An in vivo investigation of residual force enhancement in healthy hamstring muscles

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An *In vivo* Investigation of Residual Force Enhancement in Healthy Hamstring Muscles

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A thesis submitted in fulfilment of the award:

Doctor of Philosophy

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Dedication

To my wife, Rebecca, for her unwavering support and belief in me throughout our life together. At least half of this thesis belongs to you. None of this would have been possible without you. To my two beautiful daughters, Edie and Ava. I hope that when you are older, this thesis provides an example of what can be accomplished when you doggedly set your mind to achieving your goal.

"Believe that you can, and you're halfway there" – Theodore Roosevelt

Thesis Declaration

I certify that the work presented in this thesis is, to the best of my knowledge and belief, original, except as acknowledged in the text, and that the material has not been submitted, either in whole or in part, for a degree at this or any other university.

I acknowledge that I have read and understood the University's rules, requirements, procedures, and policy relating to my higher degree research award and to my thesis. I certify that I have complied with the rules, requirements, procedures, and policy of the University (as they may be from time to time).

Neil Chapman

28th Match 2021

Abstract

Background: Hamstring strain injuries are among the most prevalent in sport. Despite significant research interest, there is debate about which muscle training methodology involving eccentric muscular contractions or isometric muscular contractions is most effective and efficient at modifying hamstring strain injury risk factors and rehabilitating from injury. History-dependent contractions, namely post-stretch isometric contractions, incorporate both eccentric and isometric stimuli and have been shown to enhance isometric output, often measured as torque (termed residual force enhancement). This enhanced output is generated with greater efficiency via lower equivalent muscle activation levels. Ultimately, this combination of contraction modes and subsequent effects may provide added benefits in hamstring strain injury prevention programs. However, it is uncertain whether the hamstrings can generate residual force enhancement during post-stretech isometric contractions *in vivo* under various relevant conditions and whether this would be accompanied by actual contractile element lengthening in an eccentric phase. It is also unclear whether residual force enhancement would endure throughout multiple consecutive post-stretch isometric contractions as per a resistance training situation.

Research Aim: The overall aim of this thesis was to determine whether the knee flexors can reliably generate residual force enhancement during highly controlled post-stretch isometric contractions under a range of conditions relevant to hamstring strain injury prevention and rehabilitation training programs.

Methods: Following a broader review of the literature, a series of four focused studies were conducted to achieve the overall thesis aim. The first of these was a systematic review of residual force enhancement for *in vivo* human muscles. The systematic review synthesised the current understanding of residual force enhancement for *in vivo* human muscles using voluntary post-stretch isometric contractions and therefore informed the methodology for the three subsequent experimental studies. The first experimental study investigated the effects of post-stretch isometric contractions in the knee flexors using maximal contractions at long musculotendinous unit lengths. To further develop our understanding of hamstring behaviour during post-stretch isometric contractions, the second experimental study investigated the effects of post-stretch isometriccontractions at both maximal and submaximal intensities and over long and short joint rotations. This study used ultrasonography in the experimental design to directly observe muscle and tendon length changes of the biceps femoris long-head muscle during critical phases of the post-stretch isometric contractions. The third and final experimental study implemented knowledge gained directly from study one and two to investigate the effects of post-stretch isometric contractions during a training simulation. This involved a series of sets of consecutive submaximal post-stretch isometric repetitions. The conclusions drawn from these studies were then analysed and used to inform future research recommendations in the application of post-stretch isometric contractions as a resistance training stimulus with specific implications for hamstring strain injury prevention and rehabilitation programs.

Major Conclusions: The systematic review findings revealed that residual force enhancement of varying magnitude is observable in several muscle/joint arrangements *in vivo*. The thesis experiments showed that residual force enhancement was reliably and consistently generated in the hamstring muscles using maximal and submaximal post-stretch isometric contractions. The residual force enhancement generated was present in the absence of increased muscle activation. Therefore, we theorise that passive structures within the musculotendinous unit likely contributed additional force. This theory is further strengthened

by the direct observation of contractile element lengthening simultaneously with the joint rotation of maximal and submaximal intensity post-stretch isometric contractions of varying amplitude. Importantly, residual force enhancement was observed to consistently endure throughout a series of sets of consecutive submaximal post-stretch isometric contractions. We conclude that post-stretch isometric contractions are likely to be beneficial in resistance training programs where it is desirable to provide a controlled eccentric stimulus, coupled with elevated isometric torque at lower activation levels. Specifically, there are implications for the potential application of post-stretch isometric contractions in hamstring strain injury prevention programs.

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Thank you to the staff of SCU, particularly Associate Professor Mike Climstein, for supporting me with casual academic work over the years. I have significantly benefited from the experience I was able to gain at SCU in the MCEP and BSES degrees. I firmly believe that this experience contributed to me securing my first permanent academic role.

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Finally, and most significantly, thank you to the three most influential people in my life, my beautiful daughters Edie and Ava and my gorgeous wife, Rebecca. Edie and Ava, I hope that this thesis is a testament to the fact that you can achieve what may appear to be the most unachievable goals. Your potential is unlimited.

Bec, it is hard to describe how fortunate I am that we met all those years ago. I cannot express my gratitude that you always believed in me even when I could not believe in myself. You have trusted me and made sacrifices on my behalf. I could not ask for a better wife and best friend and cannot wait for the next chapter together!

List of Publications Included as Part of the Thesis

This thesis includes chapters that have been written based on the following published journal articles and manuscripts currently under review.

1. **Chapman, N**., Whitting, J., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2018). Residual force enhancement in humans: a systematic review. *Journal of Applied Biomechanics, 34*(3), 240-248.

2. **Chapman, N**., Whitting, J. W., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2021). Poststretch Isometric Contractions of the Hamstrings: Just a Brief Stretch to Achieve Supramaximal Isometric Force. *Journal of Applied Biomechanics*, *1*(aop), 1-7.

3. **Chapman, N**., Whitting, J., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2020). Maximal and submaximal isometric torque is elevated immediately following highly controlled active stretches of the hamstrings. *Journal of Electromyography and Kinesiology*, 102500.

   Chapman, N. D., Whitting, J. W., Broadbent, S., Crowley-McHattan, Z. J., & Meir, R. (2021). Residual Force Enhancement Is Present in Consecutive Post-Stretch Isometric Contractions of the Hamstrings during a Training Simulation. *International Journal of Environmental Research and Public Health*, *18*(3), 1154.

Statement of Contribution of Others

The Statements of Contribution signed by co-authors can be found in Appendices A-D.

Chapter 3

Chapman, N., Whitting, J., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2018). Residual force enhancement in humans: a systematic review. *Journal of Applied Biomechanics*, *34*(3), 240-248.

The candidate (NC) participated during all stages of the development of this paper and provided an overall contribution greater than that of any co-author. NC designed the experiments, collected the data, ran the analyses, and wrote the first draft of the manuscript, which was revised with feedback from the co-authors.

Chapter 4

Chapman, N., Whitting, J. W., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2021). Poststretch Isometric Contractions of the Hamstrings: Just a Brief Stretch to Achieve Supramaximal Isometric Force. *Journal of Applied Biomechanics*, *1*(aop), 1-7.

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Chapter 5

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The candidate (NC) participated during all stages of the development of this paper and provided an overall contribution greater than that of any co-author. NC designed the experiments, collected the data, ran the analyses, and wrote the first draft of the manuscript, which was revised with feedback from the co-authors.

Chapter 6

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The candidate (NC) participated during all stages of the development of this paper and provided an overall contribution greater than that of any co-author. NC designed the experiments, collected the data, ran the analyses, and wrote the first draft of the manuscript, which was revised with feedback from the co-authors.

Signed:	Signed:
Neil Daniel Chapman	Dr John Whitting (Principal Supervisor)

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Chapter 1 Background to the Problem

1.1 Introduction

Hamstring strain injuries are among the most prevalent in sport (Bourne et al., 2018; Kenneally-Dabrowski et al., 2019). The majority of hamstring strain injuries take place in the biceps femoris long-head muscle during high-speed running (Askling et al., 2013; Ekstrand et al., 2012; Woods et al., 2004). When a hamstring strain injury is sustained, the athlete's ability to compete and train is impaired, potentially leading to an extended period away from participation and recovery over an extended period (Orchard & Seward, 2013). The financial burden incurred as a direct result of hamstring strain injuries and associated recovery time is profound for both the athlete and their employer (Hickey et al., 2014). As such, primary prevention programs that seek to limit hamstring strain injuries and tertiary rehabilitative programs are of significant interest to athletes and their employers.

High-speed running as a common mechanism for hamstring strain injury is concerning given the role of high-speed running in a wide range of sports (Dorn et al., 2012; Schache et al., 2011; Schache et al., 2014). Investigation of the gait cycle of high-speed running has shown that most hamstring strain injuries occur due to high tensile forces within the musculotendinous unit (Kenneally-Dabrowski et al., 2019). These high tensile forces occur during two phases of the gait cycle; the late swing and early stance phases (Heiderscheit, Sherry, Silder, Chumanov, et al., 2010; Huygaerts et al., 2020). In fact, direct observation of hamstring strain injuries recorded in real-time deduced that the hamstring strain injuries occurred during the late swing phase of the gait cycle (Schache et al., 2010; Schache et al., 2009). For this reason, this thesis will make the late swing phase of the gait cycle of high-speed running the primary focus when discussing hamstring strain injuries incurred during high-speed running actions.

Much of the current understanding of the dynamic function of the hamstrings is limited to kinematic and kinetic analysis (Chumanov et al., 2011; Higashihara et al., 2016; Higashihara et al., 2015; Nagano et al., 2014; Schache et al., 2013; Simonsen et al., 1985; Thelen et al., 2005), computational modelling (Kenneally-Dabrowski et al., 2019), evidence from other lower limb muscles (Brockett et al., 2001, 2004; Lai et al., 2014), and in animal studies (Gillis et al., 2005). As a result, a singular theory of hamstring muscle function is yet to be proposed. As a consequence, two main theories exist within the literature to explain the contractile element behaviour of biceps femoris long head during the late swing phase of high-speed running. These are (i) an eccentric behaviour (Chumanov et al., 2007, 2011; Schache et al., 2012; Schache et al., 2013; Yu et al., 2008) and (ii) an isometric behaviour (Van Hooren & Bosch, 2017a). These two main theories give rise to opposing views on the best approach to injury prevention programs.

The first theory states that the likelihood of injury increases during active lengthening of biceps femoris long head during the late swing phase of the gait cycle due to a lack of eccentric strength and insufficient fascicle length (Bohm et al., 2018). An eccentric contraction bias, such as that produced during the Nordic Hamstring Exercise, has been recommended in injury prevention programs (Bourne et al., 2017; van der Horst et al., 2015). Current evidence suggests that hamstring strain injury prevention programs that increase eccentric hamstring strength and increase fascicle length (Bourne et al., 2017; Timmins, et al., 2016), particularly biceps femoris long head, result in a reduction in hamstring strain injury risk (Petersen et al., 2011; van der Horst et al., 2015; van Dyk et al., 2018). This evidence-based hamstring strain injury prevention recommendation of Bourne et al. (2018) is popularly known as the ‘quadrant of doom.’

The alternative theory postulates that the contractile element maintains a quasi-isometric behaviour during the late swing phase. A lack of isometric strength results in a forced eccentric contraction that is causative of injury to biceps femoris long head (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). The use of high-intensity isometric contractions such as the Single-leg Roman Chair Hold has been proposed for use in hamstring strain injury prevention programs (Macdonald et al., 2019). Presently, in comparison to the active lengthening theory of hamstring running mechanics, there is a paucity of high quality objective evidence to support the isometric strength hypothesis; however, this may be due to the relative recency of such assertions by some researchers (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018).

It is of significance to note that regardless of an eccentric or isometric bias to hamstring strain injury prevention programs, both theories share common evidenced-based goals; to increase strength (be it eccentric or isometric) (Croisier et al., 2002; Maniar et al., 2016; Silder et al., 2010; Sole et al., 2011; Van Hooren & Boscha, 2017; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018), and increase fascicle length of biceps femoris long head (Timmins, Bourne et al., 2016). To this end, it has been shown that eccentrically biased training at supra-maximal intensity is effective at improving eccentric strength, increasing fascicle length, and inducing a rightward shift in the joint angle of peak torque on the length-tension relationship (Brockett et al., 2001; Mjolsnes et al., 2004; Potier et al., 2009; Timmins, Ruddy, et al., 2016). Similarly, it is known that training with an isometric focus, particularly at long musculotendinous unit lengths is effective at improving eccentric and isometric strength, increasing fascicle length, and broadening the joint angles near the plateau of the angle of peak torque on the length-tension relationship (Herzog et al., 2015; Oranchuk et al., 2019). Nonetheless, hamstring strain injury rates have not decreased in recent years, the reasons are currently unclear and it is possible in part that the lack of engagement with current eccentrically biased injury prevention programs is a contributing factor (van der Horst et al., 2020). Notwithstanding a lack of engagement, the current injury rate is suggestive that current injury prevention programs are in need of further investigation and innovation (Orchard & Best, 2002; Orchard et al., 2013). While it is acknowledged that hamstring strain injuries are multifactorial, increasing the resilience of the hamstring muscles remains at the core of hamstring strain injury prevention programs, and as such, investigation of other novel recommendations is warranted to further develop and advance injury prevention and rehabilitation practices.

One such novel and theoretical innovation is the use of post-stretch isometric contractions. The post-stretch isometric contraction combines an active lengthening contraction immediately followed by an isometric contraction. The post-stretch isometric contraction results in a sharp increase in force during the active stretch, which reaches a steady-state during the consequent isometric phase (Abbott & Aubert, 1952). The isometric steady-state force after active lengthening is significantly greater when compared with levels of force in isometric contractions without prior stretch and is commonly termed residual force enhancement (Abbott & Aubert, 1952). The magnitude of residual force enhancement in the isometric steady-state has been observed at levels of 10-400%. The phenomenon of residual force enhancement and its functional relevance is yet to be fully understood (Seiberl et al., 2015). Apparent similarities in reasoning for each of the eccentric only and isometric only approaches to training for hamstring strain injury prevention and rehabilitation make it reasonable to suggest that a combined approach might be appropriate. The likelihood that the hamstrings function dynamically, utilising a combination of both eccentric and isometric actions during key gait phases in high-speed running, means that compared with a conventional approach, the use of chronic post-stretch isometric contractions in hamstring strain injury prevention and rehabilitation programs could result in greater resilience of the biceps femoris long head. However, before implementing post-stretch isometric contractions in hamstring strain injury prevention or rehabilitation programs, further investigation of the phenomenon of residual force enhancement in the hamstrings must be undertaken.

Therefore, a series of studies were planned to i) identify the current understanding of residual force enhancement of *in vivo* human muscle; ii) confirm the capacity of the hamstring to produce residual force enhancement using maximal and submaximal post-stretch isometric contractions at varying joint positions iii) confirm contractile element lengthening (and hence eccentric contraction) of the biceps femoris long head during post-stretch isometric contractions; and finally, iv) to confirm the capacity for the hamstring to develop residual force enhancement using multiple and consecutive repetitions and sets of post-stretch isometric contractions.

1.2 Thesis aim

The overall aim of this thesis was to determine whether hamstring muscles can reliably generate residual force enhancement during highly controlled post-stretch isometric contractions under a range of conditions relevant to hamstring strain injury prevention and rehabilitation training programs. A series of published studies, presented in three parts, was undertaken to achieve this overall aim. An overview of these studies and their contribution to the overall thesis aim is outlined below.

i) Part I of the thesis sought to clarify the current understanding of residual force enhancement of *in vivo* human skeletal muscle. Specifically, to identify the effect of the following variables on resitual force enhancement magnitude; i) contraction intensity, ii) amplitude of joint excursion during the stretch, iii) angular velocity during the stretch, and iv) joint position of the final isometric contraction. These aims were achieved via a systematic review of the literature (Chapter 3). The systematic review results provided direction for developing the resultant experimental studies 1, 2, and 3, which are presented in Part II (Chapters 4 and 5) and Part III (Chapter 6).

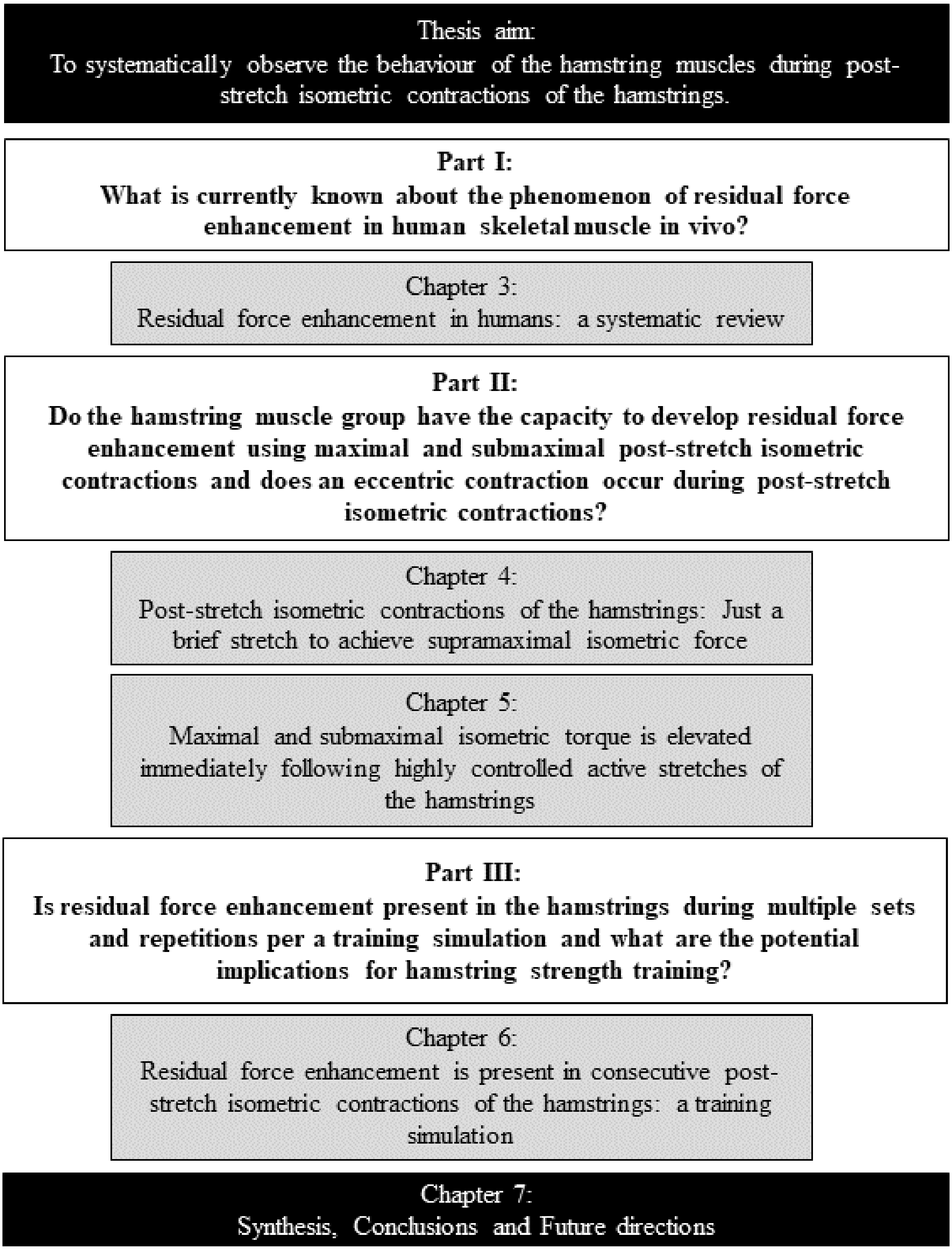
ii) Part II involved completing two experimental studies focused on the observation of the neuromuscular behaviour of the knee flexors during single post-stretch isometric contractions. The first experimental study (Chapter 4) sought to confirm that the knee flexors could exhibit residual force enhancement using post-stretch isometric contractions of maximal intensity ending at joint angles indicative of action on the descending limb of the length-tension relationship. Muscle activation of biceps femoris long head was simultaneously observed to determine the likelihood that additional motor unit recruitment was present to contribute to enhanced isometric steady-state torque. The first experimental study methodology was developed in consideration of the findings of the systematic review to optimise the likelihood that residual force enhancement would be observed. Findings from the first experimental study informed the second experimental study (Chapter 5). The second experimental study (Chapter 5) sought to extend our understanding of residual force enhancement in the knee flexors *in vivo* by; i) simultaneously observing torque output and muscle activation of the medial and lateral hamstring muscles during post-stretch isometric contractions of maximal and submaximal intensities and with different stretch amplitudes (long stretch and short stretch); and ii) to observe and measure, via ultrasound, dynamic positional change of the distal and proximal musculotendinous junctions of biceps femoris long head during post-stretch isometric contractions in each of the intensity and stretch amplitude conditions. The second experimental study's findings (Chapter 5) were then used to design the methodology for the final experimental study presented in Part III (Chapter 6).

iii) Part III of the thesis outlines the final experimental study (Chapter 6), which aimed to observe the knee flexors' neuromechanical behaviour following a series of repeated and consecutive submaximal post-stretch isometric contractions using joint positions that replicate standard knee flexor strength training methods, in the form of a training simulation. The final experimental study (Chapter 6) was designed and implemented as the culmination of knowledge gained via the systematic review (Chapter 3) and experimental studies 1 and 2 (Chapters 4 and 5). The results of the systematic review and experimental studies described above provide strong evidence upon which to develop recommendations for a novel training modality using post-stretch isometric contractions (Chapter 7). The use of post-stretch isometric contractions in the hamstrings has two potential applications; i) for use in hamstring strain injury prevention programs to increase hamstring resilience to injury, and ii) for use in rehabilitation programs to efficiently restore hamstring function following injury.

A general outline of each study and how these studies have contributed to the thesis's overall aim are presented in Figure 1. The specific hypotheses for each study are provided in the relevant chapters.

1.3 Significance of the Thesis

The prevention of hamstring strain injuries is of great importance to athletes and their organisations, as is effective and efficient rehabilitation once a hamstring strain injury has been sustained. The current practices used in hamstring strain injury prevention and rehabilitation programs are yet to influence hamstring strain injury incidence and recurrence rates effectively (Ekstrand et al., 2016; Raya-González et al., 2020). As such, there is a need to investigate other novel interventions that can reduce hamstring strain injury risk and where an injury has been incurred, rebuild function and resilience of the hamstring muscle group. Grounded in current knowledge of eccentric and isometric training modalities currently used in hamstring strain injury prevention and rehabilitation programs, an alternative contraction mode is proposed in this thesis. Via a series of progressive studies, this thesis provides the first insight into post-stretch isometric contractions and resultant residual force enhancement in the knee flexors. Based on this evidence, this thesis culminates in the provision of recommendations for future investigation into the use of post-stretch isometric contractions as a supplemental or adjunct contraction modality in hamstring strain injury prevention and rehabilitation programs with the potential to reduce hamstring strain injury prevalence and recurrence.



Thesis aim:
To systematically observe the behaviour of the hamstring muscles during post-stretch isometric contractions of the hamstrings.

Part I:
What is currently known about the phenomenon of residual force enhancement in human skeletal muscle in vivo?

Chapter 3:
Residual force enhancement in humans: a systematic review

Part II:
Do the hamstring muscle group have the capacity to develop residual force enhancement using maximal and submaximal post-stretch isometric contractions and does an eccentric contraction occur during post-stretch isometric contractions?

Chapter 4:
Post-stretch isometric contractions of the hamstrings: Just a brief stretch to achieve supramaximal isometric force

Chapter 5:
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Part III:
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Figure 2 *Schematic representation of the aim of the thesis and how the flow of studies systematically contributed to developing greater understanding of the phenomenon of residual force enhancement and its potential application to hamstring strain injury prevention and rehabilitation programs.*

Chapter 2 Literature Review

2.1 Introduction

Optimal hamstring function is an essential factor in an athlete's ability to perform in sports that required periods of high-speed running (Dorn et al., 2012; Schache et al., 2011; Schache et al., 2014). As such, an injury to the hamstring impedes the individual's ability to perform to their full capacity (Hagglund et al., 2013; Hickey et al., 2014). Hamstring strain injuries are among the most prevalent in sport, particularly in elite football codes such as Football (Soccer), Rugby Union, and Australian Rules Football (Kenneally-Dabrowski et al., 2019). Within Australian Rules Football, hamstring strain injury is the most common injury incurred, resulting in a protracted recovery before return to play (Orchard & Seward, 2013). These injuries also have a high injury recurrence (Orchard & Seward, 2013). The high hamstring strain injury rate and subsequent time spent away from competition lead to an excessive financial burden for athletes and their employers (Hickey et al., 2014).

In European Football, the first team player's financial cost of being injured for one month has been estimated to be ~$718,686AUD (Ekstrand, 2013). Using this figure and data from the Union of European Football Associations injury study, it can be estimated that an average hamstring strain injury of 14 days duration may cost approximately ~$359,409AUD (Ekstrand, Hagglund, & Walden, 2011). Accordingly, much emphasis has been placed on developing a deeper understanding of hamstring strain injury, and on identifying effective hamstring strain injury prevention techniques. Despite such interest, hamstring strain injury incidence continues to increase annually within football (Ekstrand et al., 2016), athletics (Opar, Drezner, et al., 2014), and cricket (Orchard et al., 2017). The investigation into alternative hamstring strain injury prevention and rehabilitation approaches is warranted in an effort to positively address the elevated hamstring strain injury incidence and recurrence rate (Orchard & Best, 2002; Orchard et al., 2013).

2.1.1 Hamstring strain injury mechanisms

Injury mechanisms for hamstring strain injury attract great research interest. However, there is a lack of consensus regarding hamstring strain injury mechanisms (Askling et al., 2011; Freeman et al., 2021; Huygaerts et al., 2020; Kenneally-Dabrowski et al., 2019). It has been suggested that two hamstring strain injury types are defined by injury mechanism: i) stretch-type and ii) sprint-type (Askling et al., 2011; Huygaerts et al., 2020). Stretch-type injuries occur during movements such as kicking and dancing, where hip flexion and knee extension combine to place the musculotendinous unit under considerable stretch (Huygaerts et al., 2020). In consideration of stretch-type injuries, hamstring strain injury prevention research was initially focused on flexibility as a modifiable risk factor to reduce stretch-type hamstring strain injury (van Dyk et al., 2018). However, flexibility is now accepted as a weak risk factor for hamstring strain injury (Green et al., 2020a; van Dyk et al., 2018).

The second hamstring strain injury mechanism, sprint-type injuries, often referred to as high-speed running injuries are one of the most common hamstring strain injury mechanisms in sports, including track and field (Bennell & Crossley, 1996) and football codes: American football (Feeley et al., 2008), Football (Ekstrand et al., 2011), Rugby Union (Brooks et al., 2006) and Australian Rules Football (Orchard et al., 2013). High-speed running injuries occur at or nearing maximal running velocity where high levels of tensile force are placed through the bi-articular hamstrings, at the proximal and distal musculotendinous junctions (Heiderscheit et al., 2010; Huygaerts et al., 2020). Elevated levels of tensile force generated during high-speed running result in injury to the biceps femoris long-head in 94% of instances (Askling et al., 2013; Ekstrand et al., 2012; Woods et al., 2004). Furthermore, injuries to the biceps femoris long head demonstrate significantly more involvement of the proximal region of the muscle and of the proximal musculotendinous junction compared with the distal portion of biceps femoris long head (Askling et al., 2007; Silder et al., 2010). Hence, much hamstring strain injury prevention research has focussed on the vulnerable biceps femoris long head musculotendon complex (Kenneally-Dabrowski et al., 2019) and increasingly also focused on the influence that high-speed running has on hamstring strain injury (Duhig et al., 2016).

2.1.2 The function of the hamstrings during high-speed running

In the context of hamstring strain injury, the gait cycle during high-speed running involves two main phases: the stance phase (where the foot is in contact with the ground) and the swing phase (where the foot is not in contact with the ground) (Huygaerts et al., 2020; Kenneally-Dabrowski et al., 2019). Each phase can then be broken down into early stance, late stance, early and mid-swing, and late swing (Huygaerts et al., 2020; Kenneally-Dabrowski et al., 2019). Debate exists over the hamstrings' contractile element behaviour (specifically biceps femoris long head) during the late swing phase of the gait cycle where the biceps femoris long head is proposed to be most vulnerable to injury (Kenneally-Dabrowski et al., 2019). In support of this proposal, in instances where hamstring strain injury has been captured in real-time, the moment of injury was deemed to have occurred during the late swing phase (Heiderscheit et al., 2005; Schache et al., 2010; Schache et al., 2009). As such, the focus hereafter will be on the late swing phase of the gait cycle of high-speed running.

Ongoing debate continues over the behaviour of biceps femoris long head during the gait cycle in high-speed running as, currently, no definitive explanation exists. Presently, the *in* *vivo* behaviour of the contractile element and series elastic element of biceps femoris long head is unable to be directly observed during high-speed running. Notwithstanding this, much of our current understanding of the dynamic behaviour of the hamstrings is based on kinematic and kinetic analysis, which measures the change in distance between the osteotendinous attachment points of the hamstrings (Chumanov et al., 2011; Higashihara et al., 2016; Higashihara et al., 2015; Nagano et al., 2014; Schache et al., 2013; Simonsen et al., 1985; Thelen et al., 2005), animal research (Gillis & Biewener, 2001, 2002; Gillis et al., 2005; Gregersen et al., 1998) and computational modelling (Chumanov et al., 2007; Fiorentino & Blemker, 2014; Fiorentino et al., 2014; Thelen et al., 2005). Notwithstanding current methodological limitations, two popular theories exist regarding the type of muscle action that dominates during the late swing phase of the gait cycle during high-speed running; i) an eccentric muscle action (Chumanov et al., 2007, 2011; Schache et al., 2012; Schache et al., 2013; Yu et al., 2008); and more recently ii) an isometric muscle action (Van Hooren & Bosch, 2017a).

The first theory based on kinematic and kinetic analysis as well as computational modelling suggests that the hamstrings are active during the mid to late swing phase of the gait cycle with peak musculotendinous unit stretch increasing with increasing running velocity until 80% of maximal velocity where stretch remains constant (Chumanov et al., 2007, 2011; Schache et al., 2012; Schache et al., 2013; Yu et al., 2008). Peak eccentric muscle forces occur during the late swing phase of running at approximately 85% of the gait cycle irrespective of running velocity in semimembranosus, followed by biceps femoris long head and semitendinosus , respectively (Chumanov et al., 2007, 2011; Schache et al., 2012; Thelen et al., 2005).

Based on animal research (Gillis & Biewener, 2001, 2002; Gillis et al., 2005; Gregersen et al., 1998) and computational modelling (Chumanov et al., 2007; Fiorentino & Blemker, 2014; Fiorentino et al., 2014; Thelen et al., 2005), the second theory posits that during high-speed running, the contractile element of the hamstrings passively lengthens during the initial swing phase. However, when muscle activity and forces are higher during the late swing phase, the contractile element remains chiefly isometric (Van Hooren & Bosch, 2017a). Van Hooren and Bosch (2017a) propose that their theory suggests a discrepancy between hamstring function and current injury prevention practices that focus on eccentric exercise. They posit that the hamstrings should be trained while the contractile element maintains an isometric action (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). Furthermore, Van Hooren and Bosch (2017a) state that the incongruity between their proposed model of muscle action and current injury prevention and rehabilitation practices that focus on an eccentric training stimulus, may in part, explain why hamstring strain injury incidence has remained elevated. However, the validity of the theories proposed by Van Hooren and Bosch (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018) have been questioned as their proposal is grounded in evidence from other lower limb muscles (Bohm et al., 2018; Lai et al., 2014), and in animal studies (Gillis et al., 2005), with a lack of direct experimental evidence to support their theories for hamstring training. It seems clear that hamstring strain injury prevention training recommendations, while based on reasonable theories, are not yet fully informed by directly observed evidence. Until direct observation of dynamic musculotendinous unit functioning is made and hamstring behaviour during high-speed running is confirmed, these opposing views will influence injury prevention recommendations.

2.1.3 Risk factors for hamstring strain injury

Risk factors in hamstring strain injury are classified as either extrinsic or intrinsic and non-modifiable or modifiable (Pizzari et al., 2020). Of the known risk factors, hamstring strain injury prevention and rehabilitation programs primarily focus on intrinsic, modifiable risk factors that can be influenced by training, such as eccentric and isometric hamstring strength and muscle fascicle length (Pizzari et al., 2020). While it is acknowledged that hamstring strain injury is multifactorial (Bittencourt et al., 2016; Mendiguchia et al., 2012), this literature review will discuss eccentric and isometric hamstring strength and fascicle length, which are evidenced to be related to the capacity of the hamstring muscle to withstand the rigours of high-speed running and the associated hamstring strain injury risk (Buchheit et al., 2019).

Of the available evidence, the so-called ‘quadrant of doom,’ (figure 2) which asserts that athletes with low eccentric hamstring strength and short fascicle length increase their hamstring strain injury risk substantially (Bourne et al., 2018), has seen notoriety. Consequently, the research of Bourne et al. (2018) has contributed to the focus on hamstring muscle training with an eccentric bias such as the Nordic hamstring exercise and Flywheel training, which seek to address the ‘quadrant of doom’ risk factors (Arnason et al., 2008; Askling et al., 2003; Engebretsen et al., 2008; Gabbe, Branson, et al., 2006; Petersen et al., 2011; Seagrave III et al., 2014; van der Horst et al., 2015).

