bilateral nature of cycling. Specifically, when the dominant arm is at 9 o'clock, the contralateral (non-dominant) arm is fully extended (i.e., "pushing" at 3 o'clock) therefore creating more force and allowing the dominant arm to be propelled with minimal exertion. At a higher workload (100 W), increased bilateral output may have been required to maintain a cadence of 60 rpm, therefore resulting in a significant increase in force. Similar findings have been observed in leg cycling studies, with higher intensities resulting in less asymmetrical force production between the limbs (Carpes et al. 2007a, 2007b). Carpes et al. (2010) suggested that requiring a greater force output during locomotor output may eliminate asymmetries between the limbs. In the present study, to determine whether this occurred, it would be beneficial to compare force output at each ergometer handle across workloads.

Given that an increase in motor unit activation, accompanied by an increase in the EMG signal, precedes an increase in force output according to the size principle (Henneman, 1957; Adrian & Bronks, 1929), we would expect a greater magnitude of force at higher levels of EMG. Chaytor et al. (2020) characterized the integrated EMG (iEMG) of six upper limb muscles, including the biceps and triceps brachii, during arm cycling at various workloads (5 – 50% peak power output (PPO)) and during flexion and extension phases. They found that for all muscles, there was a linear relationship between workload and iEMG, indicating there was higher muscle activity at higher cycling intensities. There were phase-dependent differences for the biceps, as iEMG was greater during flexion compared to extension, but none for the triceps. Based on these findings, it would be expected that the highest recorded force would be in the 50% PPO trial given the higher EMG from all muscles included, and furthermore a higher motoneurone pool output resulting in greater force. Such is that we have observed in the current study, as there was a moderate positive correlation between pre-stimulus EMG and force across increasing workloads (see below).

Previous studies examining force output during locomotor output have demonstrated significantly greater force at higher workloads (Sargeant & Davies, 1977; Sanderson et al., 2000). Saergeant et al. (1997) found a linear correlation between force and workload for both single leg and two-legged cycling. Likewise, Sanderson and colleagues (2000) found a consistent increase in force output as workload increased. We observed a similar result in the present study, as doubling the workload produced approximately double the force output amongst the three conditions. Collectively, the literature suggests that a linear relationship exists between force output and workload for locomotor outputs. As this was the first known study to examine upper

limb force output at varying intensities during locomotor output, this research may serve as a guide for future work investigating mechanical outcomes of arm cycling.

3.4.3 Position-dependent changes in force output during arm cycling

There were significant differences in force between positions when workloads were combined, and at individual workloads (Figure 2 and Table 1). As expected, force was greatest during the flexion phase, between 3 and 9 o'clock. Force (collapsed for workload) peaked at 5 o'clock, though was not significantly different from 4 or 6 o'clock at this position, nor 11 or 12 o'clock. This indicates there are no differences in dominant arm force output at and just before mid-flexion (6 o'clock) and mid-extension (12 o'clock) during arm cycling. Again, this may be explained by the bilateral component of cycling. Given the 6 and 12 o'clock positions correspond to opposite arm configurations during cycling (i.e., when the dominant arm is at 6, the non-dominant arm is at 12, and vice versa) there may be an equal amount of horizontal (i.e., push/pull) force from both limbs at these positions, which would result in a similar force output. As 4 to 6 o'clock corresponds to the pulling phase, it appears that many participants in the current study incorporated a pulling strategy, resulting in a greater force at these positions. Previous work by Spence and colleagues (2016) has shown that pre-stimulus EMG measured from the biceps brachii at 6 o'clock was greater than EMG measured from the triceps at 6 and 12 'clock. A potential explanation for the observed pulling strategy during arm cycling might be that participants are able to activate the elbow flexors to a greater extent than the extensors. On the contrary, it may be that greater recruitment of flexor motoneurones does not cause a tendency for higher pull force, but rather that a higher tendency to favour a pulling strategy is the cause for higher biceps EMG. To investigate whether the latter is true, it may be beneficial to examine whether training to favour a pushing or pulling strategy effects cycling tactics.