Despite a differing view of the contractile element's behaviour during high-speed running, Van Hooren and Bosch (2018) concur that an eccentric action of the hamstrings may be causative to injury. However, they suggest that a lack of isometric hamstring strength during the late swing phase of the gait cycle when muscle forces are too great to maintain an isometric muscle action, may result in a 'forced eccentric action' which promotes hamstring strain injury (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). As a result, they suggest that a lack of isometric hamstring strength may increase hamstring strain injury risk (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018).

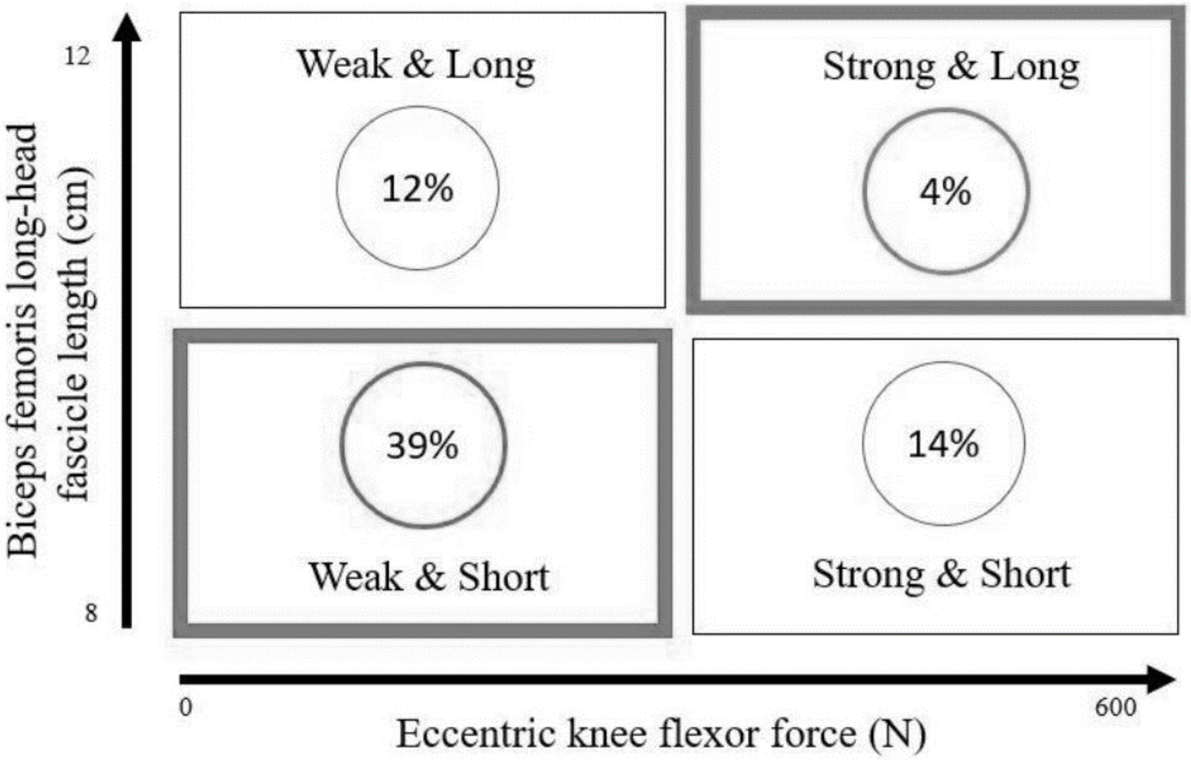


Figure 2 *The quadrant of doom depicts the risk of sustaining a hamstring strain injury as a percentage dependent upon an individual's eccentric knee flexor strength and fascicle length of biceps femoris long-head. The greater the percentage (lower left quadrant) the greater the risk of sustaining a hamstring strain injury. Adapted from Bourne et al. (2017).*

Given, and perhaps in spite of, the methodological limitations to research that to date has attempted to define muscle behaviour during the late swing phase, it is worthwhile continuing to investigate risk factors and training protocols that combine differing, but potentially congruent theories for hamstring training in hamstring strain injury prevention and rehabilitation. Namely, eccentric hamstring strength training as suggested by Bourne et al. (2018), and isometric strength training at long muscle lengths as proposed by Van Hooren and Bosch (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). In this way, until the hamstring muscles' behavior during high-speed running is confirmed, athletes may benefit by building hamstrings that have a more multifactorial resilience, particularly in terms of both eccentric and isometric strength.

2.1.3.1 Hamstring Strength as a risk factor

Low muscle strength levels have been implicated in increased hamstring strain injury occurrence (Bourne et al., 2017). Therefore, it is not surprising that the body of evidence investigating hamstring strength as a risk factor for hamstring strain injury is extensive. Previous studies have assessed hamstring strength using a range of methods, in multiple lower-limb muscles, using multiple contraction modes and angular velocities, in a range of positions, and in varying athletic populations (Freckleton et al., 2014; Freckleton & Pizzari, 2013; Green et al., 2018; Opar, Drezner, et al., 2014; Opar, Williams, et al., 2014; Opar et al., 2012; Opar et al., 2015). A lack of eccentric hamstring strength has been identified as an area of concern regarding hamstring strain injury risk owing to the proposed eccentric behaviour of the hamstring during the late swing phase of high-speed running (Croisier et al., 2002; Maniar et al., 2016; Silder et al., 2010; Sole et al., 2011). Levels of absolute and relative eccentric hamstring weakness at an angular velocity of $60^{o}.s^{-1}$ have been associated with a small predictive effect on hamstring strain injury risk (Green et al., 2018). To specifically develop hamstring strength, the use of the Nordic hamstring exercise has been investigated in two novel studies that demonstrated low levels of pre-season eccentric hamstring strength increased hamstring strain inuury risk in Australian Rules Football players (Opar et al., 2015) and Footballers (soccer) (Timmins, Bourne, et al., 2016). However, a lack of consistent association between eccentric hamstring strength and hamstring strain injury risk between different athletes and different sports suggests that eccentric hamstring strength may be specific to the athlete or sport itself (Bahr & Holme, 2003; Meeuwisse et al., 2007). Considering the uncertainty over the contractile element's behaviour during high-speed running, further investigation of the role of isometric and eccentric hamstring strength as a hamstring strain injury risk factor is warranted.

There is currently a paucity of evidence to support Van Hooren and Bosch's (2017b) assertions that isometric strength is a risk factor for hamstring strain injury. However, this may be due to the relative recency of their theory. Their theory states that an isometric muscle fascicle behaviour occurs during the late swing phase of high-speed running, and injury occurs when an extrinsic force overcomes the intrinsic tensile force required to maintain the isometric behaviour. This then leads to a forced eccentric muscle action (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018).

In a series of commentaries, Van Hooren and Bosch (2017a, 2017b, 2018) suggest that the use of high-intensity isometric strength training may be prophylactic towards hamstring strain injury. In support of this theory, the performance of isometric strength training at long muscle lengths is known to increase isometric strength (Oranchuk et al., 2019), increase peak eccentric torque (Hinks et al., 2021), broaden the range of joint angles corresponding to the plateau of the length-tension curve (Hinks et al., 2021) and increase muscle thickness and fascicle length (Oranchuk et al., 2019). On reflection of the assertions of Bourne et al. (2018), that an increase in eccentric strength and increase in fascicle length reduces hamstring strain injury risk (as per the ‘quadrant of doom’), there appears to be a congruence between the desired outcomes following the use of eccentric biased training and high-intensity isometric biased training at long muscle lengths. Although currently untested, the potential that isometric training at long muscle lengths influences hamstring strain injury risk reduction is an intriguing prospect.

2.1.3.2 Muscle fascicle length as a risk factor

Professional football (soccer) players with shorter biceps femoris long head fascicles were shown to be 4.1 times more likely to sustain a future hamstring strain injury than those with longer fascicles (Timmins, Bourne, et al., 2016). Moreover, in the same study, for every 1 cm increase in fascicle length, hamstring strain injury injury risk was decreased by ~21% (Timmins, Bourne, et al., 2016). The mechanisms contributing to the increased risk that shorter fascicles pose to hamstring strain injury remain elusive. One theory has suggested that shorter fascicles, comprising fewer sarcomeres in series, are more susceptible to damage via sarcomere ‘popping’ during active lengthening, particularly on the descending limb of the length-tension relationship (Morgan, 1990, 1994). According to this theory, sarcomere length non-uniformities occur due to the instability of sarcomeres on the length-tension relationship's descending limb. This instability is said to cause much of the stretch to occur in sarcomeres that are initially longer and weaker, rather than in sarcomeres initially shorter and more robust and therefore able to maintain a constant length (Johnston et al., 2016; Morgan, 1990, 1994). This is then proposed to cause the long and weak sarcomeres to be stretched to lengths beyond the region of actin-myosin filament overlap. Such a stretch would theoretically cause sarcomere ‘popping,’ where the force generated is said to originate from passive structural elements of muscle exclusively, such as titin (Johnston et al., 2016).

However, the sarcomere instability theory has been questioned by researchers and is not universally accepted. This is partly due to a series of investigations by Schappacher-Tilp (2018), who investigated sarcomere behaviour during lengthening contractions on the descending limb of the length-tension relationship. Further, several studies have failed to observe an increase in sarcomere length non-uniformity upon active stretch (Edman et al., 1982; Johnston et al., 2016) and have failed to observe the so-called ‘sarcomere popping’ events (Joumaa et al., 2008; Pavlov et al., 2009; Pun et al., 2010; Rassier et al., 2003; Telley et al., 2006). In addition, there is evidence suggesting that sarcomeres are more stable following active stretch (Johnston et al., 2019). Johnston et al. (2019) suggest that titin is activated during a contraction, thereby providing additional structural rigidity within and between sarcomeres in a myofibril either to increase titin stiffness or to shorten its free-spring length by binding titin to other parts of the sarcomere (Forcinito et al., 1998; Herzog, 2018; Herzog et al., 2015; Noble, 1992; Rode et al., 2009). What remains unclear is whether the activation of titin provides any protective effect from muscle damage.

Regarding muscle injury potential, it is theorised that any increase to the number of sarcomeres in a series within a fascicle will result in greater fascicle length and a reduction in the magnitude of stretch per sarcomere during an eccentric muscle action (Bourne et al., 2018). An increase in fascicle length is known to cause a rightward shift in the length-tension relationship and create greater strength on the descending limb (Lieber & Ward, 2011). As such, longer, stronger hamstring muscles are thought to be more resilient to high tensile forces at long musculotendinous unit lengths, such as those seen in the late swing phase of high-speed running (Pizzari et al., 2020). Supporting this, strong evidence exists that fascicle lengths may be increased via training that uses eccentric contractions (Potier et al., 2009; Timmins, Bourne, et al., 2016). There is also evidence showing that increases in fascicle length can result from training protocols that incorporate concentric (Blazevich et al., 2007; Franchi et al., 2014) and isometric contractions (Hinks et al., 2021; Noorkoiv et al., 2014; Oranchuk et al., 2019). Based on this evidence, both isometric and eccentric strength training can increase fascicle length, thereby potentially contributing to hamstring strain injury prevention. Therefore, the investigation of isometric and eccentric training, which seeks to address the hamstring strain injury risk factor of short fascicle length, is warranted.

2.1.4 Hamstring strain injury prevention training

The importance of hamstring strain injury prevention is well stated within the literature (van der Horst et al., 2020). It has been established that previous hamstring strain injury is the strongest predictor of future hamstring straini injury (Green et al., 2020). Thus, implementing an evidence-based, well-structured hamstring strain injury prevention program can help an athlete avoid initial injury and, therefore, the injury-reinjury cycle (van der Horst et al., 2020). Petersen et al. (2011) has identified three approaches to hamstring strain injury prevention. There are: i) primary prevention, which is focused on reducing exposure to factors that cause injury, altering practices that increase hamstring strain injury and increasing resistance to injury during exposures, ii) secondary prevention, which seeks to reduce the impact of an hamstring strain injury which has already occurred, including increasing resilience of hamstrings to injury and reinjury and iii) tertiary prevention which aims to minimise the impact of an ongoing injury with ongoing effects such as in hamstring strain injury rehabilitation where conservative treatment of the injury and primary prevention techniques have been unsuccessful.

Irrespective of whether training is for primary, secondary, or tertiary hamstring strain injury prevention or rehabilitation purposes as stated above, differing but potentially both valid views exist as to what types of muscle contractions should be incorporated in training. Although it is posited above (see section 2.3.1) that training combines eccentric and isometric contractions that may be beneficial in these injury prevention scenarios, the fact remains that two schools of thought have proliferated regarding training with either an eccentric focus or an isometric focus. The following two subsections will explore hamstring strain injury training in each of these paradigms.

2.1.4.1 Eccentric Contractions in Hamstring Strain Injury Prevention and Rehabilitation Training

The justification for and the efficacy of eccentric contractions in hamstring strain injury prevention and rehabilitation programs has generated significant research interest. With appropriate adherence levels, exercise programs that use eccentric training stimulus have been shown to reduce hamstring strain injury risk (Goode et al., 2015; Van Dyk et al., 2019). Two common examples of eccentric training exercises include flywheel training and the Nordic hamstring exercise (van der Horst et al., 2020) (figure 3). Flywheel training involves using a flywheel device that requires the athlete to initiate a concentric action to accelerate the flywheel. Once the flywheel is ‘primed,’ eccentric actions are required to decelerate the flywheel movement. The performance of active deceleration throughout a shorter range of motion initiates a period of eccentric overload (Berg & Tesch, 1994). The Nordic hamstring exercise is possibly the most well-known eccentric hamstring training exercise. This exercise is typically performed with a partner assisting the athlete performing the exercise who assumes a kneeling position while maintaining a neutral hip position and rigid trunk. The partner secures the athlete’s feet to the ground by applying pressure to the lower legs, as a form of anchor, for the duration of the exercise. The athlete then lowers their trunk towards the ground as slowly as possible, maximising the hamstring muscles' loading during the descent. The athlete uses their hands and arms to catch their descent prior to reaching the ground. Upon making contact with the ground the athlete uses a push-up action to return to the starting position which, minimises contraction of the hamstrings (concentrically) to reset the movement (Mjolsnes et al., 2004; Seagrave III et al., 2014).

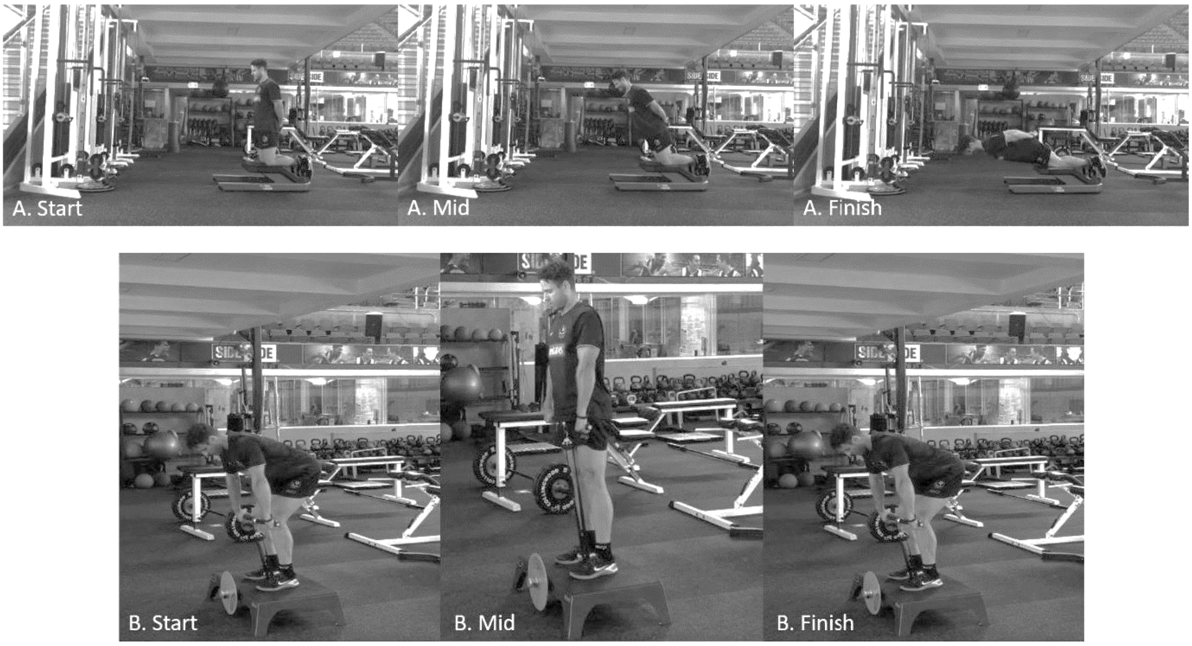


Figure 3 *The starting, midpoint and finishing point of the Nordic hamstring exercise (A) and flywheel Romanian deadlift (B). (Timmings et al,. 2021) Figure used with permission.*

The underlying motivation for using eccentrically biased exercises such as those described above, particularly during the primary prevention phase, is to mitigate the effects of modifiable hamstring strain injury risk factors (see section 2.3.1) (Petersen et al., 2011). These are namely, a lack of eccentric strength, and lack of strength on the length-tension relationship's descending limb. The effects of hamstring strain injury risk reduction appear to be more significant when the eccentric training is undertaken at long musculotendinous unit lengths (Askling et al., 2014; Askling et al., 2013).

Notwithstanding positive results for eccentric training efficacy in hamstring strain injury prevention, poor adherence to such training is seen as an issue due to perceptions of increased post-exercise muscle pain (Bahr et al., 2015; van der Horst et al., 2020). Where adherence to eccentric training has been low, the prophylactic effect has been negatively impacted (Engebretsen et al., 2008; Gabbe, Branson, et al., 2006). Despite reducing in the short to medium term (Goode et al., 2015), hamstring strain injury rates have not declined during the past decade in football and AFL (Brooks et al., 2005; Ekstrand et al., 2016; Opar et al., 2014; Orchard & Seward, 2002). This data confirms that the use of eccentric exercises in hamstring strain injury prevention training, while effective, has yet to positively influence the hamstring strain injury rate in sport. As such, other training methods for hamstring strain injury prevention, such as those that might incorporate targeted isometric exercises should also be explored.

2.1.4.2 Isometric Contractions in Hamstring Strain Injury Prevention and Rehabilitation Training

Typically, for hamstring strain injury prevention and late stage rehabilitation, dynamic resistance training involving concentric and eccentric contractions is preferred to isometric resistance training (Suchomel et al., 2018). The perception exists that isometric resistance training lacks functional relevance due to the contraction stimulus's static nature (Lum & Barbosa, 2019). However, there is evidence to indicate that isometric resistance exercise can positively influence a range of functional activities. These include; increasing dynamic strength (Behm & Sale, 1993; Chui, 1964; Folland et al., 2005; Knapik et al., 1983; Symons et al., 2005; Ullrich et al., 2010), enhancing jump performance (Bimson et al., 2017; Goldmann et al., 2013; Kubo et al., 2017; Kubo, Yata, et al., 2006), and increasing running economy (Albracht & Arampatzis, 2013; Fletcher et al., 2008). Further, isometric training has been linked to improvements to injury and pain management of soft tissue injuries (Fisher et al., 1991; Hagberg et al., 2000; Marks, 1993).

When used effectively, isometric resistance training demonstrates a number of specific benefits for individuals to:

- increase muscle hypertrophy (Alegre et al., 2014; Kanehisa et al., 2002; Kubo et al., 2001; Kubo, Ohgo, et al., 2006; Meyers, 1967; Noorkoiv et al., 2014; Schott et al., 1995),
- increase peak torque at a specific joint-angle (Folland et al., 2005; Jones & Rutherford, 1987; Kubo, Ohgo, et al., 2006; Noorkoiv et al., 2014; Noorkõiv et al., 2015),
- increase isometric peak torque and isometric peak force through a range of motion when trained at a single, long musculotendinous unit joint angle (Bandy & Hanten, 1993; Bogdanis et al., 2019; Kubo, Ohgo, et al., 2006),
- broaden the plateau of angles for peak torque on the length-tension relationship (Hinks et al., 2021), with an increase in fascicle length when isometric resistance training is performed at long musculotendinous unit lengths (Akagi et al., 2020; Hinks et al., 2021; Oranchuk et al., 2019),
- increase in fascicle lengths when isometric resistance training is performed at long musculotendinous unitlengths (Akagi et al., 2020; Hinks et al., 2021; Oranchuk et al., 2019) and vi) increase tendon stiffness and integrity (Kubo, Ohgo, et al., 2006; Rio et al., 2017).

Importantly, the research evidence shows that consistently, the magnitude of these responses appears to be greatest when isometric resistance training is performed at long musculotendinous unit lengths (Akagi et al., 2020; Alegre et al., 2014; Hinks et al., 2021; Kanehisa et al., 2002; Kubo et al., 2001; Kubo, Ohgo, et al., 2006; Meyers, 1967; Noorkoiv et al., 2014; Oranchuk et al., 2019; Schott et al., 1995).

Isometric resistance training has been shown to be an efficient mode of exercise that results in large and rapid increases in strength, of up to 40% in 8 weeks (Young et al., 1985) and 25-54% in 5 weeks (Lindh, 1979; Thepaut-Mathieu et al., 1988). Increased efficiency is of benefit to athletes and practitioners who require results in short timeframes. Furthermore, isometric strength training at both high and low loads results in similar strength gains (Schoenfeld et al., 2017). As such, the evidence has shown that isometric strength training performed at long musculotendinous unit lengths and using a moderate load of at least 50% maximal voluntary isometric contraction, has resulted in increased isometric peak torque, increased fascicle lengths, and a rightward shift and broadening of the plateau region of the length-tension relationship (Hinks et al., 2021).

Considering the evidence presented in this section and above in sections 2.1.4.1 and 2.1.4.2 detailing hamstring strain injury risk factors, there is a distinct congruence between eccentric and isometric training, each aimed at mitigating hamstring strain injury risk factors. Notwithstanding the evidence provided in sections 2.1.4.1 and 2.1.4.2, the use of a combined eccentric-isometric contraction approach has significant appeal for hamstring strain injury prevention and rehabilitation programs.

2.1.5 The use of isometric and eccentric contractions in hamstring strain injury rehabilitation

Determining the type of rehabilitation program that most effectively promotes muscle tissue and functional recovery is essential to minimise the risk of re-injury and to improve athletic performance. The fundamental objective of the acute management phase of an hamstring strain injury is to facilitate myofibre regeneration while minimising fibrosis, more commonly known as scarring (Arnason et al., 2004; Verrall et al., 2001). The latter objective is critical because scar tissue results in a less compliant region of tissue that increases re-injury risk (Arnason et al., 2004; Verrall et al., 2001). Mobilisation of the injured site via eccentric contractions is known to induce muscle sarcogenesis via mechanotransduction, which is the fundamental mechanism by which mechanical stress acts through a cell that initiates intracellular signalling (Martineau & Gardiner, 2001). Specifically, mechanotransduction promotes cellular growth and survival (Frisch et al., 1996; Ruoslahti, 1997) and governs tissue architecture in the muscle (Chicurel et al., 1998; Vandenburgh et al., 1996). The benefits of loading the injured muscle using eccentric contractions are; improved alignment of regenerating myotubes, faster and more complete regeneration, and minimisation of atrophy of surrounding myotubes (Proske et al., 2004). With greater muscle regeneration efficiency via mechanotransduction, the use of eccentrically biased training in early-stage rehabilitation may reduce residual scar tissue size, which potentially allows earlier strength restoration. This process could potentially lead to faster and more complete hamstring strain injury recovery.

Nonetheless, the use of eccentric contractions during early hamstring rehabilitation has been much maligned. The reluctance to use eccentric contractions is primarily due to perceptions that eccentric contractions used in early-stage rehabilitation increase the risk of muscle damage during the muscle-lengthening phase of a movement (LaStayo et al., 2003; Proske & Morgan, 2001; Weerakkody et al., 2003). The use of isometric contractions has traditionally been considered a safer option than eccentric contractions. Historically, in the acute stage rehabilitation setting, models of strength restoration have been limited to the use of pain-free isometric contractions. As discussed above in section 2.1.4.2, the use of isometric training effectively minimises hamstring strain injury risk factors and therefore, its use in hamstring strain injury rehabilitation may be well justified (Heiderscheit et al., 2010). However, based on the need for greater efficiency in hamstring strain injury rehabilitation and lower rates of injury recurrence, there is growing interest in the re-evaluation of criteria for progressing hamstring strain injury rehabilitation programs. With evidence that now suggests that an eccentric stimulus, can reduce the magnitude of scarring post rehabilitation (Martineau & Gardiner, 2001) and that the use of eccentric contractions earlier in the rehabilitation continuum, may actually to be safe (Hickey et al., 2016). Combining isometric and eccentric training may be warranted.

Similar to the uncertainty posed regarding hamstring strain injury prevention discussed in section 2.1.4, hamstring strain injury rehabilitation programs are yet to be optimised and require further investigation of novel and scientifically sound protocols. Analogous to the proposal of using a combined eccentric-isometric contraction training program in hamstring strain injury prevention, there may be benefits to the combined use of highly controlled, submaximal eccentric contractions and submaximal isometric contractions, to be administered earlier in the rehabilitation process. The use of a combined submaximal eccentric-isometric training protocol has the theoretical potential to reduce hamstring strain injury recovery times and, importantly, reduce injury recurrence by minimising scarring and allowing earlier strength restoration.

2.1.6 The history dependence of force

The history dependence of force is a phenomenon involving either a decrease or an increase in the expected steady-state isometric force following either an actively shortened or actively lengthened muscle, respectively (Rassier & Herzog, 2004). The steady-state isometric force that follows active shortening is consistently lower than the steady-state isometric force without previous active shortening and is termed residual force depression (Abbott & Aubert, 1952). Conversely, after active lengthening, the steady-state isometric force is consistently and significantly greater when compared with levels of force in isometric contractions at the same muscle length and without prior stretch. This second phenomenon is termed residual force enhancement (Abbott & Aubert, 1952). For *in vitro* studies, the magnitude of residual force enhancement has been observed to exceed pure isometric force by 10% - 400%; however, it is less for *in vivo* studies (Herzog & Leonard, 2000). Additionally, it is known that the enhanced force is consistently observed in the absence of increased muscle activation (Oskouei & Herzog, 2006a; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2016).

The phenomenon of residual force enhancement is thought to be primarily due to behaviour of the giant protein, and structural element titin, which several researchers believe is responsible for the enhanced post-stretch force (Herzog & Leonard, 2005). It is theorised that titin increases in stiffness during active lengthening, contributing to the contractile element's total stiffness, which is maintained, albeit at a lower level, during the isometric steady-state, thereby enhancing total force (Herzog & Leonard, 2005).

The phenomenon of residual force enhancement is yet to be fully understood, nor has its functional relevance been thoroughly defined (Seiberl et al., 2015). However, two hypotheses have been proposed by Seiberl et al. (2013b). There are; i) residual force enhancement functions to enhance or maintain force production in situations requiring high amounts of force as output, such as landings or walking downstairs, particularly when the neuromuscular system is weakened, and ii) residual force enhancement may contribute to enhancing the neuromuscular economy and reducing metabolic cost during human locomotion.

The functional relevance proposed by Seiberl et al. (2013b) may also relate to the functional requirements of high-speed running, which is associated with hamstring strain injury risk factors. For instance, mechanisms responsible for residual force enhancement may increase the resilience of the hamstring muscles when eccentric muscle actions are required for braking or absorbing external forces. This may include open chain movements such as the late swing phase of high-speed running, with is linked to hamstring strain injury (Brockett et al., 2004; Brooks et al., 2006; Heiderscheit et al., 2010). Furthermore, the potential neuromuscular efficiency is seen during contractions that illicit residual force enhancement may be beneficial by increasing the hamstrings' ability to effectively cope with excessive tensile forces incurred during high-speed running, particularly following recovery from hamstring strain injury when neuromuscular deficits are known to persist(Buhmann et al., 2020; Opar et al., 2013a, 2013b).

Considering the body of evidence presented in this literature review, history dependent contractions that combine the use of eccentric and isometric muscle contractions in conventional hamstring strain injury prevention and rehabilitation programs warrants further exploration. However, before investigating the efficacy of a history-dependent hamstring training protocol on hamstring strain injury risk and rehabilitation, it is critical that the *in vivo* acute responses of the hamstrings to history-dependent muscle contractions during a range of relevant scenarios be established first (see chapters 4, 5, and 6). Therefore, to better inform such investigations, it was first necessary to thoroughly explore the current literature related to *in vivo* muscle behaviour during history-dependent muscle contractions that generate residual force enhancement. This has resulted in the systematic review that follows, as presented in Chapter 3.

Part I:

What is currently known about the phenomenon of residual force enhancement in human skeletal muscle *in vivo?*

Chapter 3: Residual force enhancement in humans: a systematic review

This chapter is an amended* version of the following published peer-reviewed manuscript:

Chapman, N., Whitting, J.W., Broadbent, S., Crowley-McHattan, Z.J., Meir, R. (2018). Residual force enhancement in humans: a systematic review. *Journal of Applied Biomechanics, 34(3), 240-248.*

**These amendments only relate to spelling or grammatical errors that have been identified since publication. No changes to methodology, results or findings have been made.*

Abstract

A systematic literature search was conducted to review the evidence of residual force enhancement *in vivo* human muscle. The search, adhered to the PRISMA statement, of CINAHL, EBSCO, Embase, MEDLINE, and Scopus (Inception – November 2016) was conducted. Full-text English articles that assessed at least one measure of residual force enhancement *in vivo* voluntarily contracted human skeletal muscle were selected. The methodologies of concluded articles were assessed against the Downs and Black checklist. Twenty-four studies were included (n= 424). Pooled Downs and Black scores ranked "fair" ($\bar{x}$ = 17 ± 2.26). Residual force enhancement was observed in all muscles tested. The joint range of motion varied from 15º to 60º. Contraction intensities ranged from 10% to >95% maximum. Although transient force enhancement during the stretch phase may change with angular velocity, residual force enhancement in the subsequent isometric phase is independent of velocity. The magnitude of residual force enhancement was positively influenced by smaller stretch amplitudes and greatest at joint angles indicative of longer muscle lengths. Contraction and activation intensity positively influenced residual force enhancement, particularly during the initial isometric contraction phase of a post-stretch isometric contraction. residual force enhancement resulted in increased torque production, reduced muscular activation, and enhanced torque production when the neuromuscular system is weakened as seen in an aged population.

3.1 Introduction

Muscle physiology is an area of great interest for scientists. The first half of the 20th century saw contributions to the body of knowledge of muscle mechanics by notable scientists such as Hill, Abbott, Fenn, Huxley, and Katz (Abbott & Aubert, 1952; Fenn, 1924; Fenn & Marsh, 1935; Hill, 1938, 1970; Huxley, 1957; Katz, 1939). The generally accepted mechanism of active force production in a sarcomere is based on a pioneering model by Huxley (1957), the so-called “cross-bridge theory.” According to this prevailing theory, myosin heads attach to the actin filament, pulling it toward the M-line in the centre of the sarcomere, thereby producing active force as the sarcomere shortens. Besides contraction velocity, the primary determinant of the magnitude of force output in this theory is the extent of overlap of the actin and myosin filaments, a function of sarcomere length, which determines the number of available cross-bridges (Huxley, 1957).

The great success of the cross-bridge model is based on nearly flawless predictions of force output via contractions at constant sarcomere lengths (isometric contractions) and contractions where the sarcomere is allowed to shorten (concentric contractions). However, it cannot account for some prominent observations when an activated sarcomere is stretched (eccentric contractions). One such phenomenon is the so-called “residual force enhancement”, whereby an initial isometric contraction precedes an eccentric contraction, quickly followed by a final isometric contraction (post-stretch isometric contraction). Edman et al. (1982) introduced the term residual force enhancement to describe the observations made by Abbott and Aubert (1952) as early as 1952. Abbott and Aubert (1952) investigated isometric steady-state muscle force following lengthening and shortening. Of note, they observed that the isometric steady-state muscle force at a pre-stretched length was greater than the steady-state isometric muscle force at that same length for a purely isometric muscle contraction. The resultant force reaches a peak during the stretch, quickly decaying to a steady level after stretch (Peterson et al., 2004). Using whole muscle preparations, Abbott and Aubert (1952) observed that force enhancement occurred on the ascending, plateau, and descending limb portions of the curve representing the isometric force-length relationship.

Since these early observations, residual force enhancement has been demonstrated in numerous experiments involving a range of muscle models from *in vitro* preparations of half sarcomeres (Peterson et al., 2004) to voluntarily contracted multi-joint muscles *in vivo* (Rassier et al., 2003). Specific examples include observations *in vitro* with single-fibre preparations (Edman et al., 1982; Herzog & Leonard, 2000; Schachar et al., 2004) and with whole muscle preparations (Abbott & Aubert, 1952; Campbell & Campbell, 2011; Cook & McDonagh, 1995) demonstrating residual force enhancement at levels of between 10% and 400% of baseline isometric force (Lee & Herzog, 2002). Furthermore, residual force enhancement has been observed *in vivo* with electrical stimulation (Hahn et al., 2010; Oskouei & Herzog, 2005; Pinniger & Cresswell, 2007; Ruiter et al., 2000), and in voluntary contractions (Hahn et al., 2010; Rassier et al., 2003; Ruiter et al., 2000; Seiberl et al., 2012; Tilp et al., 2009), albeit at lower magnitudes of 7% to 30% (Oskouei & Herzog, 2005; Pinniger & Cresswell, 2007) and 4% to 16% (Ruiter et al., 2000), respectively. Finally, residual force enhancement has been observed *in vivo* during maximal (Rassier et al., 2003) and submaximal (Hahn et al., 2010; Seiberl et al., 2015) muscle contractions.