Force at the 8 and 9 o'clock position was significantly lower than all other positions. These positions represent a period of full elbow flexion, just preceding the onset of elbow extension (i.e., the transition between phases). One potential explanation for lower force output at these positions is therefore a relatively low degree of muscle activation in both the biceps and triceps brachii (Chaytor et al., 2020), and furthermore a lower amount of force produced (referring to the size principle discussed above). Additionally, the contralateral arm being at the 3 o'clock position or full extension (i.e., pushing) when the dominant arm is at 9 o'clock likely reduces the effort required by the dominant arm to propel forward at this position.

Force output across phases of arm cycling was previously mapped by Klimstra et al. (2011) while cutaneous nerve stimulation to the hand were delivered. There are two important differences between the methodology of the current study and the study of Klimstra and colleagues (2011) to note. First, whereas we opted to investigate vector force, the authors examined horizontal (x), vertical force (y), and diagonal (z) force. Second, cycling was completed with the handles set in a neutral position for the current research, and a pronated position for the external study. Despite these differences, the pattern of observed force output across positions were similar, as there was a lower force output in x, y, and z directions at 8 and 9 o'clock compared to the 4 – 6 o'clock positions. This finding supports the proposed existence of a potential bilateral asymmetry causing lower force output at the fully flexed elbow position during arm cycling. It remains to be investigated why a pulling strategy appears to be the favored mechanism of arm cycling.

As mentioned above, the findings from Chaytor and colleagues' (2020) study characterizing the EMG of active arm muscles during cycling demonstrated phase-dependent differences in biceps brachii iEMG, but not triceps brachii. As the biceps brachii works as the

prime elbow flexor during arm cycling, it is expected that phase-dependent EMG would translate to higher force output during the most active phase of cycling, which peaks at 6 o'clock (Forman et al., 2014; Spence et al., 2016; Chaytor et al., 2020). On the contrary, as the triceps brachii is the prime elbow extensor during arm cycling, the near consistency of muscle activity between phases (Spence et al., 2016; Chaytor et al., 2020) would not be expected to result in any increase in force production during the extension phase. This agrees with our results since we found no significant difference at the 11 and 12 o'clock (peak triceps EMG) positions compared to the 4, 5, and 6 o'clock (peak biceps EMG, some triceps EMG).

3.4.4 Methodological considerations

There are several factors that should be considered when interpreting results of the current study. Many considerations are tied to the bilateral nature of arm cycling and the activation of numerous muscles of the arm, forearm, and wrist. In the present work, we examined dominant arm force output and corticospinal excitability from the dominant arm biceps and triceps brachii. Force output of the non-dominant arm and corticospinal excitability to the non-dominant biceps and triceps brachii were not examined, nor were other muscles activated during arm cycling (e.g., brachioradialis, deltoid, extensor carpi radialis, flexor carpi radialis). Hence, correlations obtained were without insight to these inseparable components of the motor output in question, leading to potential inconclusive results.

With regards to force output, different cycling strategies were observed amongst participants, specifically "pushing" or "pulling" mechanisms. Participants who relied on pushing tended to exert more force during elbow extension to propel the limbs through cycling, while those who relied on pulling exerted more force during elbow flexion. There was no control for "pushers" or "pullers" included, thus it may have been that an inclusion of more of one type of

cycler influenced the observed force output. Investigating a difference in bilateral asymmetries (i.e., examining both dominant and non-dominant limb force) may provide insight as to whether participants are relying on said tactics, and to what degree. For this reason, it would be practical to assess and compare workload and position dependent force in both arms, rather than solely the dominant arm, as in the present study.

As noted, normalization of evoked potentials was completed by dividing MEP and CMEP amplitudes by the amplitude of M_{max} to the biceps brachii. M_{max} to the triceps brachii was not found, thus, evoked potentials to the triceps may not be representative of a percentage of the motoneurone pool output. Furthermore, normalized MEPs and CMEPs to the triceps brachii may be lower than normalized MEPs and CMEPs in the biceps brachii because of this, and not accurately represent corticospinal excitability to the triceps brachii.