Residual force enhancement is consistently observed in electrically stimulated *in vivo* human muscle (Hahn et al., 2007). However, it is essential to note an apparent disparity in magnitude of residual force enhancement between electrically stimulated and voluntarily activated contractions. In fact, the magnitude of residual force enhancement has been found to vary greatly *in vivo* voluntarily contracted human muscle (Hahn et al., 2007). Moreover, *in vivo* submaximal voluntary contraction (% maximal voluntary contraction), residual force enhancement has been found to be absent in a subset of individuals (Oskouei & Herzog, 2006a, 2006b; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2013; Seiberl et al., 2015; Tilp et al., 2009). These individuals have been termed "non-responders" (Oskouei &

Herzog, 2006a, 2006b; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2013; Seiberl et al., 2015; Tilp et al., 2009). The cause of the non-responder phenomenon is not well understood. There is debate over whether the development of residual force enhancement is limited to a subset of people displaying particular physiological characteristics, such as greater neural inhibition, influences of fibre-type distribution, subject-specific individual threshold regarding muscular activation (Hahn et al., 2007), or whether there may be insufficient task-specific motor control (Hahn et al., 2007).

By the mid-20th century, there were only a handful of unresolved observations regarding the fundamental mechanisms of muscle contraction. Most remain unexplained to some extent to the present day (Herzog et al., 2008). These remaining observations include; i) the enhancement of force with lengthening contractions (Abbott & Aubert, 1952); ii) the depression of force with shortening contractions (Abbott & Aubert, 1952); iii) the low metabolic cost of force production during the active stretch of muscle (Bigland & Lippold, 1954), although this phenomenon is yet to be confirmed *in vivo* human muscle (Kushmerick & Davies, 1969); and iv) the high thermodynamic efficiency of actively shortening muscle (Julian & Morgan, 1979).

Efforts to explain the mechanisms behind these observations led to modifications of the original cross-bridge muscle theory (Komi, 2000), as well as the development of alternative hypotheses (Komi, 2000). Scientists are yet to definitively explain the mechanisms behind residual force enhancement, as well as the role of residual force enhancement in relation to activities of daily living. Seiberl et al. (2013) identified that the fundamental characteristics of activities of daily living involved: i) contractions at a submaximal level of activation and ii) coordination of several large muscles during multi-joint movements. The standard test condition in residual force enhancement experiments (isometric-eccentric-isometric) does not necessarily represent a typical human contraction condition (Paternoster et al., 2016). Nonetheless, recently, researchers have successfully observed residual force enhancement during experiments replicating % maximal voluntary contraction during multi-muscle and multi-joint actions close to human function (Oskouei & Herzog, 2006a; Paternoster et al., 2016). Seiberl et al. (2013) suggest that residual force enhancement may play a beneficial role in human movement in a manner that is two-fold: i) to enhance or maintain force production in situations requiring high amounts of force, for example, landings, downstairs walking, and falls prevention following perturbation, particularly when the neuromuscular system is weakened such as in an aged population and ii) improvement of neuromuscular economy and reduction in metabolic cost during human locomotion.

To our knowledge, a systematic review of the scope and quality of the evidence from *in vivo* residual force enhancement experiments using voluntarily activated contractions is yet to be undertaken. Therefore, this review seeks to inform future experiments of *in vivo*, voluntarily activated post-stretch isometric contraction modalities in human skeletal muscle.

3.2 Methods

The methodology for the systematic review followed the PRISMA statement (Moher et al., 2010).

3.2.1 Literature search

A systematic literature search of the CINAHL, EBSCO, Embase, MEDLINE, and Scopus databases was conducted from inception to November 2016. Key search terms (Table 1) were chosen in accordance with the aims of the research. Retrieved references were imported into

Endnote X7 (Thomson Reuters, New York, NY), with duplicates subsequently deleted. To ensure all recent and relevant references were retrieved, reference list searches were conducted.

Table 1 Summary of Keyword Grouping Employed During Database Searches

Residual	Force	Enhancement
Human	Skeletal	Muscle
Voluntary	Contraction	*In vivo*

Note: Boolean term OR was used within search categories, while AND was used between search categories.

3.2.2 Selection criteria

Selection criteria were developed prior to searching to maintain objectivity when identifying studies for inclusion. The included studies: i) were experimental (i.e., randomised controlled trials) or quasi-experimental (i.e., pre-test/post-test cohort_ in design; ii) measured the magnitude of residual force enhancement; iii) included participants aged 18 years and over; iv) tested healthy participants with no diagnosed orthopaedic or neurologic issues that would affect their ability to gain the required range of motion; v) investigated the *in vivo* measure of voluntarily activated human skeletal muscle; vi) had the full-test journal article in English available (excluding reviews, conference abstracts, case studies/series or letters).

The title and abstract of each article were scanned by two authors (N.C. and J.W.), and articles were removed if titles and abstracts did not contain keywords. Selection criteria were then independently applied to the remaining articles by four authors (N.C., J.W., and S.B.) and another author (Z.C-M).

3.2.3 Analysis

Following evaluation of a number of quality assessment tools, the Downs and Black checklist (Downs & Black, 1998) was used in its original form despite noted limitations for assessing observational studies. Specifically, it was expected that the assessed studies would yield proportionately moderate scores. The decision was made to use a quality assessment checklist in order to provide a relative comparison of studies, knowing that the primary focus of the systematic review was to analyse the evidence and summarise the findings available concerning residual force enhancement findings *in vivo* human muscle models. Of 27 items, 25 were scored either 0 if the criterion was not met or was unable to be determined or 1 point if the item successfully met the criteria. Item 5 was scored 0 if the criterion was not med, 1 point if the criterion was partially med, and 2 points if the criterion was successfully met. Item 27, which assessed whether the study had sufficient power to detect clinically meaningful effects, was scored between 0 and 5 points as dictated in the criteria of the Downs and Black checklist. The Downs and Black checklist, therefore, allowed for a total possible score of 32 points for each article.

3.3 Results

3.3.1 Search results

The search strategy consisted of 5 steps (Figure 4). The initial search yielded 144 studies (CINAHL = 3; EBSCO = 63; MEDLINE = 31; and Scopus = 47) from all databases. After duplicates were removed, 34 studies remained. Title and abstract screening provided 24 remaining studies. Reference list hand searching and citation tracking resulted in the addition of 0 studies. Independent application of the selection criteria yielded 24 studies to be included in the review.

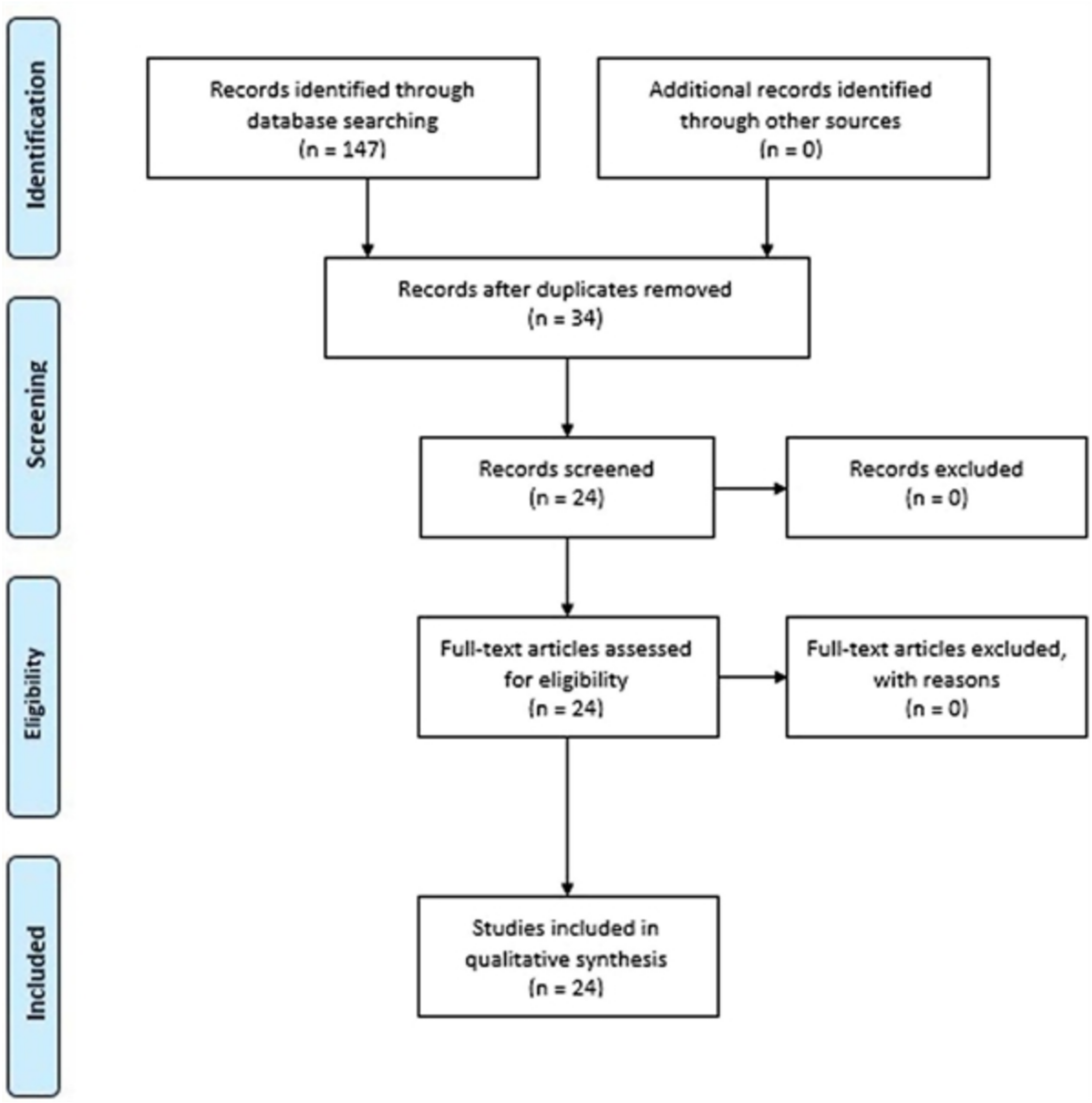


Figure 4 *PRISMA flow diagram.*

3.3.2 Risk of bias assessment

The risk of bias assessment of each publication is displayed in Table 2. It is important to note that the risk of bias assessment was not the basis of exclusion. Included studies ranged from a score of 11 to 19 of a possible 32.

3.4 Description of studies

3.4.1 Participants

A sample of 414 participants (n = 283 males, n = 68 females, n = 33 no gender specified; age range, 18-82 years) were examined in the included articles. Eleven studies included only male participants (Hahn et al., 2010; Hahn et al., 2007; Oskouei & Herzog, 2006a, 2006b; Paternoster et al., 2017; Paternoster et al., 2016a; Power et al., 2014; Power et al., 2013; Power et al., 2015; Power et al., 2012a, 2012b; Rassier et al., 2003; Seiberl et al., 2013), 10 had male and female participants (Altenburg et al., 2009; Jones et al., 2016; Lee & Herzog, 2002b; Oskouei & Herzog, 2005, 2006a; Paternoster et al., 2016a; Seiberl et al., 2016; Shim & Garner, 2012; Tilp et al., 2009; Tilp et al., 2011), and 2 studies did not specify gender of participants (Oskouei & Herzog, 2006b; Siebert et al., 2016). None of the studies exclusively included female participants.

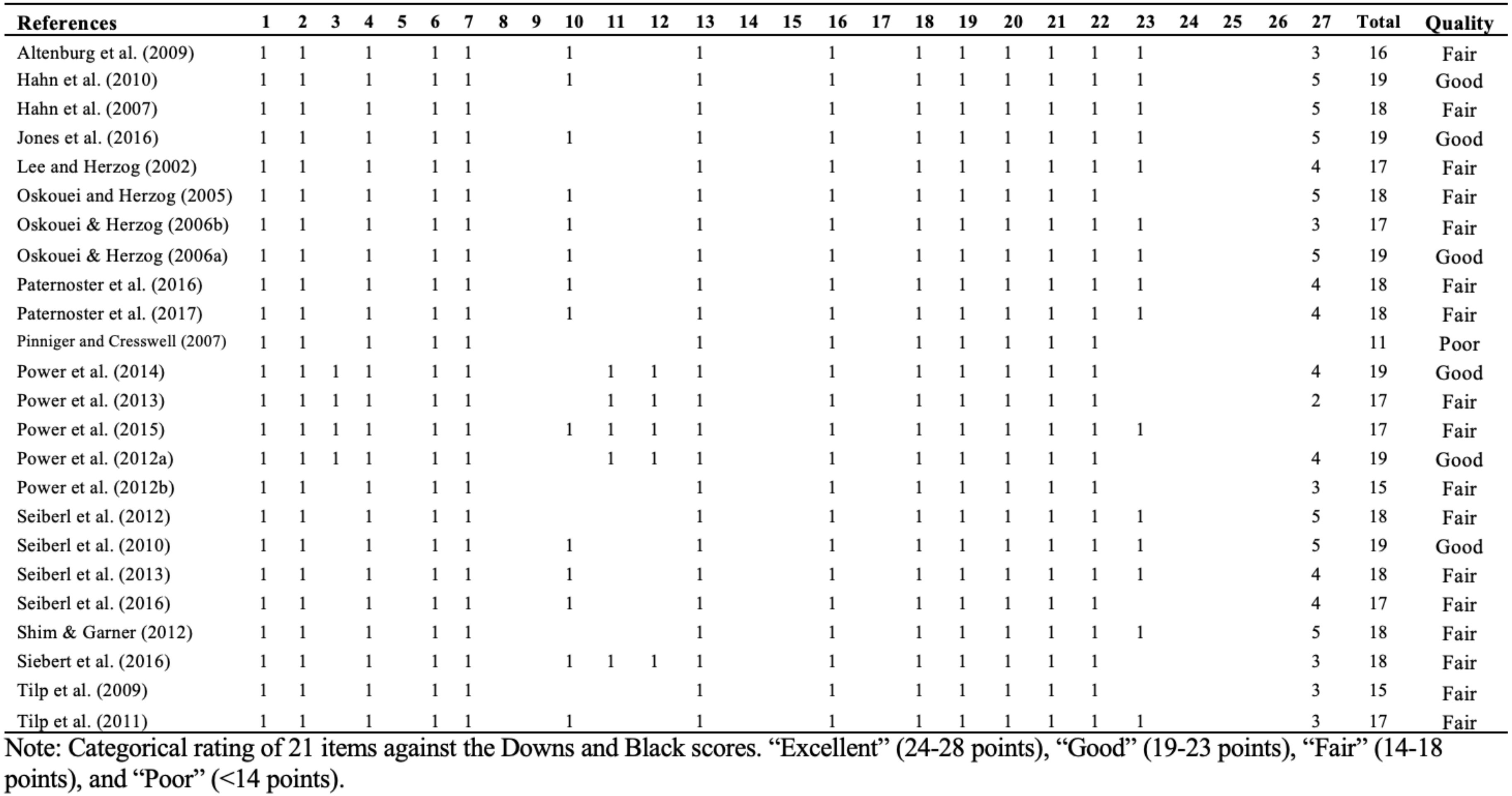
An array of joints and muscles were investigated and are identified in Table 3. Both upper and lower limb muscles were tested as were single-muscle (Jones et al., 2016; Lee & Herzog, 2002b; Oskouei & Herzog, 2005, 2006a, 2006b; Paternoster et al., 2017; Power et al., 2014; Power et al., 2012a, 2012b; Seiberl et al., 2012; Seiberl et al., 2010) and multi-muscle movements (Altenburg et al., 2009; Hahn et al., 2010; Hahn et al., 2007; Paternoster et al., 2017; Pinniger & Cresswell, 2007; Power et al., 2014; Seiberl et al., 2016; Seiberl et al., 2013; Shim & Garner, 2012; Siebert et al., 2016; Tilp et al., 2009; Tilp et al., 2011). All studies observed residual force enhancement of varying magnitudes in all muscles tested, regardless of whether the muscles crossed single or multiple joints.

The majority of studies (14 of 24) investigated residual force enhancement at contraction intensities of 95% or greater of maximal voluntary contraction intensity (Hahn et al., 2010;

Jones et al., 2016; Power et al., 2014; Power et al., 2013; Power et al., 2015; Power et al., 2012a, 2012b; Seiberl et al., 2010; Tilp et al., 2009). Four studies reported residual force enhancement in submaximal contraction intensities of 25% and 30% MVC (Altenburg et al., 2009; Oskouei & Herzog, 2005, 2006a; Paternoster et al., 2016a; Pinniger & Cresswell, 2007; Seiberl et al., 2012). One study investigated residual force enhancement in multiple submaximal and maximal contraction intensities ranging from 10% to >95% maximal voluntary contraction (Oskouei & Herzog, 2006b).

The joint angle was measured at the post-stretch isometric contraction. The included studies investigated residual force enhancement in a range of joint angles indicative of short and long muscle lengths on the ascending limb, plateau, or descending limb of the force-length relationship. Twenty studies assessed a single joint angle (Altenburg et al., 2009; Hahn et al., 2010; Jones et al., 2016; Oskouei & Herzog, 2005, 2006a, 2006b; Paternoster et al., 2017; Paternoster et al., 2016a; Pinniger & Cresswell, 2007; Power et al., 2015; Power et al., 2012a, 2012b; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2016; Seiberl et al., 2013; Siebert et al., 2016; Tilp et al., 2009; Tilp et al., 2011). Two of those studies investigated two stretch magnitudes in the tibialis anterior, namely 15º and 30º (Tilp et al., 2009; Tilp et al., 2011). The remaining four studies investigated residual force enhancement across multiple joint angles indicative of both shorts and long muscle lengths (Hahn et al., 2007; Lee & Herzog, 2002; Power et al., 2013; Shim & Garner, 2012). Two of those studies investigating multiple joint angles also investigated either two or three stretch magnitudes in the knee extensor group (Hahn et al., 2007; Power et al., 2014).

Table 2 Itemised scoring of study quality using the Downs and Black checklist



References	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Total	Quality
Altenburg et al. (2009)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				3	16	Fair
Hahn et al. (2010)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				5	19	Good
Hahn et al. (2007)	1	1		1		1	1						1			1		1	1	1	1	1	1				5	18	Fair
Jones et al. (2016)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				5	19	Good
Lee and Herzog (2002)	1	1		1		1	1						1			1		1	1	1	1	1	1				4	17	Fair
Oskouei and Herzog (2005)	1	1		1		1	1			1			1			1		1	1	1	1	1					5	18	Fair
Oskouei & Herzog (2006b)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				3	17	Fair
Oskouei & Herzog (2006a)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				5	19	Good
Paternoster et al. (2016)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				4	18	Fair
Paternoster et al. (2017)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				4	18	Fair
Pinniger and Cresswell (2007)	1	1		1		1	1						1			1		1	1	1	1	1						11	Poor
Power et al. (2014)	1	1	1	1		1	1				1	1	1			1		1	1	1	1	1					4	19	Good
Power et al. (2013)	1	1	1	1		1	1				1	1	1			1		1	1	1	1	1					2	17	Fair
Power et al. (2015)	1	1	1	1		1	1			1	1	1	1			1		1	1	1	1	1	1					17	Fair
Power et al. (2012a)	1	1	1	1		1	1				1	1	1			1		1	1	1	1	1					4	19	Good
Power et al. (2012b)	1	1		1		1	1						1			1		1	1	1	1	1					3	15	Fair
Seiberl et al. (2012)	1	1		1		1	1						1			1		1	1	1	1	1	1				5	18	Fair
Seiberl et al. (2010)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				5	19	Good
Seiberl et al. (2013)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				4	18	Fair
Seiberl et al. (2016)	1	1		1		1	1			1			1			1		1	1	1	1	1					4	17	Fair
Shim & Garner (2012)	1	1		1		1	1						1			1		1	1	1	1	1	1				5	18	Fair
Siebert et al. (2016)	1	1		1		1	1			1	1	1	1			1		1	1	1	1	1					3	18	Fair
Tilp et al. (2009)	1	1		1		1	1						1			1		1	1	1	1	1					3	15	Fair
Tilp et al. (2011)	1	1		1		1	1			1			1			1		1	1	1	1	1	1				3	17	Fair

Note: Categorical rating of 21 items against the Downs and Black scores. “Excellent” (24-28 points), “Good” (19-23 points), “Fair” (14-18 points), and “Poor” (<14 points).

Stretch magnitude, defined as the total range of movement measured in degrees between the isometric pre-activation contraction and the isometric contraction following the stretch condition, investigated within all studies varied from 8º to 60º range of movement (Table 3). Of the 24 studies, two investigated two different stretch magnitudes (i.e., 15º and 30º) (Hahn et al., 2007; Power et al., 2014), with one study investigating residual force enhancement at three stretch magnitudes (i.e., 15º, 25º, and 30º) (Hahn et al., 2007).

Stretch velocity was measured in degrees per second during the stretch condition. Stretch velocities ranged from 9 to 360º.s^{-1} (Table 3). Twenty studies assessed a single stretch velocity (Altenburg et al., 2009; Hahn et al., 2010; Hahn et al., 2007; Jones et al., 2016; Oskouei & Herzog, 2005, 2006a, 2006b; Paternoster et al., 2017; Paternoster et al., 2016; Pinniger & Cresswell, 2007; Power et al., 2014; Power et al., 2013; Power et al., 2012a, 2012b; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2016; Shim & Garner, 2012; Siebert et al., 2016). Four studies assessed two stretch velocities (Lee & Herzog, 2002; Power et al., 2014; Tilp et al., 2009; Tilp et al., 2011). One study assessed a range of stretch velocities (i.e. 15, 30, 45, 60, 120, 270, 300, 330, and 360º.s^{-1} (Power et al., 2015).

A total of 23 studies measured muscular activation via surface or intramuscular electromyography (Altenburg et al., 2009; Hahn et al., 2010; Hahn et al., 2007; Jones et al., 2016; Lee & Herzog, 2002b; Oskouei & Herzog, 2005, 2006a, 2006b; Paternoster et al., 2017; Paternoster et al., 2016; Pinniger & Cresswell, 2007; Power et al., 2014; Power et al., 2013; Power et al., 2015; Power et al., 2012a, 2012b; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2016; Seiberl et al., 2013; Tilp et al., 2009; Tilp et al., 2011). One study used intramuscular electromyography in addition to surface electromyography measurements

(Altenburg et al., 2009). Intramuscular electromyography was used to measure the activation of 42 individual muscle motor units.

Electromyography was used to measure the reduction in muscle activation during post-stretch isometric contractions at maximal voluntary contraction and % maximal voluntary contraction intensity, where torque was controlled for isometric reference and post-stretch isometric contractions. Fourteen studies used electromyography primarily to measure muscle activation reduction in maximal voluntary post-stretch isometric contractions (Hahn et al., 2010; Hahn et al., 2007; Jones et al., 2016; Lee & Herzog, 2002b; Paternoster et al., 2017; Power et al., 2014; Power et al., 2013; Power et al., 2015; Power et al., 2012a, 2012b; Seiberl et al., 2016; Tilp et al., 2009; Tilp et al., 2011), and one study used electromyography to measure activation reduction in % maximal voluntary post-stretch isometric contractions via torque control % maximal voluntary contraction (Oskouei & Herzog, 2006b). Six studies used electromyography to control muscle activation levels to achieve a set % maximal voluntary contraction intensity (Oskouei & Herzog, 2005, 2006a; Paternoster et al., 2016; Pinniger & Cresswell, 2007; Seiberl et al., 2012; Seiberl et al., 2013).

3.5 Discussion

The evidence presented in this systematic review relates to simple single-muscle/single-joint actions through to more complex multi-muscle/single-joint and multi-muscle/multi-joint actions, which correspond more closely to complex functional movements such as walking. The evidence suggests that the mechanisms underlying residual force enhancement and activation reduction are influenced by other factors such as competing neural influences between single-muscle/multi-joint actions. Much of the focus of the latest research has been concerned with more complex multi-muscle/multi-joint actions, which have attempted to elucidate our understanding of residual force enhancement for human function.

This systematic review revealed four significant findings that demonstrated or contributed to the presence, or the magnitude of, residual force enhancement *in vivo* human muscle models: i) the magnitude of residual force enhancement was greater with increasing contraction intensity, mainly when there was greater contraction intensity during the isometric pre-activation contraction – with the minimum contraction intensity required to observe residual force enhancement appearing to be specific to the individual; ii) the magnitude of residual force enhancement was greatest at joint angles indicative of the longest muscle lengths, though it is unclear whether there is a relationship between magnitude of residual force enhancement and magnitude of stretch; iii) the magnitude of residual force enhancement was unaffected by the angular velocity of stretch; and iv) the magnitude of residual force enhancement may be age-dependent, with greater magnitude of residual force enhancement being observed in older participants.

Of the included studies, residual force enhancement was observed in single-muscle/single-joint, multi-muscle/single-joint and multi-muscle/multi-joint models (T. M. Altenburg et al., 2009; Hahn et al., 2010; Hahn et al., 2007; H. D. Lee & W. Herzog, 2002b; Oskouei & Herzog, 2005, 2006a, 2006b; F. K. Paternoster et al., 2016a; Pinniger & Cresswell, 2007; Power et al., 2014; Power et al., 2013; Power et al., 2015; Power et al., 2012a, 2012b; Seiberl et al., 2012; Seiberl et al., 2010; Seiberl et al., 2013b; Shim & Garner, 2012; Siebert et al., 2016; Tilp et al., 2009; Tilp et al., 2011). No study sought to compare residual force enhancement between simple and multi-muscle/joint setups; therefore, no comparison between these simple and complex muscle/joint actions could be made. Varying magnitudes

Table 3 Best Evidence Synthesis Data

References	n	Gender		Muscles	Contraction intensity (%MVC)	Joint angle	Stretch magnitude	Stretch velocity (°.s^{-1})	EMG
		M	F						
Altenburg et al (2009)	10	5	5	VM, VL, RF	10, 50, 19	62.5°	20°	10	Y
Hahn et al (2010)	22	22	0	RF, VM, VL, BF, GM, GL, SOL, TA	>95	77.5°	17.8°	60	Y
Hahn et al (2007)	15	15	0	VM, VL, RF	>95	60°, 70°, 80°, 95°	15°, 25°, 35°	60	Y
Jones et al (2016)	20	11	9	APB	40, >95	0°	40°	20	Y
Lee & Herzog (2002)	12	8	4	APB	>95	10°, 20°, 30°	30°	10, 20, 60,	Y
Oskouei & Herzog (2005)	17	12	5	APB	30	0°	30°	9	Y
Oskouei & Herzog (2006)	12	Not stated		APB	10, 60	0°	30°	9	Y
Oskouei & Herzog (2006)	11	9	2	APB	10, 30, 60, 100	0°	30°	9	Y
Paternoster et al (2016)	13	10	3	RF, VM, VL, BF, GM, GL, SOL, TA, ST, BF	30	30°	20°	60	Y
Paternoster et al (2017)	20	20	0	GM	30	13°	26°	60	Y
Pinniger & Creswell (2007)	6	6	0	SOL, TA	25	0°	15°	5	Y
Power et al (2014)	35	35	0	G, VL	>95	40° PF, 80° KF	30° PF, 60° KE	15 PF, 30 KE	Y
Power et al (2013)	22	22	0	VL	>95	140°, 180°	60°	30	Y
Power et al (2015)	18	18	0	TA, SOL	>95	0° PF	50° PF	15, 30, 45, 60, 120, 210, 270, 300, 330, 360	Y
Power et al (2012)	10	10	0	TA	>95	40° PF	30°	15	Y
Power et al (2012)	8	8	0	TA	>95	30° PF	30°	30	Y
Seiberl et al (2012)	30	30	0	QF	30, 60	20°	20°	60	Y
Seiberl et al (2010)	18	18	0	QF	>95	20°	20°	60	Y
Seiberl et al (2013)	13	10	3	VM, GM, GL	30	100°	20°	60	Y
Seiberl (2016)	16	9	7	VL, VM, RF	60	80° KF	20°	60	Y
Shim & Garner (2012)	40	20	20	Not stated	>95	40°/100° KE, 10°/70° KF	30°	30	N
Siebert et al (2016)	21	Not stated		Not stated	>95	110°KE	20°	52	N
Tilp et al (2009)	12	7	5	TA, GM	>95	0°PF	15°/30°	10/45	Y
Tilp et al (2011)	12	7	5	TA, GM	>95	0°PF	15°/30°	10/45	Y

Abbreviations: APB, adductor pollicis brevis; BF, biceps femoris; EMG, electromyography; G, gastrocnemius; GL, gastrocnemius lateralis; GM, gastrocnemius medialis; KE, knee extension; KF, knee flexion; MVC, maximal voluntary contraction; N, no; PF, plantar flexion; QF, quadriceps femoris; RF, rectus femoris; SOL, soleus; ST, semitendinosus; TA, tibialis anterior; VL vastus lateralis; VM, vastus medialis; Y, yes.

of residual force enhancement were found in all studies for both maximal and % maximal voluntary contractions.

The pooled findings demonstrate that residual force enhancement is observable in the muscles and joints within the existing literature. Despite varying rates of residual force enhancement “responders” and “non-responders,” depending on factors such as contraction intensity, stretch magnitude, and stretch velocity, the pooled findings suggest that residual force enhancement is potentially observable in all human skeletal muscle. The magnitude of residual force enhancement was found to be dependent upon contraction and activation intensity, particularly the contraction or activation intensity during the isometric pre-activation phase. In a single-muscle/single-joint setup, residual force enhancement was observed in a greater proportion of participants with increasing contraction intensity during the isometric pre-activation and/or the lengthening phase. residual force enhancement was observed in 33% of participants at 10% maximal voluntary contraction, approximately half of participants at 30% maximal voluntary contraction, and 83.33% at 60% maximal voluntary contraction. Responders demonstrated greater post-activation potentiation and smaller resistance to fatigue than non-responders. It is notable that 16.66% of participants who did not show residual force enhancement at 60% maximal voluntary contraction did not show residual force enhancement at 10% and 30% maximal voluntary contraction. This suggests that there may be an individual-specific minimum contraction intensity threshold that needs to be met before residual force enhancement can be consistently observed.

Residual force enhancement has also been observed to be activation-dependent. Similar in nature to the possible minimum contraction threshold required to demonstrate residual force enhancement, a minimum voluntary activation level also needs to be achieved during isometric pre-activation or the lengthening contraction for residual force enhancement to be consistently observed. Oskouei and Herzog (2005) found that once residual force enhancement was present at an individual baseline submaximal voluntary activation, the participant would consistently exhibit residual force enhancement with repeats of increasing voluntary activation levels. The torque and activation traces from one participant, and regression analysis between activation level and force enhancement across all participants, showed that increasing activation was strongly associated with an increase in the magnitude of residual force enhancement. There was a significant maximal voluntary activation by participant interaction, indicating that the effect of voluntary contraction on residual force enhancement was participant-specific. Oskouei and Herzog (2006b) stated that these results clearly indicated that residual force enhancement following active stretch (eccentric contraction) depends on the level of activation (or force, or both) prior to or during the active stretch (eccentric contractions). They postulated, therefore, that residual force enhancement cannot be caused solely by a structural passive element (e.g., titin) that is activated during the stretch. Oskouei and Herzog (2006a) initially suggested that the transient force enhancement might have been associated with a fast or slow-twitch fibre type. However, the fibre-type hypothesis was rejected as residual force enhancement should not be observed at the lowest contraction intensities of adductor pollicis brevis, and residual force enhancement should be observed in 100% of participants at contraction intensities of 60% maximal voluntary contraction. The question of what causes residual force enhancement to be activation-dependent and what causes the threshold for residual force enhancement to differ among participants remains unanswered.

Concerning multi-muscle/multi-joint actions, one study found no difference in average torques following stretch compared with isometric reference contractions of the individual muscles of the quadriceps group (Altenburg et al., 2009). Altenburg et al. (2009) concluded that the muscular activation of the quadriceps muscle group during % maximal voluntary contraction was decreased in response to the enhanced force capacity following stretch, possibly by de-recruitment of motor units (activation reduction). They observed that when individual muscles were analysed, rectified surface electromyography of the vastus medialis and vastus lateralis were significantly lower than the isometric reference contraction at 10% maximal voluntary contraction, but not at 50% maximal voluntary contraction. The rectified surface electromyography of rectus femoris at 10% maximal voluntary contraction was significantly greater than the isometric reference contraction, but no difference was observed at 50% maximal voluntary contraction (Altenburg et al., 2009). No change in motor unit discharge rate was reported following a stretch of 10% and 50% maximal voluntary contraction when compared with the isometric reference contractions.

A later study of residual force enhancement in the knee extensors observed residual force enhancement of 7% to 11% above isometric reference contractions at 30% of maximal voluntary activation and residual force enhancement magnitude of 3% to 5% at 60% of maximal voluntary activation (Seiberl et al., 2012). No differences in activation levels of vastus medialis and vastus lateralis between isometric and stretch contractions were observed. Rectus femoris showed significantly higher muscular activation of about 4% of maximal voluntary activation after stretch. At 60% of maximal voluntary activation, there were no differences in activation for vastus lateralis and vastus medialis. Rectus femoris was significantly less activated (4% of maximal voluntary activation) after stretch. Siebert et al. (2016) suggested that the independence of the absolute magnitude of residual force enhancement from the level of activation had not been observed previously for voluntarily activated *in vivo* muscles but speculated that it might eventually be explained by passive components, such as titin, that may contribute to residual force enhancement (Leonard & Herzog, 2010). Further investigation into the effect of % maximal voluntary contraction of complex multi-muscle/multi-joint conditions to replicated human function should take place to confirm the findings of Altenburg et al. (2009) and Seiberl et al. (2012).