Previous work examining the effect of intensity on corticospinal excitability and background EMG has incorporated a range of both cadences and workloads. Absolute workloads up to 250 W have been used by Lockyer et al. (2019), whereas relative workloads up to 50% PPO were included in the study by Chaytor and colleagues (2020). Three absolute workloads up to 100 W were included in the present study, providing a narrow observation of the force-corticospinal relationship during dynamic motor output. Furthermore, because workload was absolute (i.e., the same for all participants) a different degree of effort was likely required by individual participants. Given differences in motoneurone pool output at increasing voluntary output, said differences in relative intensity may have influenced correlations between corticospinal excitability and force. It may be more practical to use a measure of relative intensity in future studies to eliminate this potential limitation.

Lastly, since evoked potentials were recorded at the 6 o'clock position, correlations were assessed at a single point in time during cycling. To create a more detailed picture of this relationship, it is recommended that future studies examine a broader range of cycling intensities (including relative intensities) and various positions.

3.5 CONCLUSION

This was the first study to examine force output at different workloads during arm cycling, as well as the first to examine the force – corticospinal excitability relationship during arm cycling. Force output increased by roughly 50% from 25 to 50W, and 100% from 50 to 100 W, and was greatest during the pulling phase of cycling, indicating force is workload- and position-dependent during arm cycling. There was a moderate positive correlation between force and corticospinal excitability to the biceps and triceps brachii, and a weak positive correlation between force and spinal excitability to the biceps at 6 o'clock. The results suggest that force and corticospinal excitability to the upper limb prime movers increase up to an intensity of 100 W during arm cycling. Although a strong linear correlation was not observed in the present study, it should be considered that cycling is a bilateral task that activates a number of muscles. Future studies should investigate this relationship at higher workloads, at different positions (e.g., 12 o'clock), and in multiple muscles of both the dominant and non-dominant limb to provide insight into neuromechanical mechanisms of arm cycling, and furthermore, locomotor outputs. This research would contribute to an existing body of knowledge regarding corticospinal excitability at different locomotor intensities, and a smaller existing literature examining both neural and mechanical outcomes during upper limb rhythmic motor outputs.

3.6 FIGURE LEGEND

Figure 1. Group data (mean ± SD, n = 11) for position-collapsed vector force magnitude (N) at 25, 50, and 100 W. Vector force was 18.39 ± 4.68, 30.36 ± 7.14, and 60.05 ± 15.18 N at 25, 50, and 100 W, respectively. * denotes a significant difference for workload ($p < .05$).

Figure 2. Group data (mean ± SD, n = 11) for workload-collapsed vector force magnitude (N) at clock positions 3 to 12. * denotes a significant difference for position ($p < .05$).

Figure 3. Correlations between group data for average vector force (n = 11) at 25, 50, and 100 W combined and MEP amplitude (%M_{max}) **(A)**, CMEP amplitude (%M_{max}) **(B)**, pre-stimulus EMG (prior to MEPs) **(C)**, and pre-stimulus EMG (prior to CMEPs) **(D)** (n = 10) from the biceps brachii at the 6 o'clock position. **(A)** There was a moderate positive correlation between vector force and MEP amplitude (r = 0.53). **(B)** There was a weak positive correlation between vector force and CMEP amplitude (r = 0.37). **(C)** There was a moderate positive correlation between vector force and pre-stimulus EMG prior to MEPs (r = 0.53). **(D)** There was a weak positive correlation between vector force and pre-stimulus EMG prior to CMEPs (r = 0.37).

Figure 4. Correlations between group data for average vector force (n = 11) at 25, 50, and 100 W combined and MEP amplitude (%M_{max}) **(A)**, CMEP amplitude (%M_{max}) **(B)**, pre-stimulus EMG (prior to MEPs) **(C)**, and pre-stimulus EMG (prior to CMEPs) **(D)** (n = 10) from the triceps brachii at the 6 o'clock position. **(A)** There was a moderate positive correlation between vector force and MEP amplitude (r = 0.53). **(B)** There was a moderate positive correlation between vector force and CMEP amplitude (r = 0.53). **(C)** There was a moderate positive

correlation between vector force and pre-stimulus EMG prior to MEPs (r = 0.47). **(D)** There was a moderate positive correlation between vector force and pre-stimulus EMG prior to CMEPs (r = 0.43).