The magnitude of residual force enhancement was reported to be greatest primarily on the descending limb of the muscle force-length relationship when muscles were at the longest lengths. This was particularly evident with more complex multi-muscle/multi-joint actions. Shim and Garner (2012) found that in >95% maximal voluntary contraction knee flexion and knee extension tasks, steady-state stretch-isometric torques significantly exceeded purely isometric torques at joint positions corresponding to long muscle lengths (4.2% and 4.7%, respectively), but not at joint positions corresponding to short muscle lengths. Hahn et al. (2007) did not find residual force enhancement during knee extension at any joint angle assessed. However, they observed transient force enhancement during the stretch at four different knee joint angles ranging from 60º to 95º. Importantly, peak moments were noted during the active stretch as opposed to previous observations where peak moments were evident at the end of the active stretch (Campbell & Campbell, 2011).

In contrast, investigations of multi-muscle/single-joint actions, such as the knee extensors and knee flexors (Hahn et al., 2007), and single-muscle/single-joint actions of adductor pollicis brevis (Lee & Herzog, 2002b) did observe a greater magnitude of force enhancement when stretch was initiated at joint angles indicative of shorter muscle lengths. Lee and Herzog (2002) found greater magnitude residual force enhancement at a joint angle of 10º flexion when compared with stretch being initiated at 20º flexion of adductor pollicis brevis despite the magnitude and velocity of stretch remaining constant. Lee and Herzog (2002) also observed that regardless of stretch condition, the intensity of electromyography signals before, during, and following active muscle stretching were smaller than those in the isometric reference contractions. Researchers suggest that voluntary inhibition due to the large size of the muscles may influence these findings in the knee flexors and extensors (Hahn et al., 2007; Shim & Garner, 2012).

Magnitudes of active stretch varied from 15º to 60º in experiments assessing a variety of joints. One study assessed multiple stretch magnitudes in simple single-muscle/single-joint combinations, specifically adductor pollicis brevis, where greater magnitudes of residual force enhancement were achieved with smaller stretch magnitudes (Lee & Herzog, 2002). In contrast to the single finding in adductor pollicis brevis, two studies that assessed more complex multi-muscle/single-joints of the knee and ankle found that residual force enhancement was independent of stretch magnitude (Hahn et al., 2007; Tilp et al., 2009). Tilp et al. (2009) and Hahn et al. (2007) observed that transient force enhancement was not dependent on stretch magnitudes of 15º or 30º. Furthermore, Hahn et al. (2007) found that transient force enhancement and residual force enhancement were independent of stretch magnitude. For all muscles and each stretch condition, muscle activation during and following stretch was smaller than during maximal voluntary isometric reference contractions. In addition, for all muscles, there was no systematic change in muscle activation as a function of stretch conditions. Finally, Tilp et al. (2009) found that the timing of peak forces seemed dependent upon the stretch magnitude by occurring later as stretch magnitudes increased. Similar inhibitions of force during stretching of voluntarily activated muscles have been observed by Hahn et al. (2007), Tilp et al. (2009), and Webber and Kriellaars (1997), who explained this by suggesting that “premature” force occurrence is partly caused by inhibitory pathways (likely Golgi tendon feedback) but may also be controlled in some manner voluntarily, depending on the magnitude of stretch.

The magnitude of residual force enhancement appeared to be unaffected by the angular velocity of stretch. Power et al. (2015) and Tilp et al. (2009) demonstrated that the magnitude of residual force enhancement was unaffected by angular velocity in the ankle dorsiflexors and plantarflexors, respectively. Furthermore, Tilp et al. (2009) stated that electromyography signals were also unaffected by angular velocity. These findings on torque production are consistent with previous findings, which indicate that angular velocity does not affect the magnitude of residual force enhancement (Power et al., 2012a).

Of note, in >95% maximal volunatary contraction, the magnitude of transient force enhancement increased with heightened angular stretch velocity but plateaued at 120^{o}.s^{-1}. Power et al. (2015) observed transient force enhancement and residual force enhancement over a range of stretch velocities from 15^{o}.s^{-1} up to 360^{o}.s^{-1}. Power et al. (2015) found that in both young and older adults, the eccentric strength (torque) during stretch increased as velocity increased from 15^{o}.s^{-1} up to 120^{o}.s^{-1} and plateaued in velocities greater than this value. Eccentric strength at 15^{o}.s^{-1} was 20% and 40% greater than isometric strength in young and old men, respectively, while at 360^{o}.s^{-1}, eccentric strength was 50% and 90% greater, respectively. These findings indicated that with increasing angular velocity, both young and older men have considerable increases in the eccentric: isometric ratio of torque production.

In a cross-sectional comparison of young and older men, older men were found to develop residual force enhancement 2.5 times greater in magnitude than younger men (Power et al., 2012a). Power et al. (2012a) observed that residual force enhancement was 7% to 30%, with a mean of ~25% greater than isometric reference contractions. The impetus behind the elevated residual force enhancement in older men appears to be related partly to the mechanisms responsible for the age-related maintenance of eccentric strength. In older men, passive force enhancement contributed ~17% more to residual force enhancement compared with young participants, and thus, passive force enhancement appears to be a vital component of the overall increase in force production observed following an active stretch in older adults (Power et al., 2012a). After the stretch, old and young participants followed the typical exponential decline in torque, but more time was required for the older men to reach a steady-state torque level compared with younger (Edman, 2012). This longer time to reach steady-state, with an elevated passive force enhancement, indicates structural elastic mechanisms may have a disproportionately greater contribution to transient force enhancement in old age. Power et al. (2012a) suggested that the observed residual force enhancement is probably more related to mechanical factors than to neural influences. Moreover, a posthoc analysis was conducted on previous residual force enhancement experiments in young and old men to fit and characterise the decay in force transients immediately following active lengthening. In the muscle groups assessed, the decay half-life of the first exponential was two times slower in the older compared with your men. Power et al. (2014) stated that there were significant associations between passive force enhancement and the decay in force. This suggests that a greater nonactive component of residual force enhancement in older adults, which could be due to age-related structural changes, caused increased muscle stiffness during and following stretch. Power et al. (2014) concluded that the passive components of residual force enhancement still appear to be a key mechanistic contributor to the overall increase in residual force enhancement, particularly in older adults.

3.6 Clinical implications

The findings of this systematic review indicate that there may be numerous potential benefits in using the stiffness of titin during maximal and submaximal post-stretch isometric contraction modalities to elicit residual force enhancement and/or activation reduction. The high force and low energy cost of eccentric contractions, as ween during the stretch phase of a post-stretch isometric contraction, makes them particularly well suited for athletic training and rehabilitation. There is a growing body of research investigating the influence of titin in the stretch-shortening cycle (Fukutani et al., 2017; Fukutani et al., 2016a) and the effects of weight training on the ability to increase residual force enhancement for potential benefit to athletic training (Siebert et al., 2016). Furthermore, it is recommended that investigation into the use of post-stretch isometric contractions should be undertaken in situations where eccentric contractions are commonly prescribed in exercise rehabilitation, particularly with respect to conditions such as sarcopenia, osteoporosis, tendinosis, and muscle strain injuries. Moreover, using activation reduction during post-stretch isometric contractions and the use of the titin mechanism where pure eccentric contraction modalities are in common use in athletic training and rehabilitative medicine should be a major priority for future research.

3.7 Conclusion

This systematic review reveals a growing body of evidence supporting the efficacy of residual force enhancement contraction modalities *in vivo* skeletal muscle. The methodological quality of the evidence was primarily determined to be “fair,”; although this assessment should be considered in the context of the observational nature of the current studies. The phenomena of residual force enhancement and activation reduction were consistently observed in a wide range of muscles and joints, including simple single-muscle/single-joint, multi-muscle/single-joint, through to more complex multi-muscle/multi-joint actions. A range of contraction and activation intensities, stretch magnitudes, and velocities were investigated, and residual force enhancement was observed for each variable. The magnitude of residual force enhancement and activation reduction was dependent on contraction or activation intensity, muscle length, and age but was independent of angular velocity and stretch magnitude. Moreover, the effect of these variables differed depending on the complexity of the action (single-muscle/single-joint, multi-muscle/single-joint, multi-muscle/multi-joint). It is clear that the understanding of residual force enhancement *in vivo* human muscle is still in its infancy, and much is yet to be realised to fully comprehend the mechanisms and potential applications of the titin mechanism in human function. There should be a focus on investigating the efficacy of the use of the titin mechanism in athletic training and rehabilitative medicine.

Part II:

Do the hamstrings display residual force enhancement using maximal and submaximal post-stretch isometric contractions, and does an eccentric contraction occur during post-stretch isometric contractions?

Chapter 4: Post-stretch isometric contractions of the hamstrings: Just a brief stretch to achieve supramaximal isometric force

This chapter is an amended* version of the following peer-reviewed manuscript:

Chapman, N., Whitting, J. W., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2021). Poststretch Isometric Contractions of the Hamstrings: Just a Brief Stretch to Achieve Supramaximal Isometric Force. *Journal of Applied Biomechanics*, *1*(aop), 1-7.

**These amendments only relate to spelling or grammatical errors that have been identified since publication. No changes to methodology, results or findings have been made.*

Abstract

Hamstring strain injuries are common in sport. Supramaximal eccentric or high-intensity isometric contractions are favoured in hamstring strain injury prevention. However, the effect of combining these contraction modes in hamstring strain injury prevention programs as a post-stretch isometric contraction is uncertain. Post-stretch isometric contractions incorporate an active stretch and result in greater final isometric force than isometric contractions at comparable joint angles. This study sought to compare torque and muscle activation levels between maximal voluntary isometric contraction and maximal post-stretch isometric contractions of the knee flexors. Participants (n = 9) completed baseline maximal voluntary isometric contractions at 150° knee flexion and maximal post-stretch isometric contractions at 120° knee flexion actively stretching at $60°\cdot s^{-1}$ to 150° knee flexion for final isometric contraction. Torque of the knee flexors and $sEMG_{RMS}$ of biceps femoris long-head were simultaneously recorded. Torque and sEMG were compared between baseline and post-stretch isometric contractions at 150° knee flexion. Torque was 14% greater in the post-stretch isometric condition compared with baseline maximal voluntary isometric contractions (42.4 ± 20.7 N·m 14% ±22.1, $p < 0.001$) without increase in sEMG (root mean square) of biceps femoris long-head (-0.03 mV, ± 0.06, $p = 0.130$, $d = 0.93$). Combining eccentric and isometric contractions resulted in supramaximal levels of post-stretch isometric torque without increased activation of biceps femoris long-head.

4.1 Introduction

There is considerable interest in the prevention of hamstring strain injury, which has a high incidence during high-speed running (Green et al., 2020). The majority of hamstring strain injuries occur to the biceps femoris long-head during high-speed running (Bennell &

Crossley, 1996; Brooks et al., 2006; Ekstrand et al., 2011; Feeley et al., 2008; Orchard et al., 2013). Hamstring strain injuries incurred during high-speed running are likely to occur at or near maximal running velocity where high levels of tensile force are placed through biceps femoris long-head, at the proximal and distal musculotendinous junctions (Heiderscheit et al., 2010; Huygaerts et al., 2020). The high tensile forces experienced during the gait cycle's late swing phase are theorised to contribute to muscle injury (Kenneally-Dabrowski et al., 2019). In instances where hamstring strain injuries have been captured in real-time, the moment of injury was estimated to have occurred during the late swing phase (Heiderscheit et al., 2005; Schache et al., 2010; Schache et al., 2009). Debate exists over the knee flexors' function during high-speed running, specifically whether the knee flexors act eccentrically or are passively lengthened during the late swing phase of the gait cycle (Van Hooren & Bosch, 2017a). Accordingly, research into hamstring strain injuries includes both an eccentric and isometric contraction focus.

In primary prevention of hamstring strain injuries, the alteration of intrinsic, modifiable risk factors for injury include; lack of eccentric strength and short fascicle length (Pizzari et al., 2020). The use of eccentric contractions is purported to increase knee flexors' resilience against injury via increased knee flexor eccentric strength and increase in fascicle length of biceps femoris long-head (Timmins et al., 2016). Eccentrically biased contraction modes, such as the Nordic hamstring exercise (Brooks et al., 2006) and flywheel training (Askling et al., 2003), are encouraged throughout injury prevention programs (Askling et al., 2014; Askling et al., 2013). Despite growing evidence for the efficacy of use in injury prevention programs, adherence to eccentric training has been considered by some to be sub-par (van der Horst et al., 2020). Athletes and coaches may limit athlete engagement in eccentrically biased programs, particularly of supramaximal intensity, limiting athlete’s involvement in subsequent training sessions due to delayed onset muscle soreness (van der Horst et al., 2020). Athletes and coaches may favour other contraction modes that result in lower levels of delayed onset muscle soreness, such as isometric strength training.

Van Hooren and Bosch suggest that the hamstring muscles maintain a predominantly isometric action during the late swing phase in high-speed running (Van Hooren & Bosch, 2017a). Furthermore, the knee flexors' lack of isometric strength predisposes an athlete to injury during high-speed running (Van Hooren & Bosch, 2018). Van Hooren and Bosch propose when tensile forces within the musculotendinous unit exceed maximal isometric strength, a forced eccentric lengthening of the knee flexors results, which is causative to injury (Van Hooren & Bosch, 2017a). Thus, high-intensity isometric strength training has been hypothesised to be at least as effective as eccentric contractions during injury prevention training (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b) and may provide an adjunct approach to injury prevention. However, the use of isometric contractions in isolation neglects the proven importance that an eccentric stimulus has on eccentric strength, fascicle length and resultant hamstring strain injury risk (Bourne et al., 2018; Timmins, Bourne, et al., 2016; van der Horst et al., 2015; van der Horst et al., 2020; Van Dyk et al., 2019). It is possible that by using a combined eccentric/isometric contraction approach, such as the post-stretch isometric contraction, the athlete could experience the benefits of both the eccentric and isometric stimulus.

The post-stretch isometric contraction is initiated with an isometric contraction at a shorter muscle length, immediately followed by a highly controlled eccentric contraction that ends with an isometric contraction at the new longer muscle length. During this series of contractions, torque spikes during the eccentric phase then reaches a steady-state during the final isometric contraction resulting in the phenomenon of “residual force enhancement”.

Elevated steady-state isometric force following an active stretch, termed residual force enhancement, exceeds the isometric force at the corresponding muscle length without prior stretch (Edman et al., 1982) and without increasing muscle activation (Hahn et al., 2010). The phenomenon of residual force enhancement has been observed *in vitro* in single fibre preparations and whole muscle preparations (Campbell & Campbell, 2011; Edman et al., 1982; Herzog & Leonard, 2000; Peterson et al., 2004; Pinnell et al., 2019; Rassier et al., 2003; Schachar et al., 2004), *in vivo* with electrical stimulation (Cook & McDonagh, 1995; Lee & Herzog, 2002; Pinniger & Cresswell, 2007; Ruiter et al., 2000) and voluntary contractions (Hahn et al., 2010; Lee & Herzog, 2002; Oskouei & Herzog, 2005; Pinniger & Cresswell, 2007; Tilp et al., 2009). The magnitude of residual force enhancement increases with increasing stretch magnitudes (Bullimore et al., 2007; Edman et al., 1978; Herzog & Leonard, 2005), is independent of stretch velocity (Lee & Herzog, 2002; Sugi & Tsuchiya, 1988), and is more pronounced on the descending limb of the force-length relationship (Julian & Morgan, 1979; Morgan et al., 2000; Peterson et al., 2004). Furthermore, residual force enhancement torque has been observed to exceed isometric torque by up to 400% (Campbell & Campbell, 2011). Despite these potential benefits for using a combined contraction modality in the knee flexors, the acute effects of post-stretch isometric contractions in the knee flexors *in vivo* is poorly understood. To date, only one investigation has reported residual force enhancement in the hamstring muscle group, with torque following post-stretch isometric contractions exceeding maximal voluntary isometric torques by 4-5% (Shim & Garner, 2012). Interestingly, Shim and Garner (2012) state that the residual force enhancement observed in their study may not represent the knee flexors' actual capacity and reason that methodological constraints during the isometric pre-activation phase may have limited the magnitude of residual force enhancement. They state that with appropriate levels of isometric pre-activation during the post-stretch isometric contraction, the knee flexors have the potential to generate a much greater magnitude of residual force enhancement (Shim & Garner, 2012).

The benefits of using a contraction mode, which utilises both eccentric and isometric modalities in the knee flexors, is unknown. It has been suggested that there is a discrepancy between the proposed isometric action of the knee flexors during high-speed running and eccentric training currently implemented (Van Hooren & Bosch, 2017a). The utilization of a singular approach may explain high hamstring strain injury incidence (Van Hooren & Bosch, 2017a). Therefore, further investigation of the acute effects of combining two contraction modes commonly implemented in hamstring injury prevention programs is warranted. This study aimed to observe the presence of residual force enhancement using highly controlled maximal post-stretch isometric contractions at joint angles indicative of long muscle lengths. It was hypothesised that residual force enhancement would be observed in the knee flexors without an increase in muscle activation.

4.2 Methods

4.2.1 Participants

Prior to recruitment, an apriori calculation was undertaken which noted nine participants would be required appropriately power the study. Nine physically active participants (8 males and 1 female, 24 yrs ± 6 yrs), provided written informed consent to participate in the study and were advised that they were free to withdraw at any time. All participants were confirmed to be free from diagnosed lower limb musculoskeletal injury and neurologic conditions in the preceding 12 weeks. The study and its associated methodology was approved by the Institutional Human Research Ethics Committee (ECN: 2019/090).

4.2.2 Experimental set-up

Participants were seated on a Biodex System 3 dynamometer (Biodex Medical Systems, Shirley, NY accuracy ± 7 N·m, resolution ± 0.02 N·m), which recorded torque for all experiments. In this position, each participant’s right hip was flexed to 80°, and the right knee flexed at 120° and 150° (i.e., terminal knee extension, 180°). Hip joint angle was confirmed via manual goniometer (J.A. Preston Corporation, Clifton, NJ). To confirm hip angle, the goniometer, was centred on the greater trochanter of the right hip and aligned with the lateral midline of the abdomen and lateral midline of the femur. The axis of rotation of the right knee was aligned with the axis of rotation of the dynamometer. The ankle cuff was attached 2.5 cm above the dorsal surface of the foot. Inelastic stabilisation straps were placed over the right distal femur, pelvis and chest to mitigate extraneous movements during contractions (Figure 5).

SEMG signals of biceps femoris long-head were recorded during all trials using a Trigno Wireless surface electromyography system with double differentiated surface electrodes (Delsys, Natick, MA, USA). The electrode was placed per the SENIAM guidelines (Hermens et al., 1999). The biceps femoris long-head electrode was placed on the muscle at 50% of the distance along the line between the ischial tuberosity and the tibia's lateral epicondyle. The electrode location on the skin was prepared by first shaving, abrading, then wiping the area with alcoholic wipes. A surgical adhesive tape was used along with double-sided adhesive electrode–skin interface, to secure the electrode to the skin.

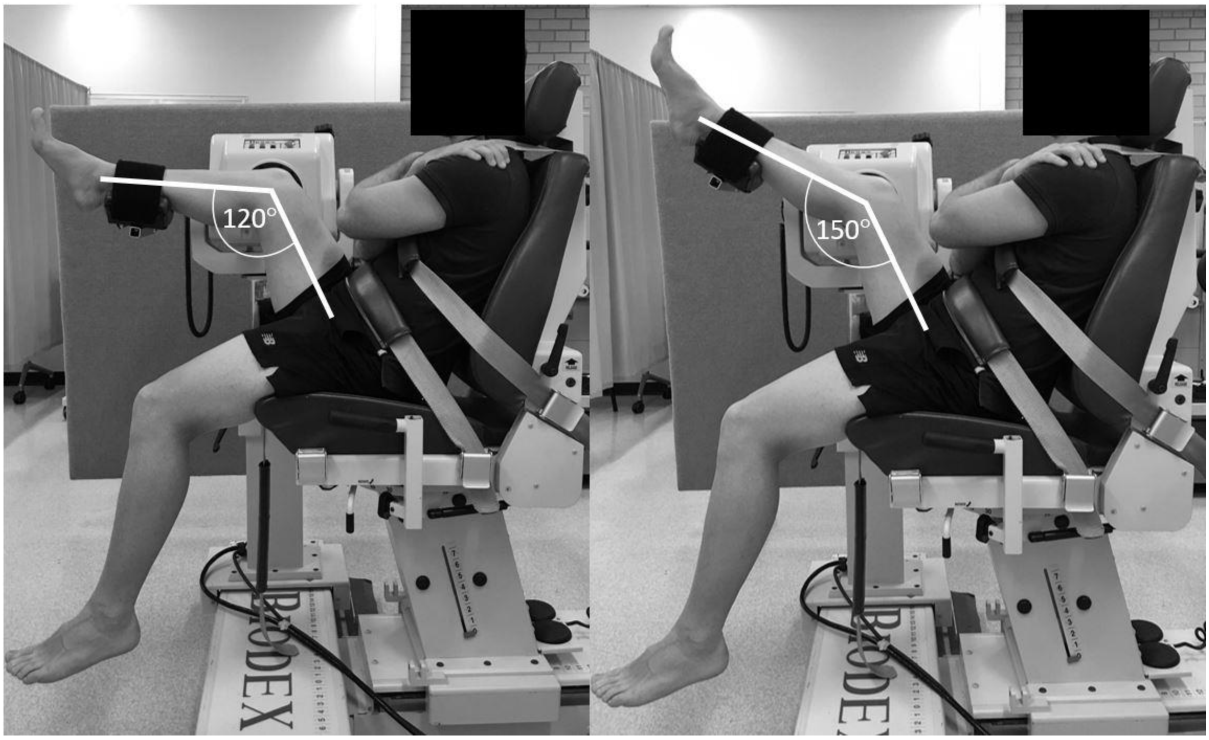


Figure 5 *Participants took an upright seated position in the Biodex chair with the involved hip flexed at 80º and knee at 120º or 150º, where 180º is full knee extension.*

The sEMG signals were sampled at 2000Hz (bandpass filtered at 10-500Hz). Biodex data was sampled at 1000Hz using a 12-bit analogue to digital converter (PowerLab System 16/35, ADInstruments, Bella Vista, Australia). Biodex and sEMG signals were synchronised with LabChart software (Pro Modules 2014, version 8, ADInstruments, Bella Vista, Australia).

4.2.3 Experimental Protocol

Following a 5-minute self-paced warmup on a cycle ergometer, each participant performed three baseline maximal voluntary isometric contractions of the knee flexors (5 s duration) at 150° knee flexion. The experimental post-stretch isometric) contraction involved three experimental trials in which the knee flexors were voluntarily activated maximally for 6.5 s, consisted of the following sequence of contractions; i) 1s maximal voluntary isometric contraction at 120° knee flexion, ii) a maximal contraction of the knee flexors during active knee extension over 30° at $60°\cdot s^{-1}$ and, iii) 5 s maximal voluntary isometric contraction at 150° knee flexion. To encourage maximal effort, each participant was provided with visual feedback of the torque traces on a television monitor and were verbally encouraged to produce their maximal effort during all voluntary efforts. It is noted that the interpolated twitch technique was not implemented in the current study, and as such, despite maximal effort on behalf of the participants, the maximal voluntary contraction was unable to be systematically confirmed. Between the individual trials, participants rested for 90 s. Between baseline and experimental conditions, participants rested for 5 minutes.

4.2.4 Data Processing and Analysis

Mean torque (N·m) was derived from a 3 s epoch for each experimental trial. Net torque (N·m) was averaged across contractions for each contraction condition in each participant. Mean $sEMG_{RMS}$ (mV) taken from raw sEMG was derived from a 3 s epoch between 2 - 5 s in the baseline maximal voluntary isometric contraction trials and 2 – 5 s following the end of the joint rotation during the isometric steady-state phase for each post-stretch isometric experimental trial. All post-stretch isometric $sEMG_{RMS}$ values recorded during isometric steady-state (2 – 5 s epoch as noted above) were normalised to baseline maximal voluntary isometric contraction during the equivalent 2 - 5 s epoch. The magnitude of residual force enhancement was defined as the absolute torque increase (N·m) and a percentage change from the reference maximal voluntary isometric contraction at 150°. The following equation previously used by Dalton et al. (2018) was used to calculate percentage change residual force enhancement (rFE):

$$rFE\ \%\ \Delta = [\frac{(Isometric\ torque\ N\cdot m\ following\ active\ lengthening - reference\ MVIC\ N\cdot m)}{Reference\ MVIC\ N\cdot m}] \times 100\%$$

All variables of interest were tested using the Shapiro-Wilk tests and found to be normally distributed. A paired T-test was performed to calculate the difference in torque and s $\mathrm{sEMG}_{\mathrm{RMS}}$ of biceps femoris long-head between the baseline maximal voluntary isometric contraction at 150° knee flexion and post-stretch isometric steady state at 150° knee flexion. Effect sizes were calculated using Cohen's d (0.20 = small, 0.50 = medium, 0.80 = large effect size) (Rice & Harris, 2005). Significance was determined based on an $\alpha = 0.05$. Descriptive data in text and figures are reported as mean and standard deviation (± SD).

4.3 Results

Compared with baseline isometric force, significantly elevated post-stretch isometric steady-state force was observed (as residual force enhancement) in the knee flexors in the absence of increased muscle activation (Figure 6). Thus, both study hypotheses were confirmed. Elevated isometric torque was recorded in the steady-state during post-stretch isometric contractions of the knee flexors (42.4 ± 20.7 N·m 14% ±22.1%, $p = < 0.01$, $d = 0.70$) compared with baseline maximal voluntary isometric contraction. Of note, all participants displayed residual force enhancement, and as such, there were no non-responders within the participant cohort.

Despite the presence of residual force enhancement in the knee flexors, there was no difference in muscle activation between baseline maximal voluntary isometric contraction and the steady-state post-stretch isometric contraction of biceps femoris long-head (raw $\mathrm{sEMG}_{\mathrm{RMS}}$) (-0.03 mV, ± 0.06, normalised $\mathrm{sEMG}_{\mathrm{RMS}}$ = 0.74 mV, ± 0.03, $p = 0.13$, $d = 0.93$).

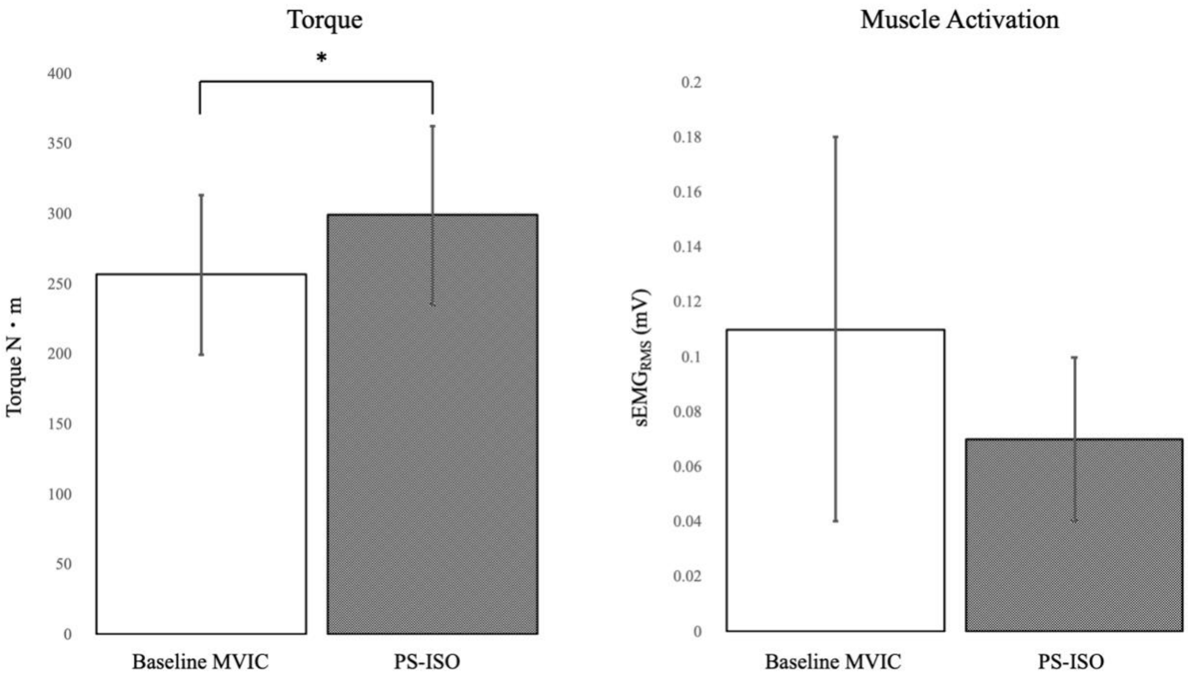


Figure 6 *Baseline maximal voluntary isometric contraction and post-stretch isometric contraction values of torque and muscle activation (M ±SD). *Significant difference (p = 0.05).*

4.4 Discussion

The present study confirmed elevated torque in the isometric steady-state during post-stretch isometric contractions without increased knee flexors' muscle activation. Hence, each of our hypotheses were confirmed. The magnitude of residual force enhancement calculated in the current study (14%) was similar to previous findings of upper and lower limb muscles (4-16%) (Chapman et al., 2018), but was notably higher than the only other investigation of the knee flexors muscle group (4-5%) (Shim & Garner, 2012). We propose that the magnitude of post-stretch isometric steady-state torque recorded in the current study meets the intensity to be categorised as supramaximal or, using the language of Van Hooren and Bosch (2017b), “high intensity” isometric torque. While it is uncertain what explicit influence muscle activation had on residual force enhancement, several factors have been identified which may explain the supramaximal magnitude of residual force enhancement in the current study; i) inter-muscle activation variation (Seiberl et al., 2010), ii) isometric pre-activation (Fukutani et al., 2016b), iii) the magnitude of stretch (Chapman et al., 2018), and iv) the position of the knee flexors on the length-tension relationship (Chapman et al., 2018).

Due to a lack of significant difference between baseline maximal voluntary isometric contraction and post-stretch isometric steady-state muscle activation amplitudes, it seems that the residual force enhancement observed in our study was not as a consequence of increased

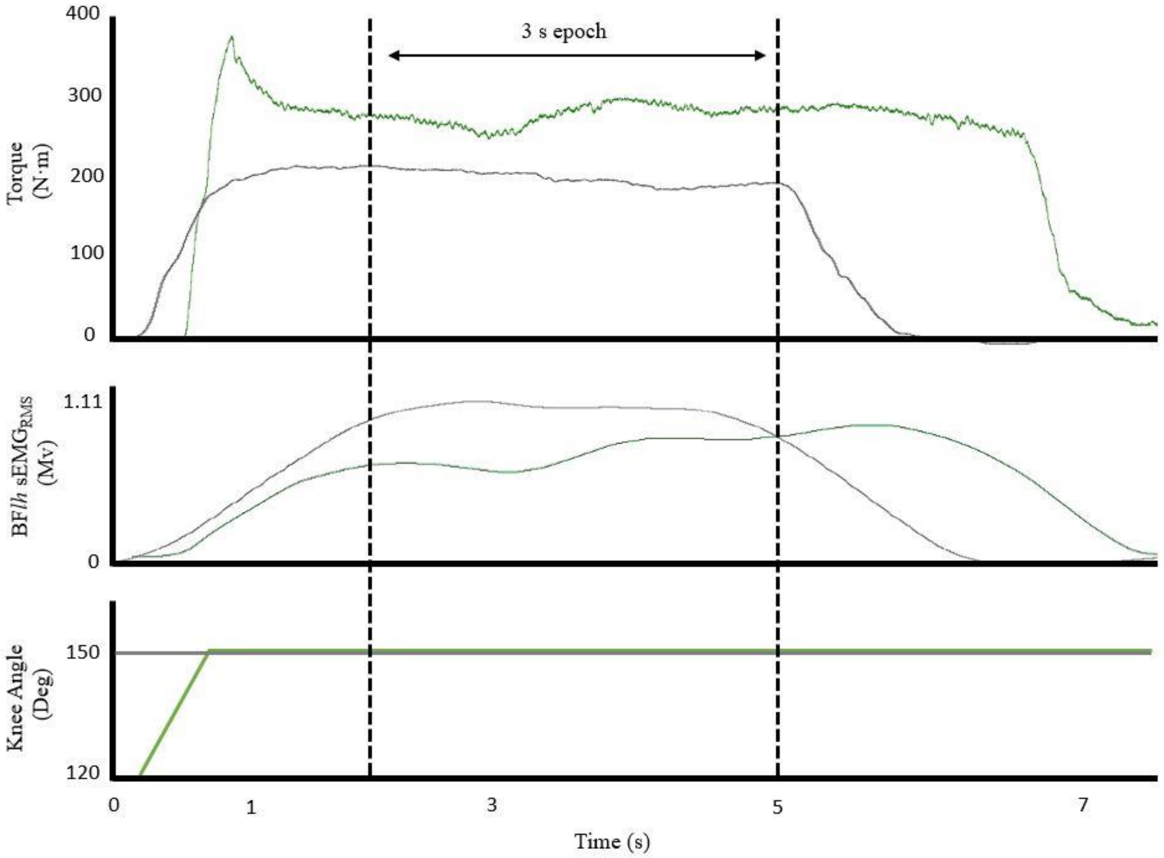


Figure 7 *A single participant's torque,* $sEMG_{RMS}$ *and joint excursion torque for baseline maximal voluntary isometric contraction (black) and post-stretch isometric contractions (colour) of the knee flexors. Torque and* $sEMG_{RMS}$ *were calculated over a 3 s epoch. The epoch, indicated by the dashed vertical lines, was over 2 – 5 s of baseline and post-stretch isometric contractions.*

activation via additional motor unit recruitment within biceps femoris long-head. In this regard, no direct comparisons can be drawn with the study of Shim and Garner (2012), as knee flexor muscle activation was not reported in their study. Nonetheless, despite our surface EMG findings we acknowledge the possibility that additional motor unit recruitment may have been present within other muscles in the knee flexor group, albeit not directly observed. While investigating residual force enhancement, Seiberl et al. (2012) observed a variation in muscle activation between individual quadriceps muscles during submaximal post-stretch isometric contractions. The activation of the rectus femoris was significantly higher at 30% contraction intensity and significantly lower at 60% contraction intensity. Simultaneously, the vastus lateralis and vastus medialis muscles did not demonstrate inter muscle activation differences at either submaximal contraction intensity. Despite the use of maximal intensity, inter muscle activation variation may have influenced the magnitude of residual force enhancement in the current study in a similar manner to that of the quadriceps group (Seiberl et al., 2012). Also, Chen and Power (2019) noted that an increase in antagonist co-activation influenced the force output of the ankle dorsiflexors, resulting in decreased residual force enhancement in their study. We posit that the level of antagonist co-activation of the knee extensors is likely to be minimal and have had little effect on the magnitude of force produced by the knee flexors in the current study. Given the complexity of muscle activation, further investigation is warranted into individual muscle activation patterns during post-stretch isometric contractions.

Secondly, Shim and Garner (Shim & Garner, 2012) identified that the isometric pre-activation protocol implemented in their study might have been suboptimal, impacting the magnitude of residual force enhancement they observed. Levels at which isometric pre-activation is performed, have been shown to influence the magnitude of residual force enhancement by increasing fascicle elongation during the active stretch (Fukutani et al., 2019). The potential exists that if lower levels of isometric pre-activation did occur in the Shim and Garner (2012) study, fascicle elongation (Fukutani et al., 2019) and titin activation (Campbell & Campbell, 2011; Edman et al., 1982; Herzog & Leonard, 2000; Peterson et al., 2004; Rassier et al., 2003; Schachar et al., 2004) might also have been affected, leading to lower levels of residual force enhancement. This theory is further strengthened by a recent *in vitro* investigation by Mahmood, Sawatsky and Herzog (2021), who reiterated that the timing of musculotendinous unit shortening before stretch is crucial for residual force enhancement. Furthermore, Mahmood, Sawatsky and Herzog (2021) state that where musculotendinous unit shortening occurs during the stretch (joint rotation) can negatively impact the magnitude of residual force enhancement. These findings may also explain decreased residual force enhancement magnitude in Shim and Garner's study (Shim & Garner, 2012). We postulate that the levels of isometric pre-activation developed in the current study, may been great enough to have influenced the magnitude of residual force enhancement by lengthening of the contractile element during the joint rotation (Bobbert & Casius, 2005; Fukutani et al., 2016b; Atsuki Fukutani et al., 2019). Lengthening is likely to have influenced tension in the giant protein titin, and therefore the capacity of titin to contribute to residual force enhancement as extensively described by investigators of *in vitro* and in-situ muscle models (Campbell & Campbell, 2011; Edman et al., 1982; Herzog & Leonard, 2000; Peterson et al., 2004; Rassier et al., 2003; Schachar et al., 2004).

In addition to suggesting that residual force enhancement was potentially affected by the level of the isometric pre-activation protocol in their study, Shim and Garner (2012) also state that their methodology may have inadvertently resulted a reduction in stretch magnitude. By instructing their participants to ramp quickly to full activation and by triggering stretch at

10% maximum effort, a portion of the 30° stretch was potentially completed before full muscle activation. The magnitude of residual force enhancement is known to increase with a greater magnitude of stretch (Bobbert & Casius, 2005; Edman et al., 1978). Thus, any reduction in stretch magnitude could reduce the magnitude of residual force enhancement. The limitation identified by Shim and Garner (2012) may contribute to understanding the disparity in residual force enhancement magnitude between their study and the current study. Interestingly, the joint rotation in the current study (30°), is relatively modest in comparison to the joint rotations seen in conventional exercise modes such as the Nordic hamstring exercise (Brooks et al., 2006). By increasing the joint rotation during the post-stretch isometric contraction to match conventional exercise modes, it is not unreasonable to expect greater residual force enhancement magnitude than that observed in the current study. However, this remains untested in the knee flexors. Finally, the position of the hip and knee in the current study, (hip flexed to 80°, knee flexed at 120° and 150°), differed with the hip and knee position used by Shim and Garner (2012) (hip flexed to 90 °, knee flexed at 120° and 150°). Compared with Shim and Garner (Shim & Garner, 2012), the hip and knee position used in the current study resulted in the knee flexors being active at comparatively longer musculotendinous unit lengths and closer to the end range of the descending limb of the length-tension relationship (Chleboun et al., 2001). It is understood that the greatest magnitude of residual force enhancement is consistently performed further into the descending limb of the length-tension relationship (Chapman et al., 2018). Thus, our findings support previous evidence which states, to maximise isometric steady-state torque, the hip and knee position should allow for post-stretch isometric contractions of the knee flexors to be performed deep into the descending limb of the length-tension relationship.

There is considerable interest in understanding the influence that eccentric and isometric contraction modes each have on the resistance of the knee flexors to injury. Due to the high rate of injury and injury recurrence (de Vos et al., 2020), it is clear that a complete understanding of hamstring strain injury prevention and rehabilitation is yet to be reached. Evidence provided here suggests that the combined use of both contraction modes on the descending limb of the length-tension relationship can yield supramaximal levels of isometric torque at muscle activation levels equivalent to maximal voluntary isometric contraction. Although untested, with chronic use, post-stretch isometric contractions could theoretically lead to an increased tolerance to high intensity eccentric and isometric forces, such as those seen during the late swing phase and early stance of the gait cycle in high-speed running. Thus, if chronic adaptation to supramaximal levels of torque is proven to occur, the use of post-stretch isometric contractions may provide an additional hamstring strain injury prevention tool for use by athletes and coaches.

Chapter 5: Maximal and submaximal isometric torque is elevated immediately following highly controlled active stretches of the hamstrings

This chapter is an amended* version of the following peer-reviewed manuscript:

Chapman, N., Whitting, J.W., Broadbent, S., Crowley-McHattan, Z.J., Meir, R. (2021). Maximal and submaximal isometric torque is elevated immediately following highly controlled active stretches of the hamstrings. *Journal of Electromyography and Kinesiology*, 56, 102500.

**These amendments only relate to spelling or grammatical errors that have been identified since publication. No changes to methodology, results or findings have been made.*

Abstract

Hamstring strain rehabilitation programs with an eccentric bias are effective but have a low adherence rate. Post-stretch isometric contractions incorporate a highly controlled eccentric contraction followed by an isometric contraction resulting in elevated torque following the stretch, compared with isometric contractions at the same joint angle. This study measured torque, activation, and musculotendinous unit behaviour of the hamstrings during post-stretch isometric contractions of maximal and submaximal levels using two stretch amplitudes. Ten male participants (24.6 years ±2.22 years) completed maximal and submaximal baseline isometric contractions at 90°, 120° and 150° knee flexion and post-stretch isometric contractions of maximal and submaximal intensity initiated at 90° and 120° incorporating an active stretch of 30° and 60° at $60°\cdot s^{-1}$. Torque and muscle activation of the knee flexors were simultaneously recorded. Musculotendinous unit behaviour of the biceps femoris long head was recorded via ultrasound during all post-stretch isometric contractions. Compared with baseline, torque was 8% and 39% greater in the maximal and submaximal post-stretch isometric conditions, respectively, with no change in muscle activation. The biceps femoris long head muscle lengthened during all post-stretch isometric contractions. Post-stretch isometric contractions may be beneficial where the effects of highly controlled eccentric contractions and elevated isometric torque are desired, such as hamstring rehabilitation.

5.1 Introduction

Despite considerable interest in injury prevention and rehabilitation strategies, the incidence and recurrence of hamstring strain injuries remain high (Brooks et al., 2006). The biceps femoris long-head is the most commonly injured of the hamstring muscle group (Gibbs et al., 2004), and high-speed running, one of the most common injury mechanisms (Gabbe, Bennell, et al., 2006). A lack of isometric strength leading to a forced eccentric lengthening during the late swing phase of high-speed running or braking during the late swing phase of high-speed running is proposed as potential causes of injury (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b). Rehabilitation of hamstring injuries typically focuses on; i) minimisation of scar tissue formation and subsequent reduction in musculotendinous unit extensibility (Proske et al., 2004), ii) the restoration of isometric and eccentric strength (Hickey et al., 2020; Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017) and iii) the correction of altered neuromuscular control following injury (Erickson & Sherry, 2017). It has also been proposed that rehabilitation programs address psychosocial factors, such as apprehension and fear of movement when completing ballistic tasks (Askling et al., 2010). However, a consensus is lacking regarding best practices in hamstring injury rehabilitation (Comfort et al., 2009), which may explain lengthy recovery times typically experienced by athletes (Orchard & Best, 2002).

Eccentric strength training such as the L-protocol (Askling et al., 2014) and the Nordic hamstring exercise (Brockett et al., 2001) are commonly used in rehabilitation. Strength training with an eccentric bias has been shown to offset the effects of scar tissue (Proske et al., 2004), increase in series compliance resulting in a rightward shift in the length-tension curve (Tyler et al., 2015). However, despite the evidence for effectiveness, negative perceptions persist that eccentric exercise increases pain, and thus adherence to eccentric exercise remains sub-par (van der Horst et al., 2020). This perception is potentially re-enforced by conventional guidelines which recommend the avoidance of pain during the treatment of acute muscle injuries (Jarvinen et al., 2005). Notwithstanding this, these conventional guidelines concede that the current treatment principles lack a scientific basis (Jarvinen et al., 2005). Nonetheless, this contradictory approach may influence the exercise selection of some practitioners towards more conservative contraction modes such as isometric contractions (Heiderscheit et al., 2010).

In contrast, isometric contractions are often favoured in early-stage rehabilitation and are advocated to be at least as effective as eccentric contractions (Van Hooren & Bosch, 2017b). There may be favourable outcomes in combining eccentric and isometric contractions by harnessing the benefits of history dependence of muscle. It is also feasible that having greater control over the intensity and angular velocity of eccentric contractions may prove to be a more palatable approach where adherence to eccentric training is sub-par (van der Horst et al., 2020).

A potential option is the post-stretch isometric contraction. A post-stretch isometric contraction is initiated with an isometric contraction at a shorter muscle length, immediately followed by a highly controlled eccentric contraction, then a final isometric contraction at the new longer muscle length. *In vitro* evidence indicates that torque spikes sharply during the eccentric phase of the post-stretch isometric before normalising somewhat; however, it remains elevated during the post-stretch isometric steady-state contraction. The post-stretch isometric steady-state torque exceeds the predicted isometric torque at the corresponding muscle length without prior stretch, termed residual force enhancement (Edman et al., 1982). It is theorised that the enhanced force is due to the giant protein titin increasing stiffness during the stretch and maintained during the steady-state isometric contraction following stretch (Herzog & Leonard, 2005). Notably, the enhanced force is observed in the absence of increased muscle activation (Herzog & Leonard, 2005). The magnitude of residual force enhancement is greatest at long muscle lengths and increases with increasing stretch amplitude (Herzog & Leonard, 2005), though it is independent of stretch velocity (Lee &

Herzog, 2002). Although *in vitro* evidence of residual force enhancement continues to build, to date, a single *in vivo* investigation has been undertaken which reported residual force enhancement of 4-5% in the hamstrings muscle group using maximal post-stretch isometric contractions (Shim & Garner, 2012). The magnitude of residual force enhancement *in vivo* has been shown to range from 3%-25% in other lower limb muscles during maximal and submaximal voluntary contractions (Chen & Power, 2019). No study has, as yet, investigated residual force enhancement in the hamstrings muscle group using activation-matched submaximal post-stretch isometric contractions which are more relevant in rehabilitation.

The evidence for the use of eccentric stimulus in rehabilitation continues to mount, yet the effects of using a combined eccentric and isometric contraction mode which is highly controlled, are as yet, unknown. Seiberl et al. (2015) have suggested that the phenomenon of residual force enhancement may be applicable in instances where high levels of force are required, particularly when the neuromuscular system is weakened. Therefore, an investigation of the acute effects of post-stretch isometric contractions of the hamstrings group is warranted. This study aimed to observe the presence of residual force enhancement using highly controlled maximal and submaximal post-stretch isometric contractions using two stretch amplitudes. The study also aimed to observe musculotendinous unit behaviour during the joint rotation of the post-stretch isometric contraction. It was hypothesised that residual force enhancement would be observed during all maximal and submaximal post-stretch isometric contractions without increased muscle activation. Secondly, it was hypothesised that the biceps femoris long-head muscle would lengthen, confirming an eccentric contraction during the joint rotation of maximal and submaximal post-stretch isometric contractions using two stretch amplitudes.

5.2 Methods

5.2.1 Participants

Prior to recruitment, a priori calculation was calculated (n = 8). Ten physically active male participants (24.6 years ±2.22 years) provided written, informed consent to participate in the study. All participants were free from diagnosed lower limb musculoskeletal injury and neurologic conditions in the preceding 12 weeks. The study was approved by the Institutional Human Research Ethics Committee (ECN: 2019/090).

5.2.2 Experimental set-up

Participants were asked to assume a prone position on a Biodex System 3 dynamometer (Biodex Medical Systems, Shirley, NY; accuracy ± 7 Nm, resolution ± 0.02 N·m), which recorded torque measurements for all experiments. The axis of rotation of the right knee was aligned with the axis of rotation of the dynamometer. The ankle cuff was attached 25 mm above the dorsal surface of the foot. Inelastic straps were placed over the L4/5 area to mitigate extraneous movements of the trunk during contractions (Figure 7). A manual goniometer (J.A. Preston Corporation, Clifton, NJ) was used to confirm that each participant’s hip angle was set between to be between 170° and 180° (180° representing neutral hip position). The goniometer was centred on the greater trochanter of the right hip and aligned with the lateral midline of the abdomen and lateral midline of the femur.

Surface electromyography (sEMG) signals of Biceps femoris long-head and semitendinosus were recorded during all trials using a Trigno Wireless sEMG system with double differentiated surface electrodes (Delsys, Natick, MA, USA). Electrodes were placed, and sites were prepared per SENIAM guidelines (Hermens et al., 1999).

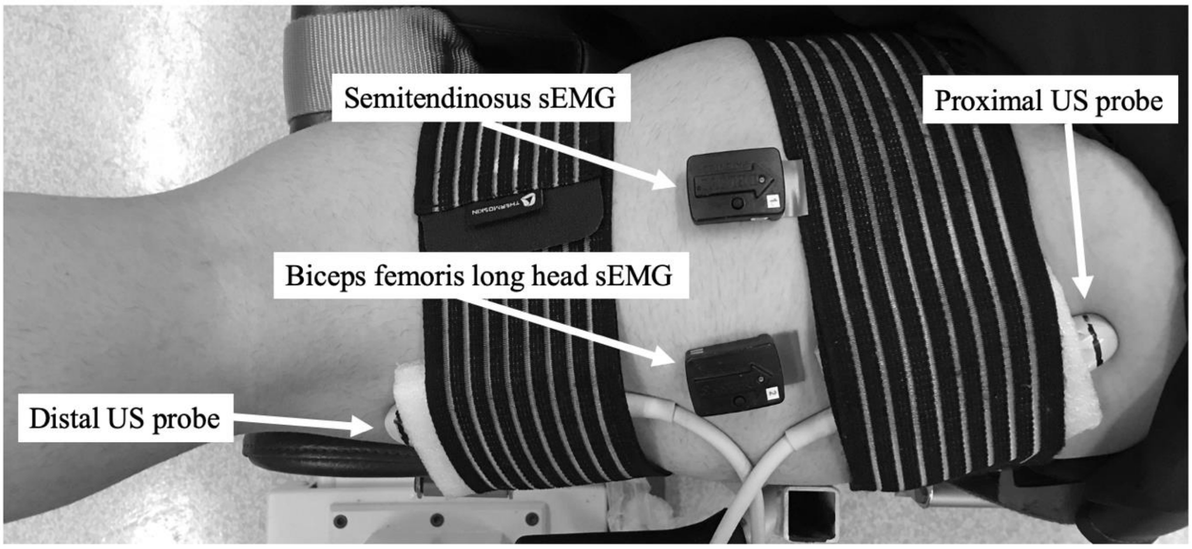


Figure 8 *The participant was positioned lying prone on the dynamometer. The positions of the proximal and distal ultrasound probes and the sEMG sensors position on biceps femoris long-head and Semitendinosus are pictured.*

Distal and proximal musculotendinous junctions were observed via B-mode ultrasound (MicrUS EXT-1H, Telemed Vilnius, Lithuania) using a dual-head linear transducer (frequency, 12Hz; depth, 8cm; field of view, 12 x 70mm). Each transducer was located over the proximal and distal musculotendinous junctions of biceps femoris long-head respectively and aligned parallel with the direction of the muscle fibres. Transducers were firmly fixed to the leg using two custom-built Styrofoam housings (Figure 8) and secured in place with elastic bandages (Tilp et al., 2011). A GoPro (GoPro Hero 7 Black, GoPro Inc, San Mateo, CA, USA), positioned directly above the participant's right leg, recorded video images of the position of each ultrasound probe. B-mode ultrasound was chosen for its reproducibility (Kwah et al., 2013), high intra-class correlation coefficients (0.99) (Aeles et al., 2017), and suitability to study dynamic muscle changes (Franchi et al., 2018). As conventional B-mode ultrasound presents field of view limitations when viewing biceps femoris long-head fascicles (Franchi et al., 2018), the investigators chose to observe and calculate the positional change of individual musculotendinous junctions during post-stretch isometric contractions to confirm whole muscle and tendon length change.

The sEMG signals were sampled at 2000Hz (bandpass filtered at 10-500Hz). Biodex data were sampled at 1000Hz using a 12-bit analogue to digital converter (PowerLab System 16/35, ADInstruments, Bella Vista, Australia). Ultrasound video images were visualised using Echo Wave II software (Telemed Vilnius, Lithuania). GoPro video images were recorded at 1080p, 60fps. Biodex, sEMG, ultrasound, and GoPro data were synchronised with LabChart software (Pro Modules 2014, version 8, ADInstruments, Bella Vista, Australia). Tracker software (Tracker Version 5.1.5) was used to plot and measure the positional change (in mm) of each musculotendinous junction during post-stretch isometric contractions in the ultrasound video images.

5.2.3 Experimental procedures

Following a 5-minute warmup on a cycle ergometer, participants performed three baseline maximal voluntary isometric contractions (MVIC), and three baseline activation matched voluntary isometric contractions of the knee flexors (5 s duration); the latter was performed at three knee joint angles (90°, 120°, and 150° knee position, 180° representing full knee extension). Participants rested for 90 s after each maximal or activation matched trial, with an additional 5 min rest between maximal and submaximal baseline trials. The activation matched baseline was calculated using the activation of the semitendinosus muscle. The mean of the root mean square (RMS) amplitude (mV) of the sEMG (sEMG_{RMS}: moving average window = 50 ms) was derived from a 3 s epoch, corresponding to seconds 2-4 in the MVIC baseline contractions. To standardise activation levels during activation matched baseline trials (50% of MVIC), a matching target was calculated from this MVIC epoch with a ± 5% tolerance. The 50% activation matched trace was visualised on a computer monitor positioned within direct sight of participants.

Participants performed three maximal and three submaximal activation matched post-stretch isometric contractions of the knee flexors at 90° knee flexion (60° stretch amplitude) and 120° knee flexion, (30° stretch amplitude) respectively (PS-ISO$_{\text{MAX-long}}$, PS-ISO$_{\text{SUB-long}}$, PS-ISO$_{\text{MAX-short,}}$ and PS-ISO$_{\text{SUB-short}}$). A total of 12 experimental contractions. All active stretches occurred at a constant angular velocity of $60°\cdot s^{-1}$ and were voluntarily activated for a total of 7 s, or 6.5 s respectively for the 60° and 30° joint excursions, respectively. Participants were verbally encouraged to produce maximal effort during all maximal experimental conditions and to closely match the activation matching target during all submaximal experimental conditions. Each participant could view either a torque trace (PS-ISO$_{\text{MAX}}$) or semitendinosus sEMG$_{\text{RMS}}$ trace (PS-ISO$_{\text{SUB}}$) on a television monitor located in their direct line of sight for visual feedback. Participants rested for 90 s between trials and 5 minutes between each experimental condition.

5.2.4 Data analysis

Mean torque (N·m) was derived from a 3 s epoch corresponding to 3-5s for each baseline isometric and post-stretch isometric steady-state experimental trial. Net torque (N·m) was averaged across contractions for each contraction condition in each participant. Mean sEMG$_{\text{RMS}}$ (mV) was derived from a 3 s epoch corresponding to 3-5s for each experimental trial. The mean of the three experimental trials in each condition was used as the overall participant mean value. The residual force enhancement magnitude was defined as the absolute torque increase (Nm) and a percentage change from the baseline MVIC and baseline

50% MVIA at 150°. The following equation was used to calculate percentage change residual force enhancement (Dalton et al., 2018):

$$rFE\ \%\ \Delta = [\frac{(Isometric\ torque\ N{\cdot}m\ following\ active\ lengthening - reference\ MVIC\ N{\cdot}m)}{Reference\ MVIC\ N{\cdot}m}] \times 100\%$$

For musculotendinous unit length change measurements, the positions of origin, insertion, and ultrasound transducers located over the proximal and distal musculotendinous junctions with the knee flexed at 90°, 120°, and 150° were determined by direct measurement (mm) at the time of data collection. Direct measurements were later confirmed by using the GoPro video images, which were visualised and measured (mm) using Tracker software. A series of ultrasound images (image sequence recordings) were used to determine musculotendinous junction positional change during post-stretch isometric contractions in each post-stretch isometric contraction. This technique was adapted from Aeles et al. (2017), who noted an average intra-rater ICC of 0.857 and SEM of 2.59mm ± 1.56mm. Positional measurements are illustrated in Figure 9. Intra-rater reliability was established for the ultrasound measurements using Cronbach's alpha; (CE = 0.980, proximal tendon = 0.995, and distal tendon = 0.982)

The length of the muscle, proximal and distal series elastic element were calculated via the equations below;

Muscle length = $c + d + e$

Proximal series elastic element length = $a + b$

Distal series elastic element length = $f + g$

To calculate the change in length of the muscle, proximal series elastic element, and distal series elastic element during the active stretch phase of the post-stretch isometric contraction, the post-stretch lengths (150° knee flexion) were subtracted from the pre-stretch lengths (either 90° or 120° knee flexion) (Figure 9).

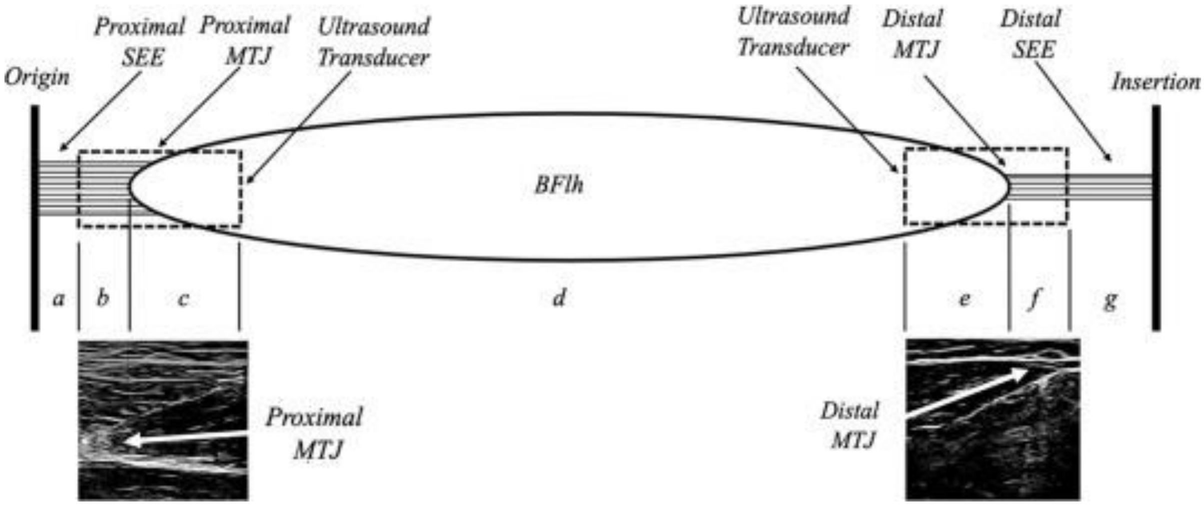


Figure 9 *Schematic of the ultrasound transducer positioning over the biceps femoris long-head musculotendinous unit and of the lengths used to calculate positional change of the CE and proximal and distal SEE. a = muscle origin to proximal edge of the proximal transducer, b = proximal edge of the proximal edge of the proximal transducer to proximal MTJ, c = proximal MTJ to the distal edge of the proximal transducer, d = distal edge of the proximal transducer to the proximal edge of the distal transducer, e = proximal edge of the distal transducer to the distal MTJ, f = distal MTJ to the distal edge of the distal transducer, g = distal transducer to muscle insertion.*

All variables of interest were tested using the Shapiro-Wilk tests and found to be normally distributed. A repeated-measures ANOVA was performed to calculate the differences in; torque, sEMG$_{RMS}$ of biceps femoris long-head and semitendinosus, and muscle and tendon length between the baseline isometric contraction at 150° knee flexion and post-stretch isometric steady state at 150° knee flexion. These calculations were made for all experimental conditions, maximal and submaximal activation matched conditions. Effect sizes were calculated using partial eta squared (0.20 = small, 0.50 = medium, 0.80 = large effect size) (Cohen, 2013). Significance was determined based on an $\alpha = 0.05$. Descriptive data in text and figures are reported as mean and standard deviation (± SD).

5.3 Results

5.3.1 Torque

A significant residual force enhancement was observed across maximal ($p = 0.013$, $\eta^2 = 0.381$) and submaximal residual force enhancement conditions ($p = 0.001$, $\eta^2 = 0.663$) (figure 10). No difference in torque was observed between joint rotations of maximal ($p = 0.056$) and submaximal ($p = 1.000$) conditions. All torque measurements and pairwise comparisons are presented in Table 4.

5.3.2 sEMG$_{RMS}$

A significant difference was observed in the maximal biceps femoris long-head sEMG$_{RMS}$ increased from baseline to post-stretch isometric condition ($p = 0.023$, $\eta^2 = 0.342$) (figure 10). There was no difference in submaximal sEMG$_{RMS}$ from baseline to post-stretch isometric conditions of biceps femoris long-head ($p = 0.957$, $\eta^2 = 0.005$) and semitendinosus ($p = 0.755$, $\eta^2 = 0.031$). There was no difference in maximal semitendinosus sEMG$_{RMS}$ from baseline to post-stretch isometric condition ($p = 0.346$, $\eta^2 = 0.111$). All sEMG$_{RMS}$ measurements, including pairwise comparisons, are presented in Table 4.

5.3.3 Muscle and tendon length

During all post-stretch isometric contractions, the muscle (60° joint rotation p = <0.001, η^2 = 0.752; 30° joint rotation p = < 0.001, $\eta^2 = 0.710$) and distal tendon (60° joint rotation p = <0.001, $\eta^2 = 0.839$; 30° joint rotation p = 0.001, $\eta^2 = 0.561$) lengthened. The proximal tendon shortened during all post-stretch isometric contractions (60° joint rotation p = 0.001, η^2 = 0.831; 30° joint rotation p = 0.001, η^2 = 0.815). All whole muscle and tendon measurements and pairwise comparisons are presented in Table 5 and visualised in Figure 11.

Table 4 *Torque and sEMG$_{RMS}$ during maximal and submaximal baseline isometric and post-stretch isometric contractions of biceps femoris long-head (BFlh) and semitendinosus (ST)*

	Torque (Nm)			BF*lh* (mV)			ST (mV)		
	M	SD	SE	M	SD	SE	M	SD	SE
Baseline Max	190.33	39.35	12.44	0.14	0.04	0.01	0.16	0.04	0.01
PS-ISO$_{MAX-long}$	196.91	32.01	10.12	0.12	0.03	0.01	0.16	0.06	0.02
PS-ISO$_{MAX-short}$	**207.34**	31.46	9.95	0.12	0.04	0.01	0.14	0.05	0.02
Baseline Sub	58.52	12.54	3.97	0.06	0.02	<0.00	0.08	0.02	<0.00
PS-ISO$_{SUB-long}$	**81.58**	19.33	6.11	0.06	0.02	<0.00	0.08	0.02	<0.00
PS-ISO$_{SUB-short}$	**81.35***	13.00	4.11	0.06	0.02	<0.00	0.08	0.02	<0.00

*Mean values (M), standard deviation (SD), and standard error (SE) presented for baseline isometric contractions and post-stretch isometric contractions. Bold values indicate significant differences (p < 0.05), additional asterisk indicate highly significant (*p < 0.001) differences between baseline and post-stretch isometric contractions.*

5.4 Discussion

This study confirmed residual force enhancement during maximal and submaximal post-stretch isometric contractions without increased muscle activation in the hamstrings muscle group. Lengthening of the biceps femoris long-head muscle was confirmed during the eccentric portion of the post-stretch isometric contractions. As such, both hypotheses were confirmed. The magnitude of residual force enhancement in the PS-ISO$_{\text{MAX-short}}$ condition (8.94%) was greater than the only other investigation of the hamstrings muscle group (4-5%) (Shim & Garner, 2012). The observed residual force enhancement in PS-ISO$_{\text{SUB-long}}$ and PS-ISO$_{\text{SUB-short}}$ conditions (39%) are the first to be recorded in the hamstrings muscle group and are greater than previous studies of submaximal intensity using other lower limb muscles (25%) (Chen & Power, 2019). It is highly likely that altered titin stiffness during muscle stretch contributed to the elevated post-stretch isometric steady-state force. However, due to the complexity of the in-vivo model used in this experiment, it must also be acknowledged that other non-contractile elements may have contributed to these post-stretch isometric steady-state forces.

5.4.1 Dynamic musculotendinous unit behaviour during post-stretch isometric contractions

This is the first investigation to observe the lengthening of the biceps femoris long-head muscle during post-stretch isometric contractions. This finding is similar to previous findings, which confirmed muscle lengthening of the knee extensors (Fukutani et al., 2016b) and plantarflexors (Fukutani et al., 2019) during post-stretch isometric contractions. Confirmation of active muscle lengthening during the post-stretch isometric contractions leads us to conclude that titin likely contributed to the increased force observed (Fukutani & Herzog, 2019). Relying on direct observations of muscle behaviour during post-stretch isometric contractions strengthens this conclusion, particularly in light of the sound body of evidence that has demonstrated such a link with in vitro experiments (Herzog & Leonard, 2005). Similar to the current study, Fukutani et al. (2016b) reported that in maximal voluntary post-stretch isometric contractions of the knee extensors, the muscle consistently lengthened

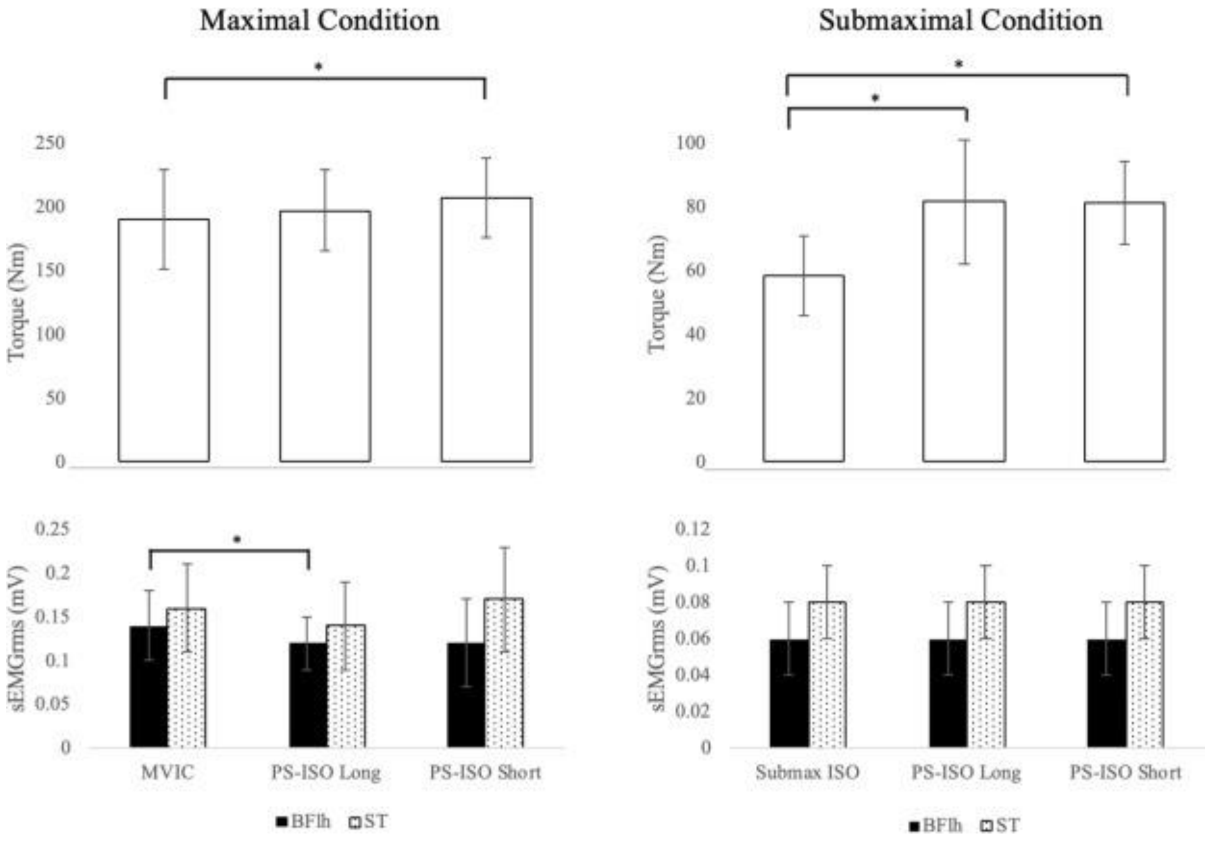


Figure 10 *Baseline and post-stretch isometric values of knee flexion torque (N·m) and sEMG$_{RMS}$ muscle activation amplitudes (mV) in maximal and submaximal conditions of long (60°) and short (30°) joint rotations. Note: In the PS-ISO$_{SUB\text{-}long}$ and PS-ISO$_{SUB\text{-}short}$ conditions, participants mediated activation levels to 50% MVIA ± 10% of sEMG$_{RMS}$. * $p = <0.05$ indicates a statistically significant difference between baseline and experimental values.*

during the eccentric phase. Previous investigators have reasoned that modulation of muscle lengthening is influenced by muscle-tendon interaction (Farris et al., 2016) or the elimination of slack (Herbert et al., 2015) within the musculotendinous unit during the isometric pre-activation phase. Our findings suggest that these modulations may also be influential during submaximal intensity post-stretch isometric contractions. Hence the current results support previous evidence that isometric pre-activation is influential in muscle lengthening during maximal and now submaximal post-stretch isometric contractions (Fukutani & Herzog, 2019; Fukutani et al., 2019).