3.7 LIST OF TABLES

Table 1. Group (*n* = 11) vector force (N) (mean ± *SD*) at individual positions and workloads.

	Position											
Workload	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**1**	**2**
25 W	25.7 ± 5.06	28.5 ± 5.33	29.4 ± 5.03	26.7 ± 4.28	19.3 ± 2.85	12.4 ± 3.77	8.3 ± 3.48	7.5 ± 2.80	11.0 ± 3.91	13.6 ± 4.38	19.0 ± 5.17	22.9 ± 6.22
50 W	44.5 ± 12.5	51.7 ± 14.3	49.9 ± 12.0	42.7 ± 7.45	27.7 ± 6.43	13.5 ± 4.07	11.9 ± 5.42	23.4 ± 7.93	27.7 ± 7.46	24.9 ± 6.46	24.3 ± 3.71	32.5 ± 7.13
100 W	67.0 ± 14.0	86.3 ± 19.6	91.8 ± 19.5	80.8 ± 11.8	52.6 ± 8.02	25.9 ± 10.5	36.9 ± 7.78	60.5 ± 9.97	71.9 ± 8.89	64.4 ± 8.16	47.6 ± 7.64	44.5 ± 9.05

Table 2. Statistical summary table of the effect of workload at individual positions on group (n = 11) vector force.

Position	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**1**	**2**
Workload Main Effect	$F_{(2,18)}$ = 46.17, p = .00	$F_{(2,18)}$ = 34.18, p =.00	$F_{(1.263,11.370)}$ = 91.33, p = .00	$F_{(1.263,11.370)}$ = 248.74, p = .00	$F_{(2,18)}$ = 131.48, p = .00	$F_{(1.170, 10.528)}$ = 11.443, p = .05	$F_{(2,18)}$ = 109.52, p = .00	$F_{(2,18)}$ = 247.18, p = .00	$F_{(2,18)}$ = 87.47, p = .00	$F_{(2,18)}$ = 191.03, p = .00	$F_{(1.23, 11.069)}$ = 102.09, p = .00	$F_{(2,18)}$ = 26.07, p = .00

3.8 LIST OF FIGURES

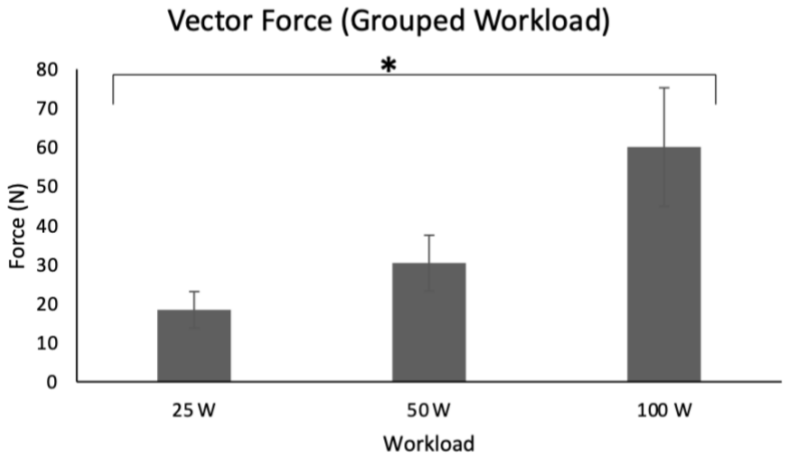

Figure 1 Grouped (n = 11) vector force at 25, 50, and 100 W, collapsed for position.

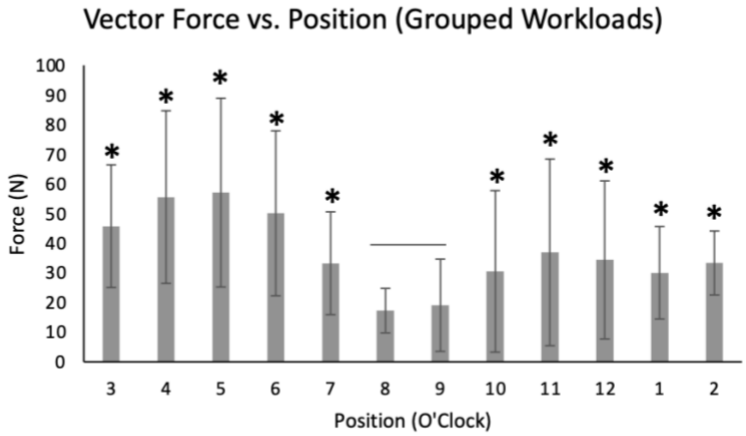

Figure 2 Grouped (n = 11) vector force at twelve clock (elbow) positions, collapsed for workload. * denotes a significant difference from the positions indicated by the bar.