Table 5 Measurements of muscle, distal tendon and proximal tendon prior to and following post-stretch isometric with 30° (short) and 60° (long) joint rotations.

	Distal Tendon (mm)			Muscle (mm)			Proximal Tendon (mm)		
	M	SD	SE	M	SD	SE	M	SD	SE
Pre-Stretch short	41.33	5.89	1.86	312.84	7.27	2.29	48.32	5.02	1.59
PS-ISO$_{MAX\text{-}short}$	**47.44***	7.18	2.72	**327.38****	7.98	2.52	**38.72****	6.84	2.16
PS-ISO$_{SUB\text{-}short}$	**48.07**	7.67	2.43	**324.19***	9.41	2.97	**41.28***	7.26	2.29
Pre-Stretch long	41.93	6.64	2.10	317.57	11.06	3.50	42.95	6.74	2.13
PS-ISO$_{MAX\text{-}long}$	**56.46****	7.59	2.40	**329.18***	7.66	2.42	**38.02***	6.77	2.14
PS-ISO$_{SUB\text{-}long}$	**56.82****	5.71	1.81	**329.91****	9.45	2.99	**38.58**	6.62	2.09

*Mean values (M), standard deviation (SD) and standard error (SE) presented for baseline isometric contractions and post-stretch isometric contractions. Bold values indicate significant differences (p < 0.05), additional asterisks highly significant differences (*p < 0.01; **p < 0.001) in length between pre-stretch and following post-stretch isometric contractions.*

The observation of variation in proximo-distal length change of biceps femoris long-head tendons during post-stretch isometric contractions is new and novel, warranting further investigation. Proximal and distal tendons behaved independently of each other during post-stretch isometric contractions in biceps femoris long-head. The proximal tendon was observed to shorten, whilst the distal tendon was observed to lengthen (Figure 11). We theorise that complex interactions occurring within the musculotendinous unit between the muscle (joint position and variation in moment arm between joints, pennation angle, fascicle length, muscle thickness, and variability in proximo-distal fibre arrangement, compartmentalisation, and inscription) (Higham & Biewener, 2011; Kellis, 2018) and series elastic element (visco-elastic properties, physiological cross-sectional area, and aponeurosis morphology function) (Lersch et al., 2012) contributed to the observed behaviour. However, these suppositions regarding variation in proximo-distal length change are largely speculative due to sparse *in vivo* evidence, particularly concerning biceps femoris long-head (Kellis, 2018). It is, therefore, recommended that further investigation is undertaken into the effect of proximo-distal length change variation in bi-articular muscles during post-stretch isometric contractions.

5.4.2 Neuromuscular influences on post-stretch isometric contractions

The magnitude of residual force enhancement during maximal and submaximal conditions (figure 10) was greater than the previous investigation of the hamstring muscle group (4-5%) (Shim & Garner, 2012). There is little evidence to suggest that underlying mechanical mechanisms of residual force enhancement (i.e., titin stiffness) are solely responsible for the disparity. It is possible that the magnitude of residual force enhancement in the maximal conditions, and particularly the PS-ISO$_{\text{MAX-long}}$ condition, was influenced by tension mediated factors from peripheral sensory inputs via altered inhibitory sensory feedback to the agonist motor neuron pool (Contento et al., 2019). This sensory feedback can result in reduced muscle activation (Sypkes et al., 2018) (figure 10). The biceps femoris long-head muscle is known to be highly prone to musculotendinous injury (Timmins, Bourne, et al., 2016); among a number of other factors, it is possible that the activation reduction may be the result of a protective response within the biceps femoris long-head muscle. It has been suggested that 1b afferent tension mediating factors may provide a protective effect by limiting tension

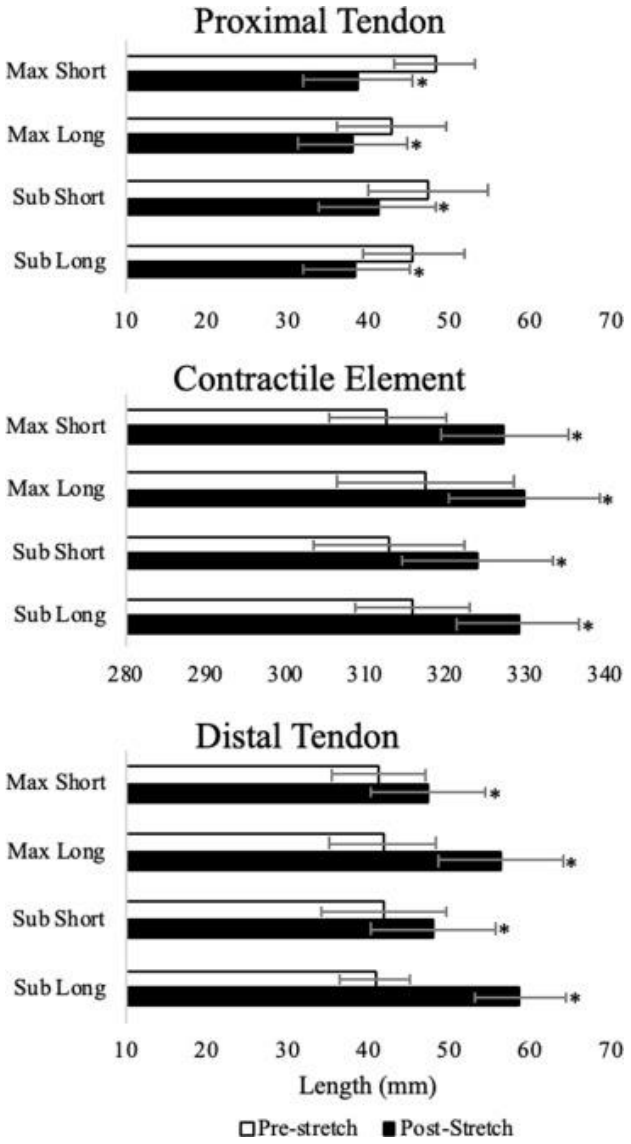


Figure 11 *Whole muscle, proximal and distal tendon lengths, at the start and end of the active-stretch phase of the post-stretch isometric contractions. Note: PS-ISO$_{MAX\text{-}long}$ and PS-ISO$_{SUB\text{-}long}$ contractions were of maximal intensity and occurred over a joint excursion of 60º at $60^{o}\cdot s^{-1}$. PS-ISO$_{MAX\text{-}short}$ and PS-ISO$_{SUB\text{-}short}$ contractions were of submaximal intensity and occurred over a joint excursion of 30° at $60°\cdot s^{-1}$. * $p = <0.05$ indicates a statistically significant difference between pre-stretch and post-stretch*

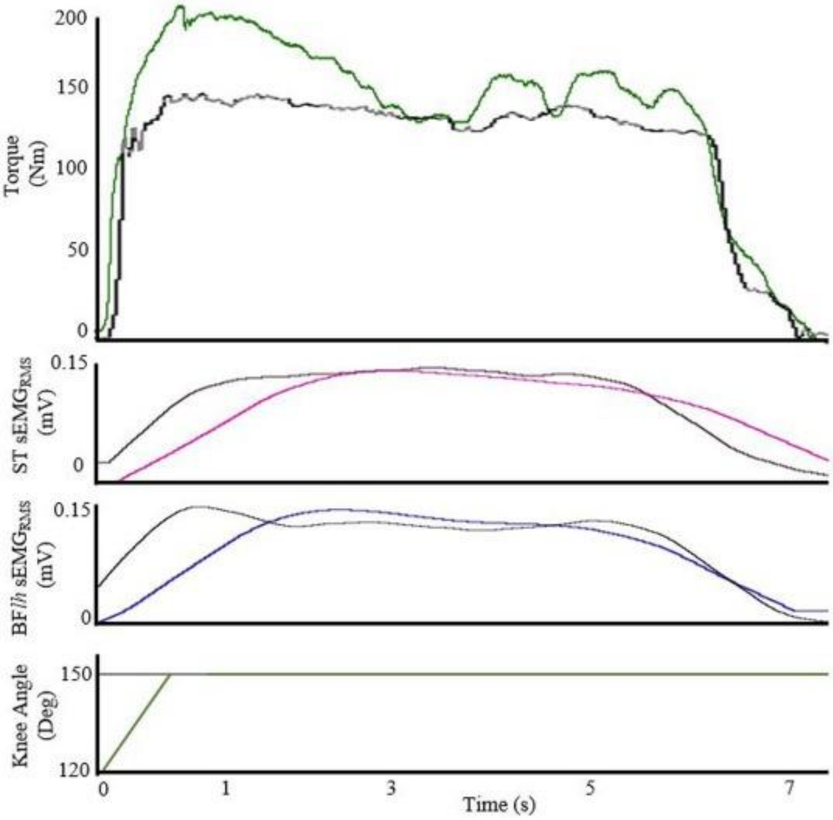


Figure 12 *Torque and muscle activation of biceps femoris long-head (BFlh) and semitendinosus (ST) during maximal baseline isometric contractions at 150° knee flexion (180° is equal to full knee extension) (in grey) and post-stretch isometric contractions with a 30° joint rotation at 60°·s^{-1} (in colour).*

within the musculotendinous unit to reduce the likelihood of musculotendinous injury (Hahn et al., 2012). This protective mechanism might have been more pronounced in the biceps femoris long-head muscle during the PS-ISO$_{\text{MAX-long}}$ condition if the response of the Golgi tendon organ was augmented due to a greater joint excursion under higher musculotendinous unit tension (Gregory et al., 2002). As activation reduction was not observed in semitendinosus sEMG$_{\text{RMS}}$, this may provide further evidence of the muscle-specific nature of corticospinal excitability (Giesebrecht et al., 2010). However, further research is required to elucidate the effect of the range of influences on the golgi tendon organ and motor neuron pool.

Where tension mediation factors may have reduced residual force enhancement in one of the maximal conditions, it is plausible that tension mediated factors may have a lesser influence on residual force enhancement in submaximal activation matched conditions. Contento et al. (2019) noted that the tension-dependent Golgi tendon organ and the 1b afferent fibres were the most likely contributors in modulating agonist motor neuron excitability during voluntary control of submaximal contractions in the residual force enhancement steady-state. The current findings present the possibility that submaximal post-stretch isometric contractions may result in a relatively greater proportion of residual force enhancement. A greater proportion of residual force enhancement may be of benefit where elevated force is desirable without increased muscle activation. Although currently untested, submaximal post-stretch isometric contractions in series (as per traditional strength training) may be of benefit in situations such as in injury rehabilitation.

Whilst great care was taken in designing and undertaking this investigation, and it should be noted that limitations exist with the collection and interpretation of 2-D ultrasound images of a dynamic muscle contraction moving in a 3-D space, as well as interpretation of sEMG of the hamstring muscle group where the effect of cross-talk can influence the interpretation of sEMG signals.

5.5 Conclusion

Consistent with our major hypothesis, this study provides novel evidence confirming residual force enhancement in the knee flexors during maximal and submaximal post-stretch isometric contractions over two stretch magnitudes. The present study was the first to observe muscle length change in knee flexors during maximal and submaximal post-stretch isometric

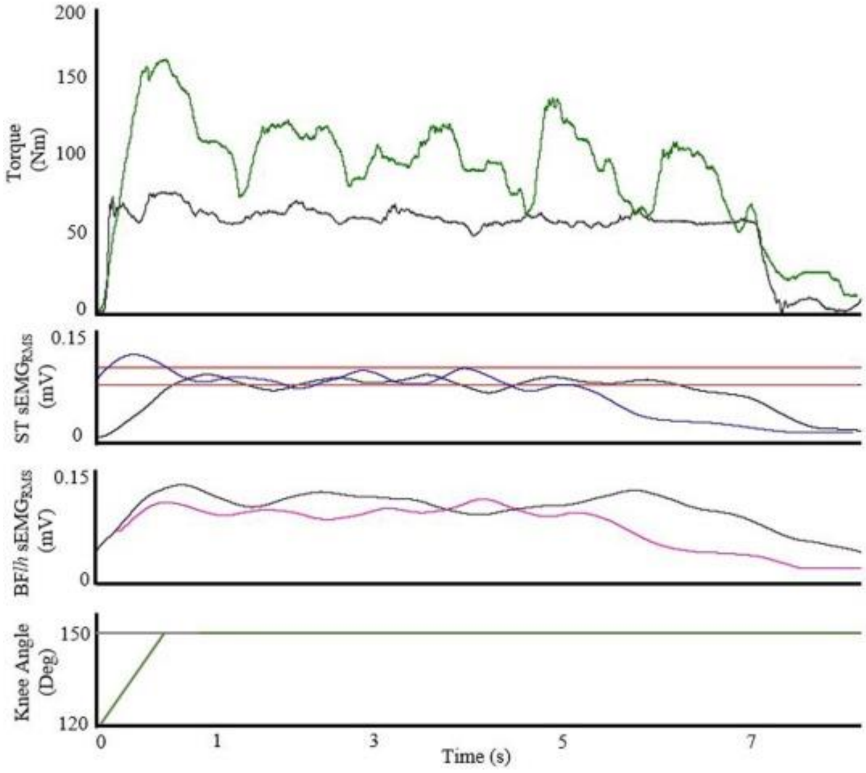


Figure 13 *Torque and muscle activation of biceps femoris long-head (BFlh) and semitendinosus (ST) during activation matched submaximal baseline isometric contractions at 150° knee flexion (180° is equal to full knee extension) (in grey) and activation matched submaximal post-stretch isometric contractions with a 30° joint rotation at* $60°·s^{-1}$ *(in colour). Semitendinosus activation matching target indicated by red guidelines.*

contractions. It is also the first to observe proximo-distal length change in any muscle during post-stretch isometric contractions. We postulate that tension-mediated neuromechanical factors may influence residual force enhancement in maximal post-stretch isometric contractions of the knee flexors. The enhanced isometric steady-state force in submaximal post-stretch isometric contractions may be of particular interest to those looking to rehabilitate injured muscle, restore strength and minimise excessive scar tissue formation. Future research should investigate the potential hypertrophic effect of consecutive bouts of post-stretch isometric contractions simulating a training stimulus.

Part III:

Is residual force enhancement present in the hamstrings during multiple sets and repetitions per a training simulation and what are the implications for hamstring training?

Chapter 6: Residual force enhancement is present in consecutive post-stretch isometric contractions of the hamstrings: a training simulation

This chapter is an amended* version of the following published peer-reviewed manuscript:

Chapman, N., Whitting, J.W., Broadbent, S., Crowley-McHattan, Z.J., Meir, R. (2021). Residual force enhancement is present in consecutive post-stretch isometric contractions of the hamstrings: a training simulation. *International journal of environmental research and public health*, 18(3), 1154.

**These amendments only relate to spelling or grammatical errors that have been identified since publication. No changes to methodology, results or findings have been made.*

Abstract

Residual force enhancement is observed when isometric force following an active stretch is elevated compared to an isometric contraction at corresponding muscle lengths. Acute residual force enhancement has been confirmed in vivo in upper and lower limb muscles. However, it is uncertain whether residual force enhancement persists using multiple, consecutive contractions as per a training simulation. Using the knee flexors, ten recreationally active participants (seven males, three females; age 31.00 years ± 8.43 years) performed baseline isometric contractions at 150° knee flexion (180° representing terminal knee extension) of 50% maximal voluntary activation of semitendinosus. Participants performed post-stretch isometric contractions (three sets of 10 repetitions) starting at 90° knee extension with a joint rotation of 60° at $60°\cdot s^{-1}$ at 50% maximal voluntary activation of semitendinosus. Baseline isometric torque and muscle activation were compared to post-stretch isometric torque and muscle activation across all 30 repetitions. Significant residual force enhancement was noted in all repetitions (37.8–77.74%), with no difference in torque between repetitions or sets. There was no difference in activation of semitendinosus or biceps femoris long-head between baseline and post-stretch isometric contractions in all repetitions (Semitendinosus; baseline ISO = 0.095–1.000 ± 0.036–0.039 Mv, post-stretch isometric = 0.094–0.098 ± 0.033–0.038 and biceps femoris long-head; baseline ISO = 0.068–0.075 ± 0.031–0.038 Mv). This is the first investigation to observe residual force enhancement during multiple, consecutive submaximal post-stretch isometric contractions. Post-stretch isometric contractions have the potential to be used as a training stimulus.

6.1 Introduction

There is much interest in the prevention and rehabilitation of hamstring strain injuries. Hamstring strain injuries have a high incidence, particularly during high-speed running

(Green et al., 2020). The function of the hamstring muscles during high-speed running is vigorously debated. One theory proposes that in high-speed running, the hamstring muscles act eccentrically (actively lengthen) during the late swing phase of the gait cycle (Van Hooren & Bosch, 2017a). Whereas the alternate postulation states that the hamstrings remain predominantly isometric during the late swing phase and act isometrically (no change in length to the muscle) during foot contact (Van Hooren & Bosch, 2017a). Much of our current understanding of the dynamic function of the hamstrings is based on a kinematic and kinetic investigation, which measures the change in distance between attachment points of the hamstrings (Chumanov et al., 2011; Higashihara et al., 2016; Nagano et al., 2014; Schache et al., 2013; Simonsen et al., 1985; Thelen et al., 2005). Methodological limitations exist whereby the change in distance between origin and insertion attachment points of the musculotendinous unit is used to infer the behaviour of the contractile element (Van Hooren & Bosch, 2017a). The actual behaviour of the series elastic element and other non-contractile tissues such as aponeurosis and fascial tissues lack direct focus (Van Hooren & Bosch, 2017a). This ongoing debate concerning hamstring function, although worthwhile, may prove to be somewhat academic if the critical functioning of the hamstrings during the gait cycle is found to be specific to the individual (Maniar et al., 2020).

Uncertainty over the dynamic function of the hamstrings has led to conjecture over appropriate training methods for the hamstring muscles, be it for; performance, injury prevention, or rehabilitation. Eccentric strength, fascicle length, and neuromuscular functioning have been identified as important modifiable risk factors for injury and are often the focus of injury prevention programs (Pizzari et al., 2020). Flywheel training and the Nordic hamstring exercise are examples of eccentrically biased training methods purported to be effective in injury risk minimisation (Askling et al., 2003; Askling et al., 2014; Askling et al., 2013; Brooks et al., 2006). However, if an isometric action of the contractile element exists, there is a cause to utilize isometric specific exercise (Morrissey et al., 1995). Van Hooren and Bosch (2017b) suggest that isometric exercises such as the Roman Chair Hold (and variations) can generate sufficient overload whilst maintaining positive transfer for improvements in performance and reduction in injury risk. Van Hooren and Bosch (2017a) hypothesise that high-intensity isometric contractions may prove more effective than eccentric contractions in preventing hamstring strain injuries during high-speed running (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). However, Van Hooren and Bosch advocate for the use of both eccentric and isometric contractions to be included in hamstring strain injury prevention programs (Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). Therefore, the use of both eccentric and isometric contractions has the potential to be most beneficial for reducing hamstring injury risk.

The post-stretch isometric contraction, which combines both eccentric and isometric stimulus, may provide benefits of both contraction modes. A post-stretch isometric contraction is initiated with an isometric contraction at a shorter musculotendinous unit length, then moved through an active stretch phase, ending with a sustained isometric contraction at the new longer muscle length (Chapman et al., 2018). Torque peaks during the active stretch phase before normalising somewhat during the final sustained isometric steady-state. The torque observed during the post-stretch isometric steady-state is consistently greater than isometric torque without active stretch (Chapman et al., 2018). This elevated post-stretch isometric torque is referred to as residual force enhancement (Edman et al., 1982). Residual force enhancement has been observed *in vitro* in single fibre and whole muscle preparations (Campbell & Campbell, 2011; Edman et al., 1982; Herzog & Leonard, 2000; Peterson et al., 2004; Rassier et al., 2003; Schachar et al., 2004) and *in vivo* with electrical stimulation (Cook & McDonagh, 1995; Lee & Herzog, 2002b; Pinniger & Cresswell, 2007; Ruiter et al., 2000) and voluntary contractions (Chapman et al., 2020; Hahn et al., 2010; Lee & Herzog, 2002; Oskouei & Herzog, 2005; Pinniger & Cresswell, 2007; Tilp et al., 2009). The magnitude of residual force enhancement is greater at joint angles indicative of longest muscle lengths (Julian & Morgan, 1979; Morgan et al., 2000; Peterson et al., 2004) and increases with increasing stretch magnitudes (Bullimore et al., 2007; Edman et al., 1978; Herzog & Leonard, 2005).

Residual force enhancement has been observed in the hamstrings muscle group in maximal and submaximal voluntary post-stretch isometric contractions (Chapman et al., 2020). The maximal post-stretch isometric steady-state torque was found to be almost 9% greater than baseline isometric torque without prior stretch. A 39% increase in torque between isometric steady-state and post-stretch isometric torque was found using submaximal post-stretch isometric contraction intensity (50% activation). Confirmation of contractile element lengthening (eccentric contraction) coupled with a lack of increased muscle activation led to the postulation that the giant protein titin increased stiffness during the active stretch of the post-stretch isometric contractions. The authors' reason that the resultant torque increase via titin contribution is congruent with titin elasticity theory (Herzog & Leonard, 2005). Thus, post-stretch isometric contractions which involve both eccentric and isometric contraction modes, have the potential to significantly increase isometric torque output without increased muscle activation of the hamstrings muscle group.

It is known that chronic use of eccentric contractions results in increased; eccentric strength and fascicle length (de Vos et al., 2020). A rightward shift in the optimal operating angle on the length-tension relationship is also known to occur (Brughelli & Cronin, 2007). The chronic use of isometric exercise at long musculotendinous unit lengths is known to increase; isometric strength, pennation angle, fascicle length, and hypertrophy (Oranchuk et al., 2019). A broadening of the plateau region of the length-tension relationship has also been observed in chronic isometric training at long musculotendinous unit lengths (Akagi et al., 2020). The potential benefits of combining eccentric and isometric contraction modes using post-stretch isometric contractions in chronic resistance training are unknown. However, they have the potential to experience both eccentric and isometric benefits.

Presently, it is unknown whether residual force enhancement endures beyond single post-stretch isometric contractions. Prior to a training study being undertaken, it is necessary to confirm residual force enhancement in the hamstring muscle group. It was hypothesized that residual force enhancement would be observed across all contractions without an increase in muscle activation.

6.2 Materials and Methods

Ten recreationally active participants (7 males, 3 females; 31.00 years ±8.43 years) provided written informed consent to participate in the study. All participants were confirmed to be free from diagnosed lower limb musculoskeletal injury and neurologic conditions in the preceding 12 weeks. The study was approved by the Institutional Human Research Ethics Committee (ECN: 2019/090).

Each participant assumed a prone position on a Biodex System 3 dynamometer (Biodex Medical Systems, Shirley, NY), which recorded torque measurements for all experiments. A goniometer (J.A. Preston Corporation, Clifton, NJ) was used to confirm the participant’s hip angle to be between 170º and 180º (180º represents neutral hip position). The goniometer was centred on the greater trochanter of the involved hip and aligned with the lateral midline of the abdomen and lateral midline of the femur. The axis of rotation of the participant's involved knee was aligned with the axis of rotation of the dynamometer. The ankle cuff was attached 25mm above the dorsal surface of the foot. Inelastic straps were placed over the L4/5 area to mitigate extraneous movements during contractions.

Surface electromyography (sEMG) signals of semitendinosus and biceps femoris long head muscles were recorded during all trials using a Trigno Wireless sEMG system with double differentiated surface electrodes (Delsys, Natick, MA, USA). The electrodes were placed as per SENIAM guidelines (Hermens et al., 1999). The semitendinosus electrode was placed on the muscle at 50% of the line between the ischial tuberosity and the medial epicondyle of the tibia in the direction of the line between the ischial tuberosity and the medial epicondyle of the tibia. The biceps femoris long-head electrode was placed on the muscle at 50% of the line between the ischial tuberosity and the lateral epicondyle of the tibia in the direction of the line between the ischial tuberosity and the lateral epicondyle of the tibia. The electrode locations were prepared by first shaving and abrading, then wiping the site with alcoholic wipes. In addition to the double-sided adhesive electrode-skin interface, a surgical adhesive tape was used to secure the electrodes to the skin.

The Biodex data was sampled at 1000Hz using a 12-bit analogue to digital converter (PowerLab System 16/35, ADInstruments, Bella Vista, Australia). The sEMG signals were sampled at 2000Hz (bandpass filtered 10-500Hz). Biodex and sEMG were synchronised with LabChart software (Pro Modules 2014, version 8, ADInstruments, Bella Vista, Australia).

6.2.1 Protocols and measurements

At the completion of a 5-minute warmup on a cycle ergometer, each participant performed three baseline maximal voluntary isometric contractions (MVIC) of the knee flexors (5 s duration) at 150º knee flexion (180º being representative of terminal knee extension). To ensure that all MVIC attempts were maximal, each participant was provided with verbal encouragement and visual feedback of the torque traces on a computer monitor within the participant's direct line of sight. The activation matching intensity, 50% ±5% MVIA, was calculated using the activation of the ST muscle. The baseline MVIC grand mean of semitendinosus root mean square (RMS) amplitude (mV) sEMG ($sEMG_{RMS}$: moving average window = 50 ms) was derived from a 3 s epoch, corresponding with a 2-4 s window in the MVIC baseline contractions. The values of 50% ±5% were entered into the LabChart software, which were visualised as guidelines on a computer monitor located in front of the participant. Each participant performed three sets of 10 baseline activation matching isometric contractions of the knee flexors (7 s duration at 150º knee flexion), a total of 30 contractions. To ensure that activation matching attempts were within ±5%, each participant was provided with verbal encouragement and visual feedback of the ST $sEMG_{RMS}$ trace on the computer monitor within direct line of sight. Participants rested for 3 s between activation matching repetitions, 30 s between activation matching sets and a minimum of 5 min between baseline and post-stretch isometric experimental condition.

The experimental condition consisted of three sets of 10 repetitions of activation matched post-stretch isometric contractions, a total of 30 post-stretch isometric contractions. Each activation matching post-stretch isometric repetition was initiated at 90º knee flexion, followed by an active stretch over a joint excursion of 60º at a constant angular velocity, $60^{\circ}\cdot s^{-1}$, then immediately followed by a post-stretch isometric contraction at 150º knee flexion, which was activation matched. To ensure that activation matching post-stretch isometric attempts were within ±5%, each participant was provided with verbal encouragement and visual feedback of the ST sEMG_{RMS} trace on a computer monitor located within the direct line of sight of the participant. At the completion of each repetition, the dynamometer arm automatically and immediately returned to the starting position with no effort on behalf of the participant. All activation matching post-stretch isometric repetitions were voluntarily activated for a total of 7 s. Each repetition within a set was completed concurrently with 3 s rest between repetitions. Participants rested for 30 s between each set. A counterbalanced design was used whereby 50% of participants completed the baseline isometric activation matched contractions prior to experimental post-stretch isometric activation matched contractions. The remaining 50% of participants completed the experimental post-stretch isometric activation matched contractions prior to the baseline isometric activation matched contractions (figure 14).

6.2.2 Data analysis

Mean torque output (N·m) was derived from a 3 s epoch corresponding to 3-5 s for each baseline isometric repetition and 3-5 s for each post-stretch isometric steady-state repetition. Net torque (N·m) was averaged across contractions for each contraction condition in each participant. Mean sEMG_{RMS} (mV) was derived from a 3 s epoch corresponding to 3-5 s for each experimental trial. The mean of the three experimental trials in each condition was used as the overall participant mean value. The residual force enhancement magnitude was defined as the absolute torque increase (Nm) and as a percentage change from the activation matched isometric baseline contraction at 150º knee flexion. The following equation previously used by Contento et al. (2019), was used to calculate percentage change residual force enhancement (rFE):

$$\text{rFE\%}\Delta = \left[\frac{(\text{ isometric torque Nm following active lengthening} - \text{baseline isometric torque Nm})}{\text{baseline isometric torque Nm}}\right] \times 100\%$$

6.2.3 Statistical analysis

A repeated-measures ANOVA was used to calculate the difference in torque and sEMG$_{\text{RMS}}$ of ST and biceps femoris long-head and between activation matched isometric baseline and activation matched post-stretch isometric steady-state. Where a main effect was noted, a posthoc test (Bonferroni's correction) was conducted. These calculations were made for all repetitions within a set and all sets of repetitions. Effect sizes were calculated using partial η^2(0.20 = small, 0.50 = medium, 0.80 = large effect size) (Cohen, 2013). Significance was determined based on an α = 0.05. Descriptive data in figures are reported as mean values.

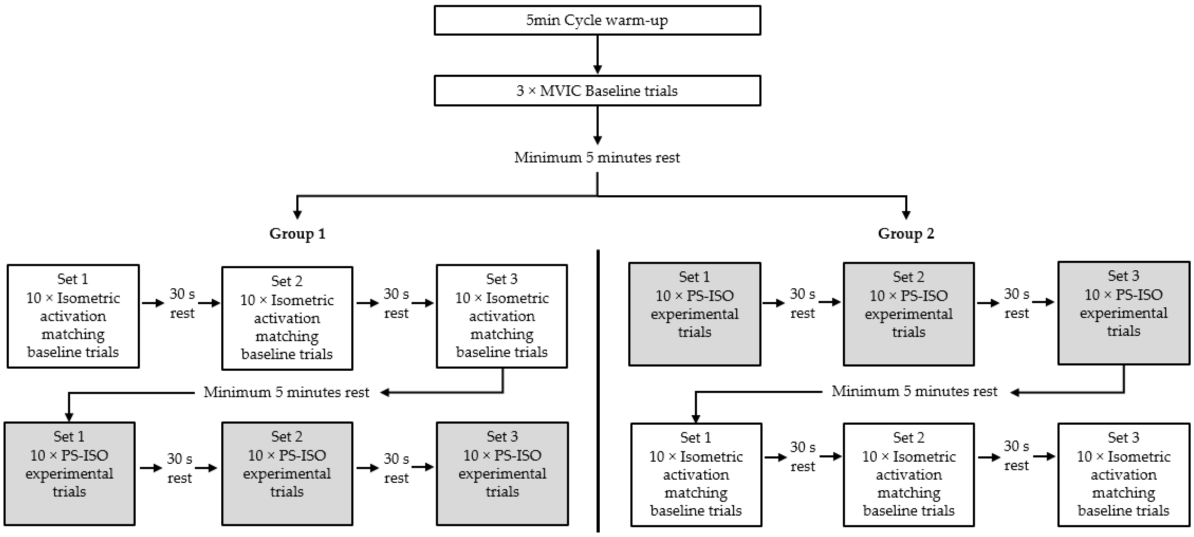


Figure 14 *Baseline and experimental protocols for Group 1 and Group 2. Participants were randomly allocated into each group.*

6.3 Results

6.3.1 Torque

The mean torque (Nm) for each repetition is presented in Table 6. A main effect of the contraction type revealed that the activation-matched post-stretch isometric contraction torque was significantly greater than the activation-matched baseline isometric torque (baseline ISO;

CV = 36.67–69.50; post-stretch isometric; CV = 20.27–38.61, F = 32.558, p = <0.001, partial η^2 = 0.783). However, no significant main effect of set (F = 0.640, p = 1.000, partial η^2 = 0.138) or repetition (F = 3.555, p = 1.00, partial η^2 = 0.970) was found. All interactions between contractions, sets and repetitions were non-significant (F = 1.197–3.442, p = 0.060–1.000, partial η^2 = 0.340–0.989). To examine the main effect of contraction, the posthoc analysis revealed that there were no differences in baseline isometric torque output between repetitions (F = 3.422, p = 1.00, partial η^2 = 0.969) or sets (F = 2.058, p = 1.000, partial η^2 = 0.340). Further, there were no differences in torque output in post-stretch isometric between repetitions (F = 0.697, p = 1.000, partial η^2 = 0.863) or sets (F = 0.193, p = 1.000, partial η^2 = 0.046). However, a significant difference between contraction modes at each repetition within each set was found (F = 15.474–41.735, p = <0.001–0.003, partial η^2 = 0.632–0.823). This demonstrated that the post-stretch isometric torque was consistently elevated above the baseline isometric torque (Figure 15).

6.3.2 sEMG$_{RMS}$

No main effect of contraction type (Semitendinosus; baseline ISO = 0.095–1.000 ± 0.036–0.039 Mv, post-stretch isometric = 0.094–0.098 ± 0.033–0.038, F = 0.312, p = 0.590, partial η^2 = 0.033 and biceps femoris long-head; baseline ISO = 0.068–0.075 ± 0.031–0.038 Mv, post-stretch isometric = 0.071–0.079 ± 0.030–0.038, F = 1.931, p = 0.198, partial η^2 = 0.177), set

(Semitendinosus; F = 1.280, p = 1.000, partial η^2 = 0.242 and biceps femoris long-head; F = 0.247, p = 1.000, partial η^2 = 0.058) or repetition (Semitendinosus; F = 1.000, p = 1.000, partial η^2 = 0.900 and biceps femoris long-head; F = 1.111, p = 1.000, partial η^2 = 0.909) were found for muscle-activation variables. No interactions were found for all muscle activations between main effects of contraction, sets and repetitions for semitendinosus and biceps femoris long-head (Semitendinosus; F = 1.000–1.500, p = 0.110–1.000, partial η^2 = 0.600–0.700 and biceps femoris long-head; F = 0.224–9.472, p = 0.052–1.000, partial η^2 = 0.343–0.988) (Figure 16).

6.4 Discussion

This is the first study to confirm residual force enhancement , in the absence of increased muscle activation, in the hamstrings during multiple and consecutive submaximal post-stretch isometric contractions. As such, the hypotheses were supported. The magnitude of residual force enhancement in the current study (55%) was greater than that of the previous investigation of the hamstring muscle group (39%) (Chapman et al., 2020) and other lower limb muscles (25%) (Chen & Power, 2019). It is evident from the findings that an increase in muscle activation cannot account for the elevated post-stretch isometric torque during the series of post-stretch isometric contractions. Thus, we posit that passive mechanisms, possibly titin for example, are likely primarily responsible for the torque increase. In submaximal post-stretch isometric conditions (50%MVIA), there is no reduction in the magnitude of residual force enhancement during multiple, consecutive post-stretch isometric contractions. These findings are the first to observe the repeatability of enhanced torque (i.e., residual force enhancement) using post-stretch isometric contractions as per a traditional training simulation. These findings may have practical application to chronic resistance training exercises focused on hamstring injury prevention.

Table 6 Torque values (Nm) for baseline and post-stretch isometric contractions.

Rep	Set 1		Set 2		Set 3	
	BL	**PS-ISO**	**BL**	**PS-ISO**	**BL**	**PS-ISO**
1	46.43	77.29	50.29	77.86	48.34	73.40
	(27.00)	(21.97) *	(24.57)	(24.03) *	(20.11)	(19.08) *
2	41.18	73.20	48.92	78.81	48.42	73.29
	(24.47)	(21.01) *	(22.19)	(18.50) *	(17.76)	(17.78) *
3	44.09	73.35	48.07	74.22	47.15	73.27
	(27.79)	(26.20) *	(26.55)	(20.11) *	(17.77)	(19.16) *
4	43.29	75.12	47.43	76.22	47.43	72.59
	(30.09)	(23.98) *	(23.02)	(22.65) *	(20.40)	(17.60) *
5	45.28	70.84	47.45	71.01	44.06	67.19
	(24.11)	(27.35) *	(23.19)	(20.04) *	(18.74)	(19.34) *
6	45.81	70.14	45.02	68.74	46.01	74.62
	(28.76)	(24.25) *	(21.67)	(20.98) *	(17.07)	(15.12) *
7	50.11	69.63	42.83	70.43	44.85	63.48
	(30.22)	(23.06) *	(23.85)	(19.59) *	(18.98)	(17.55) *
8	44.63	70.53	45.84	67.13	39.74	66.23
	(25.91)	(21.78) *	(21.14)	(18.81) *	(22.10)	(15.38) *
9	47.90	66.01	44.91	65.38	42.63	64.23
	(30.78)	(20.04) *	(17.86)	(20.58) *	(18.06)	(16.61) *
10	46.28	67.72	45.94	68.34	40.25	66.66
	(27.02)	(20.76) *	(20.90)	(21.43) *	(18.69)	(15.98) *

*Note. Torque values mean (SD). All values in Nm. * indicates a significant difference between baseline (BL) and post-stretch isometric (PS-ISO) repetitions.*

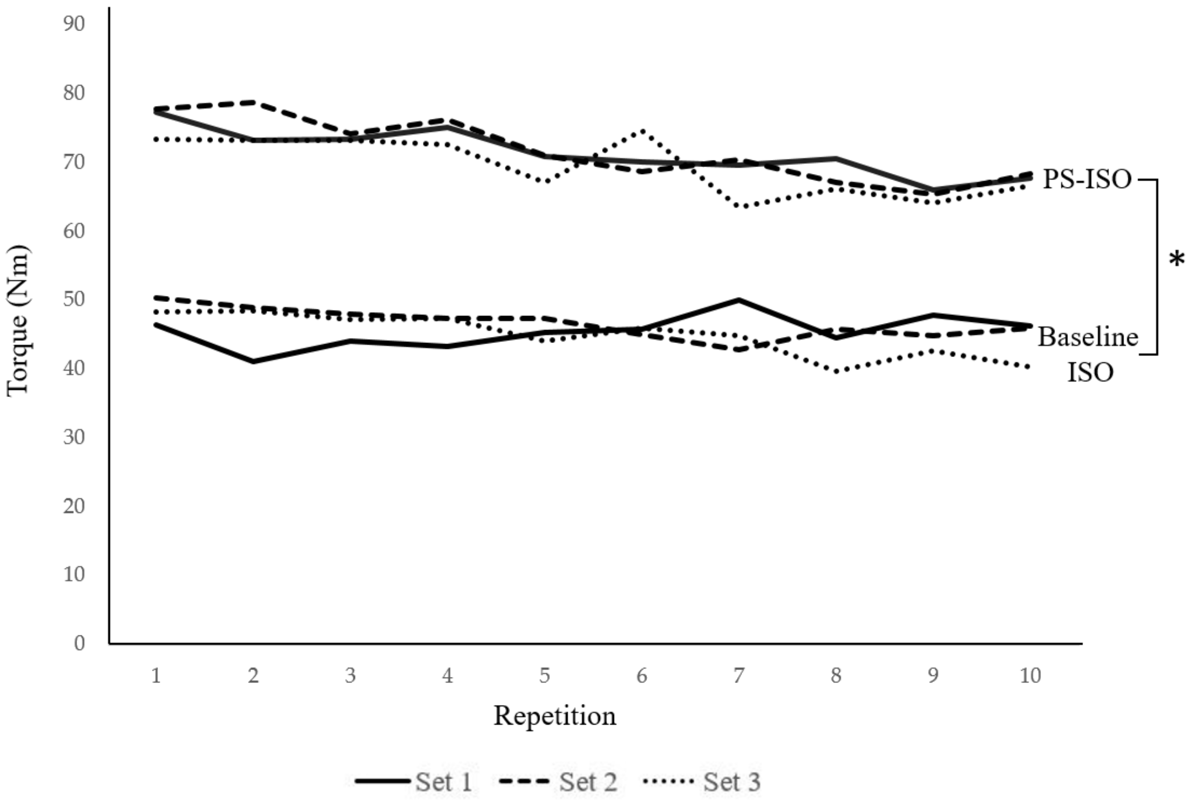


Figure 15 Mean baseline isometric and post-stretch isometric torque during 10 consecutive repetitions over three sets. * Indicates a significant increase in mean torque between baseline isometric and post-stretch isometric contraction for all repetitions and all sets (p = <0.001).

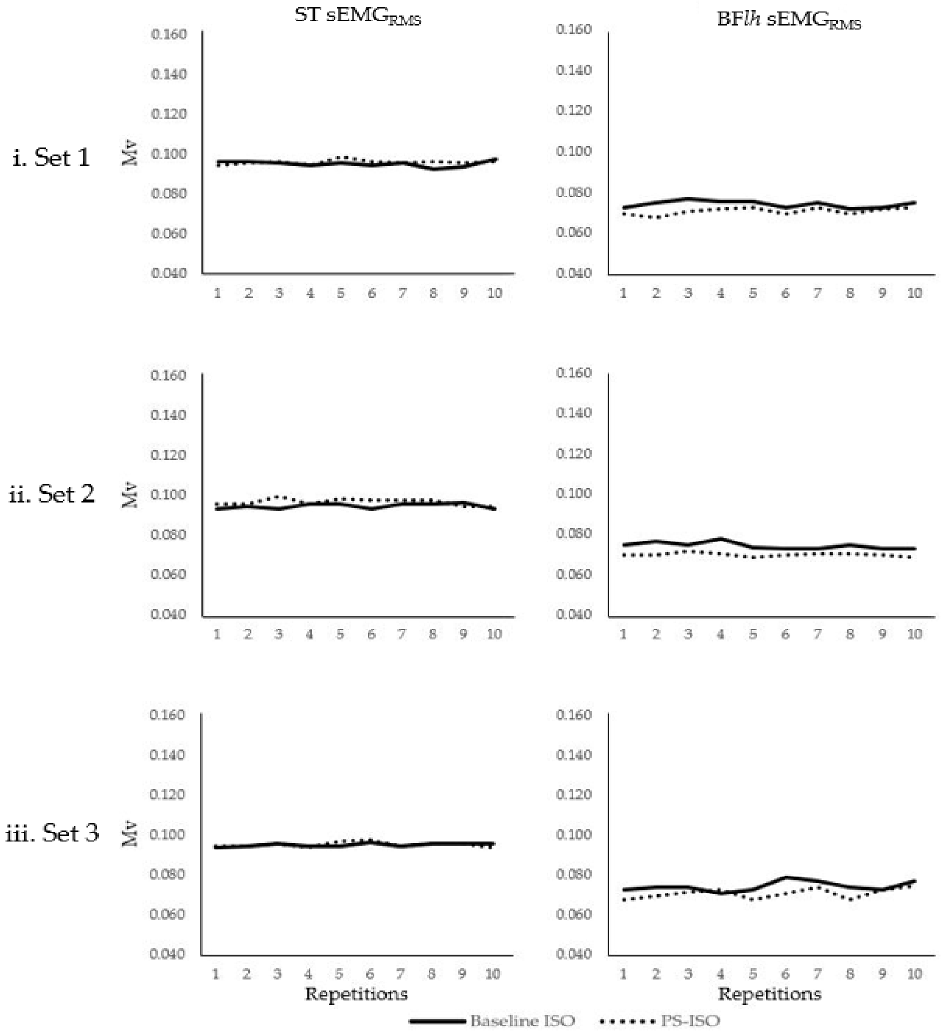


Figure 16 *Mean baseline isometric and post-stretch isometric muscle activation (sEMG$_{RMS}$) measured in millivolts (Mv) of semitendinosus (ST) and biceps femoris long-head (BFlh) muscles during 10 consecutive repetitions during 3 sets (i. Set 1, ii Set 2 and iii Set 3). No difference in muscle activation was observed between baseline isometric and post-stretch isometric contractions for all repetitions and sets of semitendinosus ($p = 0.590$) and biceps femoris long-head ($p = 0.198$). ST sEMG$_{RMS}$ is depicted in the left column and biceps femoris long-head sEMG$_{RMS}$ is depicted in the right column for Set 1 (i Set 1), Set 2 (ii. Set 2) and Set 3 (iii. Set 3). Repetitions in each set are visualized on the x axis and sEMG$_{RMS}$ on the y axis of each graph.*

The current study demonstrates that the mechanisms responsible for residual force enhancement persist beyond a single bout. We posit that this mechanism is most likely to be the giant protein titin. Titin elasticity theory states that during muscle stretch, titin binds to the actin filament, reducing the free-spring length. This, in turn, increases sarcomeric stiffness, thereby contributing additional passive force to total force output (Fukutani & Herzog, 2019; Heidlauf et al., 2016; Herzog & Leonard, 2005; Nishikawa, 2020). Furthermore, as a consequence of titin involvement, it has been suggested that forces in the enhanced state come at a reduced metabolic cost (Joumaa & Herzog, 2013). Although muscle lengthening was not directly observed in the current study, the assertion that titin contributed force during an active stretch in the current study is further supported by the following;

(i) a lack of increased muscle activation during post-stretch isometric contractions which suggests that increased torque was primarily mechanical in nature and minimally influenced by neuromechanical factors (Contento et al., 2019; Hahn et al., 2012; Sypkes et al., 2018),

(ii) the levels of isometric pre-activation in the current study was sufficient to influence muscle lengthening and activation of titin. Previous investigations have suggested that modulation of muscle lengthening is influenced by muscle-tendon interaction (Farris et al., 2016) and the elimination of muscle slack (Herbert et al., 2015) during the isometric pre-activation phase. The influence of sufficient isometric pre-activation on muscle stretch and magnitude of residual force enhancement has been demonstrated in maximal and submaximal post-stretch isometric contractions (Chapman et al., 2020; Fukutani & Herzog, 2019; Fukutani et al., 2019) and

(iii) a recent investigation of submaximal post-stretch isometric contractions was undertaken by the current authors who directly confirmed muscle lengthening of biceps femoris long-head via ultrasound during post-stretch isometric contractions (Chapman et al., 2020). This study used the same body position, joint excursion, angular velocity, and submaximal contraction intensity as the current study (Chapman et al., 2020). We, therefore, surmise that it is highly likely that muscle lengthening and activation of titin took place in the current study. However, it is acknowledged that other non-contractile elements may have made some contribution to enhanced post-stretch isometric steady-state force.

This study demonstrates that the phenomenon responsible for residual force enhancement is reproducible during consecutive post-stretch isometric contractions, similar to resistance training protocols (Ahtiainen et al., 2005). The potential benefits of a contraction mode which benefits for an eccentric stimulus leading to enhanced isometric steady-state force at reduced metabolic cost (Joumaa & Herzog, 2013), are intriguing. Evidence suggests that with chronic use of eccentric contractions, increased eccentric strength and increased fascicle length (de Vos et al., 2020) often occur concomitantly with a rightward shift in the optimal operating angle on the length-tension curve (Brughelli & Cronin, 2007). These changes to the structure and behaviour of the muscle have been found to increase the resilience of the hamstring to strain injury (Timmins, Bourne, et al., 2016). However, athlete compliance with eccentrically biased programs remains an issue (van der Horst et al., 2020). Notwithstanding the evidence for the benefits of eccentric contractions in hamstring resilience, the importance of isometric hamstring strength has recently been proposed (Macdonald et al., 2019; Van Hooren & Bosch, 2017a; Van Hooren & Bosch, 2017b; Van Hooren & Bosch, 2018). It is known that with the chronic implementation of isometric exercise at long musculotendinous unit lengths, increases in isometric strength, pennation angle, fascicle length, and hypertrophy occur (Oranchuk et al., 2019). Furthermore, a broadening of the plateau region of the length-tension curve is also known to occur with the implementation of chronic isometric training at long musculotendinous unit lengths (Akagi et al., 2020), which have the potential to provide similar prophylactic effects to hamstring strain injury. The results of the current study indicate that the use of post-stretch isometric contractions that incorporate both an isometric and eccentric stimulus results in enhanced force output of the muscle during both the eccentric and post-eccentric isometric steady-state phases. This increase in force was found to occur in the absence of increased muscle activation; hence, post-stretch isometric contractions that result in residual force enhancement may be more metabolically efficient when compared to eccentric or isometric contractions to achieve similar levels of force (Joumaa & Herzog, 2013; Seiberl et al., 2012). However, the effects of the combined use of these contraction modes shown to be beneficial to hamstring injury resilience are currently unknown.

Therefore, based on the findings of this study, future research should test the efficacy of the chronic use of post-stretch isometric contractions in hamstring strain injury prevention. The potential exists that with the chronic use of post-stretch isometric contractions, athletes could experience benefits including increased muscle hypertrophy, increased eccentric and isometric strength, increased fascicle length, and a rightward shift or broadening of the plateau of the optimum angle in the length-tension curve (Askling et al., 2003; Brockett et al., 2001; Hinks et al., 2021; Oranchuk et al., 2019; Timmins et al., 2016).

An intermediate consideration, however, is the possibility that chronic performance of post-stretch isometric contractions in resistance training may modify the history dependence of force. For instance, a modification to the history dependence of force could result in a decrease in residual force enhancement. This is because it has been hypothesized that increased fascicle length in a muscle may result in less stretching of titin per sarcomere, leading to a reduction in passive force following active lengthening and a reduction in residual force enhancement (Chen & Power, 2019). The influence of muscle architecture changes on residual force enhancement has recently been investigated, with varied effects found (Chen & Power, 2019; Siebert et al., 2016). For example, Hinks et al. (2021) found no significant changes in residual force enhancement following chronic isometric training at long or short muscle lengths, despite the fascicle length increasing and decreasing, respectively (Hinks et al., 2021). In contrast, evidence of the effect of concentric and eccentric training on residual force enhancement is less certain. Chen and Power (2019) observed an increase in residual force enahancement magnitude following concentric training and a decrease following eccentric training that corresponded to changes in fascicle lengths. These findings are tempered by their conclusion that their results were influenced by a change in non-responder rates and antagonist co-activation between conditions (Chen & Power, 2019). Thus, the influence of chronic isometric, concentric and eccentric training on history dependence of force deserves greater attention. Notwithstanding the need for further investigation of the influence that resistance training may have on residual force enhancement, it is clear that alternative injury-prevention strategies are needed to arrest the high levels of hamstring strain injury incidence. Post-stretch isometric contractions have the potential to benefit from both eccentric and isometric stimulus, with the added benefits of enhanced torque output (residual force enhancement) at a lower metabolic cost. Therefore, an investigation into the effects of a training study using post-stretch isometric contractions of the hamstrings is recommended.

6.5 Conclusions

This is the first investigation to observe residual force enhancement during multiple, consecutive submaximal post-stretch isometric contractions. The absence of increased muscle activation during post-stretch isometric contractions suggests that passive structures within the musculotendinous unit, possibly the giant protein titin, were the primary contributor of passive force to the enhanced state (Chapman et al., 2020). Debate exists over the most efficient way to improve hamstring function; however, the use of chronic eccentric and isometric training is often advocated for hamstring injury prevention (Van Hooren & Bosch, 2017b). Eccentric and isometric strength training are known to share similar benefits (increase in strength, fascicle length increases, and a broadening or rightward shift in the optimum angle of peak torque (Askling et al., 2014; Brockett et al., 2001; Hinks et al., 2021; Oranchuk et al., 2019; Timmins et al., 2016). Post-stretch isometric contractions incorporate both an eccentric and isometric stimulus with the added benefits of enhanced isometric torque at reduced metabolic cost. It would appear intuitive that the use of post-stretch isometric contractions in resistance training could combine the benefits of eccentric or isometric training in isolation. The investigation into the effect of chronic resistance training using post-stretch isometric contractions, particularly in the hamstring muscles, is certainly warranted.

Chapter 7 - Synthesis

7.1 Summary

Elevated hamstring strain injury incidence and recurrence rates are of concern to athletes, coaches, sports organisations and researchers alike. Athletes who sustain a hamstring strain injury typically endure an extended absence from competition while rehabilitating in preparation for return to play. Further, upon return to play, evidence suggests that they will have an elevated risk of re-injury. Despite an exponential increase in research in the past decade, much of it targeting the development of more effective hamstring strain injury prevention and rehabilitation programs, the elevated risk of hamstring strain injury and injury recurrence remains a concern.

Current injury prevention and rehabilitation programs which typically rely on either an eccentric or isometric contraction bias, are yet to lead to significant reductions in hamstring strain injury prevalence and recurrence, which over the previous 20 years, arguably remain stagnant. Nonetheless, based on the current literature on hamstring strain injury mechanisms and existing knowledge of rehabilitation strategies, there is a justifiable need to investigate alternative hamstring strain injury prevention and rehabilitation techniques that seek to potentially address hamstring strain injury incidence and recurrence. On this basis, a theoretical potential exists for a combined eccentric-isometric contraction approach, which, uses history-dependence of muscle contractions, while potentially optimising sarcogenesis, to benefit hamstring strain injury prevention and rehabilitation. However, history dependent behaviour of the knee flexor muscles during contractions that are relevant for injury prevention and rehabilitation was unknown prior to this thesis. Therefore, this thesis's overall aim was to determine whether knee flexor muscles could reliably generate residual force enhancement during highly controlled post-stretch isometric contractions (which incorporate eccentric and isometric contractions) under a range of conditions relevant to hamstring strain injury prevention and rehabilitation programs.

This overall thesis aim was achieved by conducting a series of studies presented in three parts (see Figure 1, Chapter 1). Firstly, a review of the literature was undertaken (Chapter 2), which identified hamstring strain injury aetiology, risk factors, current approaches to hamstring strain injury prevention and rehabilitation. Importantly, it was noted that the goals of hamstring strain injury prevention and rehabilitation programs between those implementing an eccentric or isometric bias were mostly congruent. Furthermore, sections 2.1.4.1 and 2.1.4.2 outlined that the functional outcomes of using an eccentric or isometric training bias were mainly in agreement.

Based on the evidence reported from this review of current practices, a proposal for the potential use of a combined eccentric-isometric contraction mode was posited. As a result the post-stretch isometric contraction and the phenomenon of residual force enhancement were identified as having theoretical benefits for hamstring strain injury prevention and rehabilitation programs. This then led to a systematic review (Chapter 3) resulting in Part I of the thesis clarifying the current understanding of residual force enhancement *in vivo* human skeletal muscle.

The systematic review identified the effect of contraction intensity, stretch amplitude, angular velocity, and joint position of the final isometric contraction on residual force enhancement magnitude. The systematic review results provided direction for the development of three experimental studies, presented in Part II (Chapters 4 and 5) and Part III (Chapter 6) of this thesis.

Part II involved completing two experimental studies focused on the observation of the neuromuscular behaviour of the knee flexors during single post-stretch isometric contractions. Study 1 (Chapter 4) confirmed residual force enhancement in the hamstring muscle group using post-stretch isometric contractions of maximal intensity ending at joint angles indicative of action on the descending limb of the length-tension relationship. The findings of study 1 informed the methodology of study 2 (Chapter 5, section 5.2), which extended our understanding of residual force enhancement in the knee flexors *in vivo* using maximal and submaximal post-stretch isometric contraction intensity with a long and short stretch amplitude. Study 2 also confirmed muscle lengthening during the stretch phase of post-stretch isometric contractions. The knowledge gained from the systematic review, study 1, and study 2 led to the design of study 3 (Chapter 6) and Part III of the thesis. In Part III of the thesis, the final study, study 3 (Chapter 6), observed the hamstring muscles' neuromechanical behaviour using a series of repeated and consecutive submaximal post-stretch isometric contractions that replicated standard hamstring strength training methods, in the form of a training simulation. This final experimental study (Chapter 6) was designed and implemented as the culmination of knowledge gained via the systematic review (Chapter 3) and experimental studies 1 and 2 (Chapters 4 and 5). The results of the systematic review and experimental studies described above provide strong evidence upon which to develop recommendations for a novel training modality using post-stretch isometric contractions (Chapter 7). The key findings from each part of the thesis are summarised below.

7.1.1 Part I: What is currently known about the phenomenon of residual force enhancement in human skeletal muscle *in vivo*?

Via a systematic review (Chapter 3), Part I of the thesis sought to clarify the current understanding of residual force enhancement *in vivo* human skeletal muscle. To this end, Chapter 3 provided the basis to identify the need for investigation of a combined eccentric-isometric contraction approach in hamstring strain injury prevention and rehabilitation programs. In this systematic review, 24 studies were included (n = 424), which observed residual force enhancement *in vivo* human skeletal muscle using voluntary post-stretch isometric contractions. In summary, residual force enhancement was observed in all muscles tested, ranging from single-joint/single-muscle to multi-joint/multi-muscle arrangements. The phenomenon of residual force enhancement was observed using a range of contraction and activation intensities, stretch magnitudes, and velocities. The magnitude of residual force enhancement depended on contraction intensity, muscle length, and age but was independent of angular velocity and stretch magnitude. The methodological quality of the observational studies was categorised as “fair.”

One study was identified which observed residual force enhancement in the knee flexors, and the findings of the systematic review indicated that residual force enhancement can be generated by the hamstring muscle group and is likely to be of greater magnitude where the intensity of post-stretch isometric contractions is near maximal and performed at joint angles indicative of long muscle lengths. These findings are congruent with hamstring strain injury prevention program goals. Individually, the chronic use of eccentric and isometric contractions performed at long muscle lengths, increases eccentric strength, muscle fascicle length and induces either a rightward shift or a broadening of the range of angle of peak torque on the plateau on the length-tension relationship. As such, the use of post-stretch isometric contractions of near-maximal intensity at joint angles indicative of long muscle lengths has the potential, with chronic use, to achieve current hamstring strain injury prevention and rehabilitation program goals. Therefore, an experimental study whereby the methodology was developed using the systematic review information was warranted.

7.1.2 Part II: Does the hamstring muscle group have the capacity to develop residual force enhancement using maximal and submaximal post-stretch isometric contractions, and does an eccentric contraction occur during post-stretch isometric contractions?

Although Part I confirmed the hamstrings muscle group's capacity to generate residual force enhancement, there is a paucity of evidence documenting residual force enhancement in the hamstrings using maximal and submaximal intensity post-stretch isometric contractions. Similarly, there is limited evidence of residual force enhancement in the hamstrings when using multiple stretch magnitudes. Despite the systematic review indicating that the magnitude of residual force enhancement was minimally influenced by stretch magnitude, to date, no direct observation of the hamstrings during post-stretch isometric contractions had been undertaken. It was uncertain whether the post-stretch isometric contraction's stretch magnitude influenced the magnitude of contractile element or series elastic element stretch. Accordingly, Part II involved completing two experimental studies focused on the observation of the neuromuscular behaviour of the knee flexors during single post-stretch isometric contractions of varying contraction intensity and stretch magnitude. The first experimental study (Chapter 4), using a methodology directly informed by the systematic review, confirmed residual force enhancement in the hamstring muscle group. The magnitude of residual force enhancement was observed to be 14% following post-stretch isometric contractions of maximal intensity, and at joint angles indicative of long muscle lengths with a stretch magnitude of 60°. It was also noted that residual force enhancement was observed in the absence of increased muscle activation, measured via sEMG.

Notwithstanding this, as muscle activation was observed in biceps femoris long-head only, there is the potential that other muscles in the hamstring group (semitendinosus or semimembranosus) may have increased their activation, potentially contributing to the enhanced forces observed, which were interpreted as residual force enhancement.

Study 1 (Chapter 4) provided further evidence that the hamstring muscle group can generate supramaximal levels of eccentric force (during the stretch phase of post-stretch isometric contractions) as well as supramaximal levels of steady-state isometric force (during the final isometric phase of post-stretch isometric contractions) using post-stretch isometric contractions of maximal intensity. Interestingly, the application of supramaximal levels of eccentric and isometric force is indicated for use in hamstring strain injury prevention programs that utilise either an eccentric or isometric bias, as discussed in sections 2.1.4.1 and 2.1.4.2, respectively. This is further evidence that post-stretch isometric contractions have the potential to benefit hamstring strain injury prevention programs. What was less certain was whether the hamstring muscle group could generate residual force enhancement using post-stretch isometric contractions of submaximal intensity.

The second experimental study (Chapter 5) extended our understanding of residual force enhancement in the hamstrings *in vivo* by; i) simultaneously observing torque output and muscle activation of the medial and lateral hamstring muscles during post-stretch isometric contractions of maximal and submaximal intensity and stretch amplitude (long stretch and short stretch); and ii) by using, ultrasound to measure and show dynamic positional change of the distal and proximal musculotendinous junctions of biceps femoris long-head during post-stretch isometric contractions of varying intensity and stretch amplitude (long stretch and short stretch).

Study 2 (Chapter 5) further confirmed residual force enhancement of 8% magnitude in the hamstrings using post-stretch isometric contractions of maximal intensity, using a short stretch magnitude. However, residual force enhancement was not observed using maximal intensity post-stretch isometric contractions and long stretch magnitude. Despite an absence of residual force enhancement in the short stretch magnitude, in the maximal intensity post-stretch isometric contraction condition, the contractile element of biceps femoris long-head was observed to stretch to a similar magnitude as the long stretch condition. It was postulated that tension-mediated factors from peripheral sensory inputs via altered inhibitory sensory feedback to the agonist motor neuron pool, reduced force output.

It was posited that neural influences limited torque output and resultant residual force enhancement in this condition. It is also posited that owing to the maximal contraction intensity and larger stretch amplitude, that it was possible that the observed activation reduction of semitendinosus could be a protective response by the neural system. This may functionr to reduce muscle strain and potential for injury to the muscle. Therefore, when using maximal post-stretch isometric contraction intensities, which can result in supramaximal output, a lesser stretch amplitude should be utilised to minimise the effect that tension-mediated neural factors may have. However, when using submaximal intensity post-stretch isometric contractions in study 2, the amplitude of stretch had no significant effect on torque output. Therefore, the amplitude of stretch appears to be of lesser importance in submaximal post-stretch isometric contractions of the hamstrings ending at long musculotendinous unit lengths. As such, study 2 findings reinforce the complex nature of *in vivo* residual force enhancement.

Notwithstanding the absence of residual force enhancement in the aforementioned maximal intensity condition, residual force enhancement was observed in the submaximal intensity post-stretch isometric contractions (39% magnitude) in the absence of increased muscle activation as measured by sEMG of the medial (semitendinosus) and lateral (biceps femoris long-head) hamstrings. Additionally, the stretch of the contractile element was observed during all contractions regardless of stretch magnitude. Study 2 (Chapter 5) is the first to demonstrate residual force enhancement in the hamstrings muscle group using submaximal intensity post-stretch isometric contractions. Additionally, Study 2 is also the first to observe dynamic contractile element lengthening (a true eccentric contraction) during post-stretch isometric contractions. Given these findings, study 2 provides evidence to support the use of post-stretch isometric contractions of submaximal intensity during hamstring strain injury rehabilitation programs. As a result, the goals of hamstring strain injury rehabilitation when using eccentric contractions should include; i) the use of eccentric contractions to induce sarcogenesis and alignment of myotubes during the regeneration phase of muscle recovery, resulting in decreased scar tissue size and result as a weak point of the muscle, ii) increases in eccentric strength, iii) increased muscle fascicle length, and iv) induce a rightward shift in the angle of peak torque on the length-tension relationship. Furthermore, hamstring strain injury rehabilitation goals when using isometric contractions include i) increases in isometric strength, ii) increases in muscle fascicle length, and iii) broadening the plateau of angles of peak torque on the length-tension relationship. The second experimental study's findings (Chapter 5), with particular reference to the submaximal intensity, long stretch magnitude conditions, were then used to design the methodology for the final experimental study presented in Part III (Chapter 6).

7.1.3 Part III: Is residual force enhancement present in the hamstrings during multiple sets and repetitions per a training simulation, and what are the potential implications for hamstring strength training?

Part III of the thesis outlines the final experimental study (Chapter 6), which observed the hamstring muscles' neuromechanical behaviour following a series of repeated and consecutive submaximal post-stretch isometric contractions. This was achieved using joint positions that replicate standard hamstring strength training methods, in the form of a training simulation. The final experimental study (Chapter 6) was designed and implemented as the culmination of knowledge gained via the systematic review (Chapter 3) and experimental studies 1 and 2 (Chapters 4 and 5).

Study 3 (Chapter 6) is the first to observe residual force enhancement using multiple and consecutive post-stretch isometric contractions. The magnitude of residual force enhancement ranged between 37-77% during the submaximal post-stretch isometric contractions. Of note is that residual force enhancement was observed in all 30 post-stretch isometric contractions (3 sets of 10 repetitions). The enhanced steady-state isometric torque (residual force enhancement) was not accompanied by an increase in muscle activation of the medial (semitendinosus) and lateral (biceps femoris long-head) hamstrings as measured by sEMG. Like the findings in studies 1 and 2 (Chapter 4 and 5 respectively). Furthermore, study 3 demonstrated that residual force enhancement can be reliably generated by the hamstrings muscle group and furthermore study 3 confirmed that residual force enhancement can endure beyond a single repetition. This is the first evidence presented whereby the hamstrings muscle group demonstrates the potential for post-stretch isometric contractions to be used in conventional resistance training.