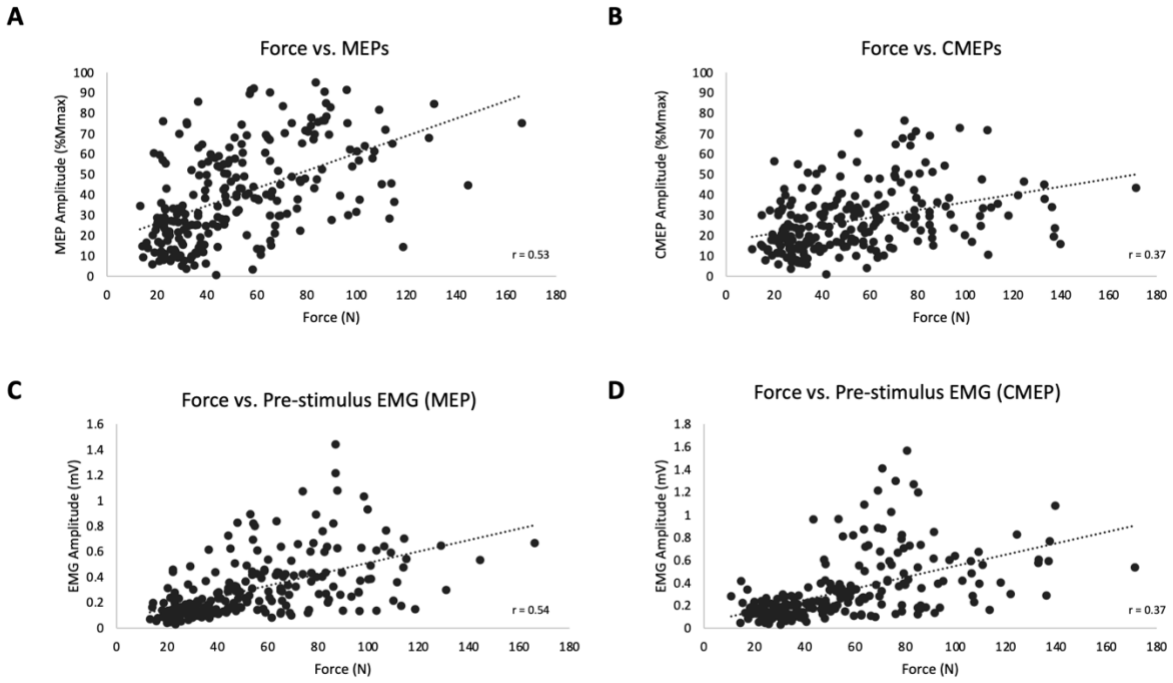

Figure 3 Correlations between grouped vector force (N) (n = 11), MEP, CMEP, and pre-stimulus EMG amplitude (n = 10) from the biceps brachii at 6 o'clock.

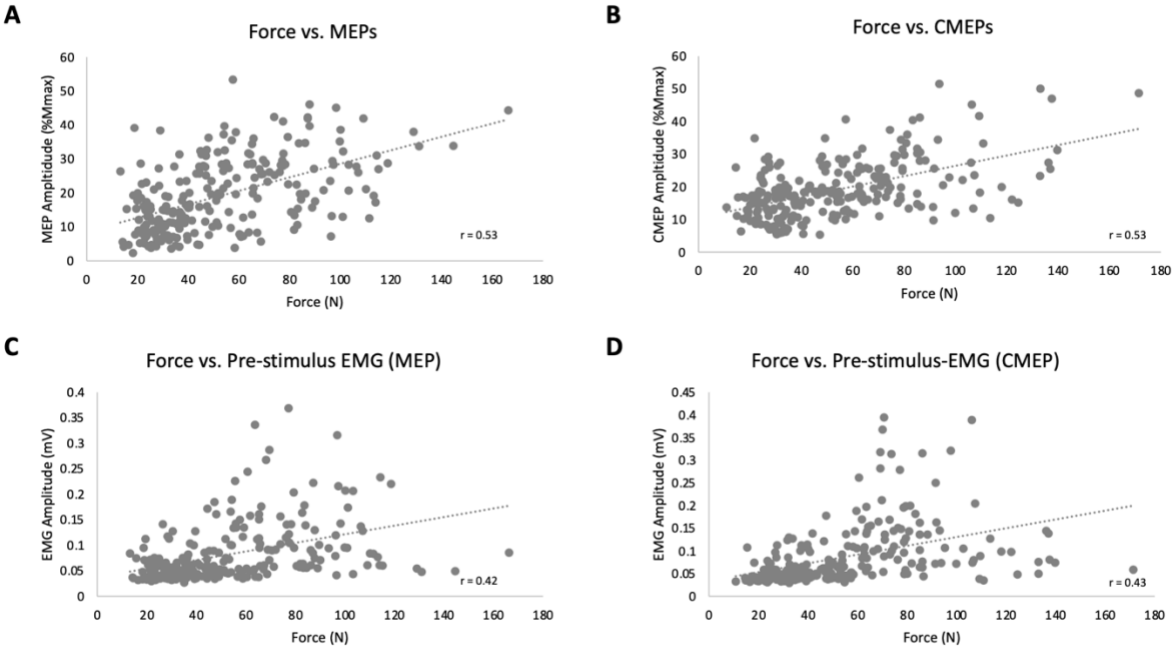

Figure 4 Correlations between grouped vector force (N) (n = 11), MEP, CMEP, and pre-stimulus EMG amplitude (n = 10) from the triceps brachii at 6 o'clock.

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Chapter 4 Summary and Future Directions

This research came to be based on the findings and recommendations of previous work done in the Human Neurophysiology Lab (HNL) at Memorial University of Newfoundland. The goal of the HNL since its inception in 2010 has been to characterize how the central nervous system produces locomotor outputs in humans. As mentioned throughout this thesis, the effect of intensity on corticospinal excitability to the dominant arm biceps and triceps brachii has been shown in work previously done in our lab. During arm cycling, corticospinal excitability to both muscles increases with workload (both relative and absolute). In recent years, research characterizing the muscle activity pattern of the biceps and triceps, amongst four other muscles, across phases of arm cycling at relative workloads ranging from 5% to 50% maximal output was completed. Of these studies, there were two primary conclusions: (1) both corticospinal excitability and muscle activity (EMG) to the biceps and triceps are workload-dependent, with the latter increasing linearly with intensity, and (2) phase-specific differences exist for the biceps brachii, which shows greater activity and excitability during flexion, whereas there were no differences in phase for the triceps brachii.

This thesis consists of the first research done in the HNL measuring both a neural (i.e., corticospinal excitability) and mechanical (i.e., force) outcome during arm cycling. Notably, there were two novel findings surrounding force output during arm cycling that emerged from this work. Firstly, force output during arm cycling increased with workload. Roughly a 50% increase in force was measured from 25 to 50 W, while a 100% increase in force was measured from 50 to 100 W. Secondly, force output was lowest at the 8 and 9 o'clock positions compared to all other positions, and greatest at 4 and 5 o'clock. These positions correspond to the onset of

elbow extension, and mid-flexion, respectively. For the first time, according to current knowledge, phase and intensity specific force output during arm cycling has been characterized.

Measures of corticospinal excitability (e.g., MEPs and CMEPs) were assessed in the present study in the same fashion as discussed above. These measures made it possible to test correlational data between force and corticospinal excitability as well as background EMG to the biceps and triceps brachii during arm cycling, which was also a first for the HNL and to the scientific literature in general. Correlations were moderate, at best, indicating that the mechanical and neural measures included may be linearly related, however the current results were inconclusive. Several important considerations were highlighted regarding the difficulty in obtaining an accurate correlation between variables, with the most prominent considerations being the bilateral nature of locomotor output, and the involvement of various muscles during arm cycling that are often omitted from such studies (including the present work, which was highly exploratory).

Asymmetries in force output between the limbs has been previously recorded during rhythmic and alternating motor outputs, such as leg cycling. On several occasions, it appears as if said asymmetries were intensified at relatively lower intensities. This leads me to bring to attention perhaps one of the most influential factors of this and previous work completed, relative versus absolute intensity. Whereas absolute intensity consists of the same physical workload presented to all subjects, it does not take into account differences in individual's force generating capacity, and therefore creates a task that is not equal in exertion for all participants. In other words, what might be considered an easy intensity of 50 W for one participant may be difficult or unrealistic for another participant. A higher voluntary effort increases excitability of the motoneurone pool, and therefore influences measures of corticospinal excitability. To

maintain consistency and to make reliable conclusions, it therefore would be beneficial to conduct this research and similar studies to follow using relative intensities.

Continuing to investigate biomechanical relationships is a promising direction for developing an understanding of locomotor output production in humans. Future studies should incorporate measures (e.g., force, corticospinal excitability, background EMG) taken from both the dominant and non-dominant limb. Additionally, it is recommended to include the neural outcomes of other muscles along with the biceps and triceps brachii, and in both limbs (which is currently ongoing in the HNL). These modifications to research may enable discoveries relating to bilateral asymmetries that could result in strategies for exercise, sport training, and rehabilitation to reduce potential injuries and impedances in performance caused by asymmetries. Likewise, this line of research may contribute to bettering neurorehabilitation protocols for persons with spinal cord injury or other neurological impairments that result in mobility impairments.

Appendix A: Ethical Approval

MEMORIAL UNIVERSITY

Interdisciplinary Committee on Ethics in Human Research (ICEHR)

St. John's, NL Canada A1C 5S7
Tel: 709 864-2561
icehr@mun.ca

www.mun.ca/research/ethics/humans/icehr

ICEHR Number:	**20190632-HK**
Approval Period:	September 13, 2018 – September 30, 2019
Funding Source:	NSERC (RGCS: 20161819; PI: Power)
Responsible Faculty:	Dr. Kevin Power School of Human Kinetics and Recreation
Title of Project:	*Bilateral force outputs and corticospinal excitability during arm cycling*

September 12, 2018

Miss Fattaneh Farahmand
School of Human Kinetics and Recreation
Memorial University of Newfoundland

Dear Miss Farahmand:

Thank you for your correspondence of September 5, 2018 addressing the issues raised by the Interdisciplinary Committee on Ethics in Human Research (ICEHR) concerning the above-named research project. ICEHR has re-examined the proposal with the clarification and revisions submitted, and is satisfied that the concerns raised by the Committee have been adequately addressed. In accordance with the *Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans (TCPS2)*, the project has been granted *full ethics clearance* to September 30, 2019. ICEHR approval applies to the ethical acceptability of the research, as per Article 6.3 of the *TCPS2*. Researchers are responsible for adherence to any other relevant University policies and/or funded or non-funded agreements that may be associated with the project.

The *TCPS2* **requires** that you submit an Annual Update to ICEHR before September 30, 2019. If you plan to continue the project, you need to request renewal of your ethics clearance and include a brief summary on the progress of your research. When the project no longer involves contact with human participants, is completed and/or terminated, you are required to provide an annual update with a brief final summary and your file will be closed. If you need to make changes during the project which may raise ethical concerns, you must submit an Amendment Request with a description of these changes for the Committee's consideration prior to implementation. If funding is obtained subsequent to

approval, you must submit a Funding and/or Partner Change Request to ICEHR before this clearance can be linked to your award.

All post-approval event forms noted above can be submitted from your Researcher Portal account by clicking the *Applications: Post-Review* link on your Portal homepage. We wish you success with your research.

Yours sincerely,

Kelly Blidook, Ph.D.
Vice-Chair, Interdisciplinary Committee on Ethics in Human Research

KB/lw

cc: Supervisor – Dr. Kevin Power, School of Human Kinetics and Recreation
Director, Research Grant and Contract Services