Based on the findings of studies 1, 2, and 3, it is clear that the combined use of eccentric and isometric contractions as produced by post-stretch isometric contractions in the hamstrings results in residual force enhancement. Furthermore, generation of residual force enhancement in the order of 8-77% magnitude is possible in the hamstrings muscle group. There is theoretical support provided in this thesis for the potential use of post-stretch isometric contractions in hamstring strain injury prevention and rehabilitation programs.

The previously identified hamstring strain injury prevention and rehabilitation goals were mostly compatible with the findings of these studies, i.e., increased eccentric strength, increase muscle fascicle length, and induce either a rightward shift or broadening of the plateau of range of angles of peak torque on the length-tension relationship. These neuromuscular and muscle architecture changes have been identified as being protective of future hamstring strain injury and/or beneficial in recovery from hamstring strain injury. The findings provided in this thesis demonstrate that post-stretch isometric contractions may have in influencing the direction of hamstring strain injury prevention and rehabilitation programs.

7.2 Recommendations for future use

Based on this thesis's results, the following evidence-based recommendations are made to improve hamstring strain injury prevention and rehabilitation programs using post-stretch isometric contractions.

i) To assess the hamstring muscles' ability to generate residual force enhancement in a training situation with the goal of reducing the incidence of hamstring strain injury, further investigation of multiple and consecutive post-stretch isometric contractions of maximal intensity (study 3 Chapter 6) should be undertaken.

ii) Investigation into the effect of fatigue in multiple post-stretch isometric contractions of maximal intensity is warranted where maximal contraction intensity is desired for performance enhancement.

iii) The potential exists that post-stretch isometric contractions may benefit other injury prevention and injury rehabilitation training scenarios. As such, following on from study 3 (Chapter 6), it is recommended that investigation of multiple and consecutive post-stretch isometric contractions of a range of upper and lower limb muscles is warranted.

iv) Before using post-stretch isometric contractions in rehabilitation programs, it is recommended that an investigation of the acute use of submaximal post-stretch isometric contractions in injured hamstring muscles be undertaken. It is not known whether injured hamstrings can generate residual force enhancement. A novel approach would be to use subjective pain experience (i.e., the visual analogue scale) as the mediator of intensity for the post-stretch isometric contractions. Pain-mediated hamstring strain injury rehabilitation has recently been investigated by Hickey et al. (2020).

v) Before post-stretch isometric contractions are adopted in hamstring strain injury prevention programs, an investigation of the chronic use of post-stretch isometric contractions that result in residual force enhancement is warranted. Specifically, the observation of the effect of using post-stretch isometric contractions in a training program on hamstring strain injury risk factors such as, eccentric strength, muscle fascicle length, and angle of peak torque on the length-tension relationship should be investigated.

vi) Before post-stretch isometric contractions are recommended for use in hamstring strain injury rehabilitation programs, an investigation of the chronic use of post-stretch isometric contractions that result in residual force enhancement is warranted. This should include observation of the effect of pain-mediated post-stretch isometric contractions on hamstring strain injury recovery markers, specifically, scar tissue size, eccentric strength, muscle fascicle length, and angle of peak torque on the length-tension relationship. Furthermore, it is recommended that the timeframe to achieve standardised strength benchmarks should be compared using conventional hamstring strain injury rehabilitation practices with pain mediated post-stretch isometric contractions. A long-term follow-up of injury rates following the use of both a conventional approach to hamstring strain injury rehabilitation and an approach that utilises post-stretch isometric contractions should be undertaken to assess the effect of post-stretch isometric-focused rehabilitation on hamstring strain injury recurrence rates.

The recommendations outlined above have the potential to influence currently accepted hamstring strain injury prevention and rehabilitation practices. It is hoped that incorporating the recommendations of this thesis in relation to hamstring strain injury prevention practices will benefit athletes by decreasing hamstring strain injury incidence. Furthermore, the use of these recommendations may influence rehabilitation practices that have the potential to reduce rehabilitation timeframes and increase the effectiveness of rehabilitation, leading to a more efficient and sustainable return to play.

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Appendix A: Statement of Co authorship Chapter 2

Chapman, N., Whitting, J., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2018). Residual force enhancement in humans: a systematic review. *Journal of applied biomechanics*, *34*(3), 240-248.

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Author 2 provided a primary supervisory role, conducted risk of bias assessments and contributed to interpretation of results and the finalisation of the manuscript.

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Appendix B: Statement of Co authorship Chapter 3

Chapman, N., Whitting, J., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2021). Post-stretch isometric contractions of the hamstrings: Just a brief stretch to achieve supramaximal isometric force. *Journal of applied biomechanics, (in press).*

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Author 3 provided a co-supervisory role, contributed to the interpretation of the results and to the finalisation of the manuscript.

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Appendix C: Statement of Co authorship Chapter 4

Chapman, N., Whitting, J., Broadbent, S., Crowley-McHattan, Z., & Meir, R. (2020). Maximal and submaximal isometric torque is elevated immediately following highly controlled active stretches of the hamstrings. *Journal of Electromyography and Kinesiology*, *56*, 102500.

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Appendix D: Statement of Co authorship Chapter 5

Chapman, N.D., Whitting, J.W., Broadbent, S., Crowley-McHattan, Z.A., & Meir, R. (2021). Residual force enhancement is present in consecutive post-stretch isometric contractions of the hamstrings: a training simulation. *International Journal of Environmental Research and Public Health (in press)*

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Candidate contribution: The candidate was the primary author and with authors 2 – 5 contributed to the conception and design of the research project. The candidate collected all data, extracted the data, performed all analysis and drafted the manuscript.

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Appendix E: Ethics Submission

Can Residual Force Enhancement and Activation Reduction be Observed in Healthy and Injured Muscles?

Project Team Roles and Responsibilities

Neil Chapman	PhD Candidate, Chief Investigator/Researcher
Dr John Whitting	Primary Supervisor, Principal Investigator
A.Prof Suzanne Broadbent	Supervisor, Principal Investigator
Dr Zac Crowley-McHattan	Supervisor, Principal Investigator
Dr Rudi Meir	Supervisor, Principal Investigator

Resources

Resources for each study are being provided by Southern Cross University, as part of the PhD candidature. Each study will be conducted at the Sports Science Laboratories at either Lismore or Gold Coast campus of Southern Cross University. Equipment is in place to conduct the studies and includes the Biodex dynamometer, Delsys EMG and Ultrasound. Consumables will be catered for in the PhD Candidate's allocated budget.

Literature Review

Hamstring muscle injuries: background and current perspectives on rehabilitation

Athletes participating in professional football codes (Football [Soccer], Rugby Union and Australian Football League [AFL]), have a substantial risk of injury, which is approximately 1000 times higher than typical high-risk industrial occupations (Drawer & Fuller, 2002). Hamstring strain injuries (HSI) are amongst the most prevalent across the majority of the elite football codes, and in sport more broadly (J. H. Brooks et al., 2006; Evans & Williams, 2017; Gabbe, Bennell, et al., 2006a; J. Hickey et al., 2014; Orchard et al., 2014). Among all reported injuries within an AFL club, HSI had the highest incidence, ranked second highest for injury recurrence, and resulted in the greatest number of missed games per club per season (5.2 new injuries per season) (J. Orchard & H. Seward, 2013). The excessive financial costs attached to recovery from HSI are also of concern to athletes and their employers (J. Hickey et al., 2014). In one of the world's highest paid professional sports, European football, the financial cost of a first team player being injured for one month has been estimated to be approximately €500,000 (Ekstrand et al., 2013). Using this Figure, and data from an injury study commissioned by the Union of European Football Associations, it can be estimated that an average HSI of 14 days duration may cost approximately €250,000 (Jan Ekstrand et al., 2012). This data reinforces the substantial effect of HSI on an athlete's career, and for the professional sporting organisation that employs them, and highlights the need for more efficient HSI rehabilitation techniques. Potential benefits of improved HIS rehabilitation may include reduced recovery times for the athlete resulting in an expedited return to play, reducing the associated costs of rehabilitation, including the significant cost to the club of lost playing time.

The use of eccentric contractions in hamstring strain injury rehabilitation

Determining the type of rehabilitation program that most effectively promotes muscle tissue and functional recovery is essential to minimise the risk of re-injury, and to improve athletic performance. Evidence based rehabilitation requires consideration of muscle remodelling while minimising modifiable hamstring strain injury (HSI) risk factors, returning eccentric hamstring strength and balancing between-limb strength (David A Opar et al., 2012). Eccentric strength training has therefore been advocated in HSI rehabilitation (Heiderscheit, Sherry, Silder, Chummanov, et al., 2010). The commonality amongst these types of programs is the focus on using eccentric loading at long muscle lengths. This approach induces change in fascicle length, hypertrophy in the injured muscle, and increases eccentric muscle contraction strength (R. G. Timmins, J. D. Ruddy, et al., 2016). The primary outcomes sought from this approach are to decrease return to play time and overcome the modifiable HSI risk factors, while also minimising subsequent HSI risk.

The aforementioned eccentric focused programs have traditionally been implemented well after the acute phase of injury rehabilitation. The use of eccentric contractions during early hamstring rehabilitation has been much maligned due to perceptions of increased risk of muscle damage during the muscle-lengthening phase of a movement (LaStayo et al., 2003; U. Proske & D. Morgan, 2001; Weerakkody et al., 2003). Traditionally, in an acute stage rehabilitation setting, models of strength restoration have been limited to the use of pain-free isometric and concentric contractions only. With regard to concentric contractions, this has also involved brief duration contractions performed through a limited range of motion (Jarvinen et al., 2007). Until recently, these contraction modes have been considered safer options (Heiderscheit, Sherry, Silder, Chummanov, et al., 2010), however there is growing interest in the re-evaluation of criteria for progressing HSI rehabilitation programs (J. Hickey et al., 2016). Accordingly, some emerging evidence suggests that the progression of rehabilitation should not necessarily always be pain-free. For instance, Hickey (2017) showed that allowing for a moderate pain threshold (4/10 on a visual analogue scale [VAS] where a higher score indicates greater pain intensity) during rehabilitation progression results in comparable return to play times when compared to a pain-free progression model (Hickey et al., 2017). The pain threshold group in that study also had the added benefit of increased knee flexor strength, thus mitigating a key modifiable HSI risk factor (Hickey et al., 2017). Although this new evidence exists, changing long-held practice, that avoids the use of eccentric contraction during acute stage HSI rehabilitation, poses a challenge. Hamstring strain injury rehabilitation is yet to be optimised and requires further investigation of novel and scientifically sound protocols. Such protocols may necessitate the use of highly controlled eccentric contractions, administered earlier in the rehabilitation process, to reduce the risk of re-injury by minimising scarring, among other potential benefits.

Post stretch isometric contractions: A potential new paradigm for early stage muscle rehabilitation?

A contraction modality that uses a brief duration eccentric contraction phase in a highly controlled manner, is that of a post-stretch isometric contraction. A post-stretch isometric contraction requires an active pre-stretch (eccentric phase), followed by an isometric contraction. When this isometric phase is long enough to achieve steady state force, it can result in force enhancement of between 10% and 400% of a pure steady-state isometric force generated without the pre-stretch (Stuart G Campbell & Kenneth S Campbell, 2011; Wolfgang Seiberl et al., 2015). Thus, a critical phenomenon of the post-stretch isometric contraction is that force output exceeds the isometric output predicted by traditional muscle models, which is proportional only to sarcomere length and the corresponding number of cross-bridges. (Stuart G Campbell & Kenneth S Campbell, 2011; Wolfgang Seiberl et al., 2015). Conversely, research also demonstrates that the mechanism behind this phenomenon leads to reduced muscular activation levels during post-stretch isometric contractions that match steady-state isometric forces without a pre-stretch (Teatske Maria Altenburg et al., 2009; Hahn et al., 2007).

Post-stretch isometric contractions, residual force enhancement and activation reduction.

There is a growing body of evidence to explain the history dependent mechanism for force enhancement in post-stretch isometric contractions in-vitro (Herzog, 2014; Herzog et al., 2010a, 2010b). Similarly, although numerous studies have demonstrated the existence of enhanced forces in-vivo (H. D. Lee & W. Herzog, 2002a; Florian Kurt Paternoster et al., 2016; Tilp et al., 2009), there remains much to learn about these mechanics in complex, multi-joint muscles such as the hamstrings. Therefore, while there appears to be an exciting potential for utilising these types of contractions in early stage HSI rehabilitation, more work is required to systematically investigate these mechanisms and their effects in healthy and injured muscles, in-vivo.

The term to describe the phenomenon of a residual force enhancement, elicited during a post-stretch isometric contraction, was introduced by Edman, Elzinga and Noble (1982) to articulate earlier observations made by Abbott and Aubert (1952). Abbott and Aubert (1952) observed that the resultant force reaches a peak during the eccentric phase and then quickly decays to a steady level during the isometric phase, albeit at a higher than predicted, or ‘enhanced’, level (Pinniger & Cresswell, 2007). Using whole muscle preparations, Abbott and Aubert (1952) observed that residual force enhancement occurred on the ascending, plateau and descending limb portions of the force-length relationship.

Since the initial experiments of Abbott and Aubert (1952), residual force enhancement has been demonstrated in numerous muscle models, including *in vitro* for single fibre preparations (Edman et al., 1982; Peterson et al., 2004; Rassier, Herzog, et al., 2003a), whole muscle preparations (Abbott & Aubert, 1952; Herzog & Leonard, 2000; Schachar et al., 2004), *in vivo* with electrical stimulation (Cook & McDonagh, 1995; H. D. Lee & W. Herzog, 2002a; Pinniger & Cresswell, 2007; Ruiter et al., 2000b), and with voluntary contractions (Hahn et al., 2010; H. D. Lee & W. Herzog, 2002a; Oskouei & Herzog, 2005; Pinniger & Cresswell, 2007; Tilp et al., 2009). Residual force enhancement has also been observed during maximal (Hahn et al., 2010), and submaximal (Pinniger & Cresswell, 2007; Seiberl et al., 2012) contraction intensities.

Over the last few decades, investigations into the phenomenon of residual force enhancement have also shed musch light on the inderlying mechanism that causes it. It is now understood that the structural protein titin, acting as a molecular spring, contributes to the enhanced force. Titin spans the half sarcomere inserting in the M-band, thereby connecting myosin (distally) to actin and the Z-line (proximally). In the I-band region, titin spans freely, elongating under load and shortening when load is removed. Titin is behaves elastically prior to the unfolding of a series of immunoglobulin domains (Ig), but becomes highly viscous once Ig unfolding occurs. Titin has also been observed to alter its spring stiffness in the presence of calcium, which binds to a specific Ig region during muscle activation, thereby increasing stiffness and force output upon stretch (Labeit et al., 2003). Furthermore, during activation, titin also binds to actin in the presense of calcium , thereby shortening its spring length, increasing stiffness and therefore force, upon stretching (Herzog et al., 2015; Herzog et al., 2016). Understanding the role of titin in enhancing the forces generated by cross-bridges during a contraction, especially when sarcomeres are lengthened, is critical for understanding how the mechanism creates the phenomena of residual force enhancement and, converseley, AR.

When force is matched between a pure submaximal isometric contraction and the final isometric phase of a post-stretch isometric contraction, there is a resulting reduction in the magnitude of muscular activation for the post-stretch isometric contraction (Altenburg et al., 2008; Oskouei & Herzog, 2005; Pinniger & Cresswell, 2007; Seiberl et al., 2012). This phenomenon has been termed activation reduction (AR).. The increased stiffness of titin, elicited during the eccentric phase of a pre-stretch isometric contraction, necessitates lower force requirements from cross-bridges in order to achieve the force output predicted for pure isometric contractions at the same muscle lengths. By supplementing force output from active elements within a sarcomere, with enhanced forces generated by titn, the largest structural protein in the body [ref], post stretch isometric contractions performed at targetted submaximal force levels result in AR which is highly efficient energetically and likely to reduce metabolic cost (Herzog, 2017).

There has been much research confirming the presence of residual force enhancement and AR in functional, multi-muscle, multi-joint actions of the hip, knee and ankle (T. Altenburg et al., 2009; Hahn et al., 2010; Hahn et al., 2007; F. K. Paternoster et al., 2016b; Power et al., 2014; Power et al., 2013; Power et al., 2015; Seiberl et al., 2013a; Tilp et al., 2009; Tilp et al., 2011). Current evidence demonstrates that residual force enhancement and AR can be observed consistently in healthy human muscle at submaximal contraction intensities and for hamstrings, at similar joint angles to those used in traditional methods of rehabilitation for restoring strength and function (Seiberl et al., 2012). In addition, Power, Rice and Vandervoort (2012b) have demonstrated that the mechanical and neuro-motor mechanisms underlying residual force enhancement may actually generate greater force enhancement (approximately 100%-250% greater) in injured muscle than in healthy muscle. The converse of this phenomenon is to achieve desired levels of force output at substantially lower activation levels, thereby minimising expenditure.

The findings of Power et al. (2012b) suggest that if muscle damage has no detrimental effect on residual force enhancement or AR, the mechanism for this phenomenon is likely to be regulated by structural components of healthy sarcomeres that can add to cross-bridge output . This would not be surprising when one considers that numerous researchers over the last couple of decades have demonstrated that residual force enhancement and AR are determined largely by titin (Herzog et al., 2015; Herzog et al., 2016). Interestingly, this is more evidence that contradicts long-held beliefs that any contractions involving an eccentric phase will increase the risk of further damage and therefore be detrimental to healing in early stage rehabilitation (LaStayo et al., 2003; U. Proske & D. Morgan, 2001; Weerakkody et al., 2003). On the contrary, it is reasonable to speculate that highly controlled, submaximal post-stretch isometric contractions using small ROM eccentric phases may be more beneficial, rather than more risky than traditional methods.

From this review of the literature so far, current and emerging evidence indicates that the potential benefits of using scientifically justified doses of post-stretch isometric contractions in acute and sub-acute injury rehabilitation may include: i) optimised alignment of collagen fibres during fibrosis and remodelling that can reduce scarring and reduce subsequent re-injury risk; ii) up-regulated sarcogenesis through mechanotransduction that can lead to faster strength gains; iii) earlier gains in strength should expedite progression into later stage functional rehabilitation protocols; and iv) rehabilitation that can minimise expenditure by reducing muscular activation at targeted submaximal training intensities. Nonetheless, there also appears to be a number of gaps in the literature that require investigation before studies should attempt to develop or test the efficacy of rehabilitation protocols that use post-stretch isometric contractions in HSI rehabilitation. Therefore, a systematic review is essential for summarising and critically analysing the current evidence of voluntarily activated post-stretch isometric contractions. Furthermore, a systematic review should identify areas requiring further investigation to inform any future experiments of post-stretch isometric contractions in multi-joint healthy and injured muscle. Evidence gathered from such future experiments should underpin the development of optimised HSI rehabilitation protocols.

Research Aims and Hypotheses

Overall aims

The overall aim of the experimental aspect of this research is to better understand the post-stretch isometric contraction modality in healthy and injured multi-joint muscle models, specifically the hamstrings muscle group. The scientific paradigm in this thesis will take the epistemological position of positivism. The design methodology will involve two experimental studies using quantitative research methodology to test a series of hypotheses. The purpose of these studies will be to: (i) confirm muscle fibre lengthening in healthy hamstring muscles during the eccentric phase of a post-stretch isometric contractions; (ii) determine the presence of residual force enhancement and AR in healthy hamstring muscles as a result of post-stretch isometric contractions; and (iii) determine the presence of residual force enhancement and AR in injured hamstring muscles as a result of post-stretch isometric contractions.

Main hypotheses

H1 (experiment 1): In healthy hamstring muscles, fascicle length will significantly change when measured during the eccentric stretch phase of a voluntary post-stretch isometric contraction.

H2 (experiment 1): There will be no significant difference in fascicle length change between different contraction and activation intensities at a single joint angle.

H3 (experiment 2): In healthy hamstring muscles, torque will be greater (i.e. enhanced) during the final isometric phase of a voluntary post-stretch isometric contraction when compared with a voluntary isometric contraction at a corresponding muscle length.

H4 (experiment 2): The magnitude of torque during the final isometric phase of a post-stretch isometric contraction will be greatest at joint angles indicative of longest muscle lengths.

H5 (experiment 2): In healthy hamstring muscles, muscle activation will be present during the final isometric phase of a voluntary post-stretch isometric contraction when compared with a voluntary isometric contraction at a corresponding muscle length.

H6 (experiment 2): The magnitude of activation reduction during the final isometric phase of a post-stretch isometric contraction will be greatest at joint angles indicative of longest muscle lengths.

H7 (experiment 3): In injured hamstring muscles, muscle activation will be lower during the final isometric phase of a pain matched voluntary post-stretch isometric contraction when compared with a pain matched voluntary isometric contraction at a corresponding muscle length.

H8 (experiment 3): In injured hamstring muscles, fascicle length will significantly change when measured during the eccentric stretch phase of a voluntary post-stretch isometric contraction.

Methodology

Experiment 1 – Muscle and Tendon behavior during post-stretch isometric contractions in the hamstring muscle

Aim and hypotheses

The primary aim of this experiment is to determine whether fascicles lengthen during the eccentric stretch phase of post-stretch isometric contractions. The specific hypotheses for experiment 1 are listed and detailed as *H1* and *H2* above in section *"Main hypotheses"*.

Participants

An A *priori* estimation [G*power 3 (version 3.1.9.3)] (Faul, Erdfelder, Lang, & Buchner, 2007) was used to estimate the sample size needed for experiment 1 (alpha = 0.05 and power = 0.80). It was found that a minimum of 9 participants would be required to satisfy the statistical approach outlined in section "Statistics". A convenience sample i.e. residents residing in the areas of the North Coast of New South Wales and South East Queensland and students attending Southern Cross University, will be recruited. All volunteers recruited for the study will then be asked to provide informed consent. The following inclusion and exclusion criteria will be applied to all volunteers.

Inclusion criteria will be:

i) currently healthy (i.e. not suffering from any acute or chronic illnesses) as established by completing the "Exercise and Sports Science Australia Pre-Exercise Screening Tool" (appendix 1);

ii) aged between 18 and 50 years; and

iii) consent to participate in all aspects of the study.

The exclusion criteria will be:

i) recent lower limb injuries, including sprains or strains sustained within the previous 12 weeks;

ii) diagnosed neurologic or lower extremity orthopaedic conditions (including spinal or lower back injuries); and

iii) acute illness (e.g. the common cold, viral infections).

Volunteers who satisfy the inclusion and exclusion criteria will be asked to participate in a familiarisation session.

Experimental design and protocol

To satisfy the primary aim, muscle fascicle lengths of biceps femoris long head (biceps femoris long-head) will be measured during post-stretch isometric contractions at 30^0 from full knee extension using two different ultrasound methodologies. Each volunteer will be required to visit the laboratory on one occasion. All participants, prior to the familiarisation and experimental procedures will undertake a standardised 10 min cycle ergometer warm-up. All testing sessions will be carried out at the exercise physiology laboratories of the School of Health and Human Sciences, Southern Cross University, Australia.

Materials and experimental set up

All trials will be performed using a Biodex Dynamometer (System 4, Biodex Medical Systems, Shirley, NY, USA) to measure torque produced by the knee flexors. A Telemed Echo Blaster Ultrasound (64 EXT-1T, LV7.5/65/64D, Vilnius, Lithuania) in B-mode using a 7.5 MHz linear array probe will be used to measure instantaneous fascicle lengths and angles of pennation during each contraction.

Torque Measurements

Using the Biodex Dynamometer, torque data will be sampled and recorded at an analogue to digital conversion rate of 2000Hz via a custom written Lab View program (version 8.2 LabView, National Instruments, Austin Texas). During all strength testing sessions, one seat belt will be placed over the participant's hips and consistently fastened to minimise pelvis motion. Participants will be in a prone position with a hip flexion angle of 180°. The dominant leg, selected by the participant, will be fitted into the attachment for knee flexion with the leg strap being approximately 2cm above the medial malleolus of the ankle. The rotational axis of the knee joint will be aligned with the rotational axis of the dynamometer for all testing conditions.

Ultrasound Measurements

For the Ultrasound measurements, two methodologies will be tested. Methodology and setup 1 will be adapted for use from (Brennan et al., 2017). Muscle thickness, pennation angle and fascicle length of the biceps femoris long-head will be determined from ultrasound images taken along the longitudinal axis of the muscle belly utilising a two dimensional, B-mode ultrasound (frequency, 12<Hz; depth, 8cm; field of view, 14 x 47mm). The scanning site will be determined as the half-way point between the ischial tuberosity and the knee joint fold, along the line of the biceps femoris long-head. These landmarks include the ischial tuberosity, fibula head, and the posterior knee joint fold at the mid-point between biceps femoris and semitendinosus tendon. In this position the probes will be firmly fixed to the leg using custom-built Styrofoam casing and elastic bandages (Tilp et al., 2011). All architectural assessments will be performed with participants in a prone position with a fixed hip angle of 180° following at least 5 minutes of inactivity. Assessments at rest will always be performed first followed by the graded isometric contraction protocol.

Methodology and setup 2; One ultrasound probe will be located over the proximal musculotendinous junction of biceps femoris long-head whilst the second probe will be located over the distal musculotendinous junction of biceps femoris long-head. Synchronised video images will be taken utilising a two dimensional, B-mode ultrasound (frequency, 12<Hz; depth, 8cm; field of view, 14 x 47mm). In these positions the probes will be firmly fixed to the leg using custom-built Styrofoam casing and elastic bandages (Tilp et al., 2011). All architectural assessments will be performed with participants in a prone position with a fixed hip angle of 180° following at least 5 minutes of inactivity. The ischial tuberosity will be marked and a scale used to determine the distance from the edge of the ultrasound probe and the ischial tuberosity. The lateral condyle of the fibula will also be marked and a scale used to determine the distance from the edge of the ultrasound probe and the ischial tuberosity. Concurrently with the ultrasound video images, 2D video will be taken from above the position of the participant in order to view the marked portions of the origin and insertion of the biceps femoris long-head. Assessments at rest will always be performed first followed by the graded isometric contraction protocol.

Data collection and analysis

Maximal Isometric Strength Measurements

Maximal isometric strength will be determined at 30^0 from full knee extension for the knee strength assessment. This joint angle was chosen, being commonly used by practitioners when assessing strength restoration in early stage hamstring rehabilitation (Schmittt, 2012). The participant will be asked to progressively increase their isometric contraction effort and maintain the maximal isometric contraction for a period of 3 s. The maximal torque value of the three contractions will be selected as the maximal isometric contraction value. The average muscular activation level over the 3 s period will be selected as the maximal isometric activation value.

Experimental Trials

The maximal and submaximal experimental trials will commence at 60° from full knee extension. The post-stretch isometric contractions will involve an eccentric phase through a 30° joint excursion for each contraction ending with the final isometric phase at 30° (Seiberl et al., 2012a) at a velocity of 60°/s. Each contraction will be started and stopped upon the researcher's verbal instruction and will have a duration of approximately 2 s to 3 s for isometric MVC.

Three sub-maximal post-stretch isometric contractions will be performed using visual feedback control at levels of 30% MVC of the biceps femoris long-head. During stretch contractions, participants will first match the target line visible on the LabView program interface at 60° knee flexion angle for 3 s. The dynamometer will then be moved 30° at 60°/s^{-1} and subjects will be asked to continue to match the target activation line at 30° knee flexion angle for a further 10 s. All trials will be completed in the order outlined in Table 1. Subjects will receive a minimum of 3 min and maximum of 5 min rest as needed between contractions (Seiberl et al., 2012a).

The best trial for each contraction condition, determined by the lowest standard deviation (SD) from the target level, will be used for analysis. Residual force enhancement will be assessed over intervals of 2 s between 2-4 s after stretch (AS1), 4-6 s (AS2), and 8-10 s (AS3). 'After stretch' will be defined as the instant in time when the angular velocity of the dynamometer achieves zero following the eccentric phase of each contraction (Seiberl et al., 2012).

Statistics

Descriptive statistics will be calculated for all variables of interest and expressed as mean ± standard deviation for use in further statistical analyses. Data will be tested for normality via the Kolmogorov-Smirnov test and with visual interpretation of histograms, boxplots and Q-Q Plots. Statistical significance will be set at $p < 0.05$.

Values for residual force enhancement and AR, calculated over each 2 s interval will be submitted to a single factor [angle (30°) × intensity (30% and 95%)] repeated measures General Linear Model (GLM) with both angle and intensity as the within-subject factors. If a significant main effect or angle-intensity interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values.

Fascicle length data will be submitted to a single factor [angle (30°) × intensity (30% and 95%)] repeated measures GLM with both angle and intensity as the within-subject factors. If a significant main effect or angle-intensity interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values.

Expected outcomes

It is expected that Experiment 1 will confirm the presence of residual force enhancement and AR in a multi-joint muscle model using maximal and sub-maximal voluntary post-stretch isometric contractions. It is also expected that this study will confirm muscle fascicle lengthening during the eccentric phase of maximal and sub-maximal post-stretch isometric contractions in a multi-joint muscle model. This evidence will inform future investigations (including experiment 2 of this thesis) of sub-maximal post-stretch isometric contraction protocols in an injured multi-joint muscle model such as the hamstrings.

Experiment 2 – Residual force enhancement and activation reduction in the hamstring muscle group using maximal and submaximal voluntary post-stretch isometric contractions

Aim and hypotheses

The primary aim of this experiment is to determine the magnitude of residual force enhancement and AR during the final isometric phase of a voluntary post-stretch isometric contraction undertaken at two different joint angles, and at maximal and two submaximal activation and contraction intensities. The secondary aim of this experiment is to determine whether fascicles lengthen during the eccentric stretch phase of these contractions. The specific hypotheses for experiment 2 are listed and detailed as *H3* through *H6* above in section *“Main hypotheses”.*

Participants

An A *priori* estimation [G*power 3 (version 3.1.9.3)] (Faul, Erdfelder, Lang, & Buchner, 2007) was used to estimate the sample size needed for experiment 1 (alpha = 0.05 and power = 0.80). It was found that a minimum of 9 participants would be required to satisfy the statistical approach outlined in section “Statistics”. However, a sample size with even numbers (n=10) will be used in order to allow for a balanced crossover design. A convenience sample i.e. residents residing in the areas of the North Coast of New South Wales and South East Queensland and students attending Southern Cross University, will be recruited. All volunteers recruited for the study will then be asked to provide informed consent. The following inclusion and exclusion criteria will be applied to all volunteers. Inclusion criteria will be:

i) currently healthy (i.e. not suffering from any acute or chronic illnesses) as established by completing the "Exercise and Sports Science Australia Pre-Exercise Screening Tool" (appendix 1);

ii) aged between 18 and 50 years; and

iii) consent to participate in all aspects of the study.

The exclusion criteria will be:

i) recent lower limb injuries, including sprains or strains sustained within the previous 12 weeks;

ii) diagnosed neurologic or lower extremity orthopaedic conditions (including spinal or lower back injuries); and

iii) acute illness (e.g. the common cold, viral infections).

Volunteers who satisfy the inclusion and exclusion criteria will be asked to participate in a familiarisation session.

Table 7 Experimental protocol experiment 1

	Allocation 1	***Allocation 2***
Day 1	*Explanation of experimental procedures by the researcher and provision of informed consent*	
	Completion of the ESSA Pre-Exercise Screening Tool	
	Cycle ergometer warm-up protocol (10mins)	
	Familiarisation of all experimental procedures including the practice of all testing conditions	
Rest Period	*48-72 hours rest period*	
Day 2	*Cycle ergometer warm-up protocol (10mins)*	
	Familiarisation of all experimental procedures including the practice of all testing conditions	
	3 x MVIC baseline assessment trials at 30° knee flexion	*3 x MVIC baseline assessment trials at 60° knee flexion*
	3 x 30%MVC trials at 60° knee flexion	*3 x 30%MVC trials at 90° knee flexion*
	3 x 30%MVA trials at 60° knee flexion	*3 x 30%MVA trials at 90° knee flexion*
	3 x 60%MVC trials at 60° knee flexion	*3 x 60%MVC trials at 90° knee flexion*
	3 x 60%MVA trials at 60° knee flexion	*3 x 60%MVA trials at 90° knee flexion*
	3 x >95%MVC trials at 60° knee flexion	*3 x >95%MVC trials at 90° knee flexion*
Rest Period	*48-72 hours rest period*	
	Cycle ergometer warm-up protocol (10mins)	
	Familiarisation of all experimental procedures including the practice of all testing conditions	

Day 3	*3 x MVIC baseline assessment trials at 60° knee flexion*	*3 x MVIC baseline assessment trials at 30° knee flexion*
	3 x 30%MVC trials at 90° knee flexion	*3 x 30%MVC trials at 60° knee flexion*
	3 x 30%MVA trials at 90° knee flexion	*3 x 30%MVA trials at 60° knee flexion*
	3 x 60%MVC trials at 90° knee flexion	*3 x 60%MVC trials at 60° knee flexion*
	3 x 60%MVA trials at 90° knee flexion	*3 x 60%MVA trials at 60° knee flexion*
	3 x >95%MVC trials at 90° knee flexion	*3 x >95%MVC trials at 60° knee flexion*

Experimental design and protocol

In order to test the hypotheses of this experiment, the experimental protocol detailed in Table 1 will be used. To satisfy the primary aim the magnitude of residual force enhancement and AR will be determined from the measurement of joint torque output and the electrical activity of muscles during voluntary post-stretch isometric contractions at two knee joint angles (30° and 60° from full knee extension), using three contraction (30%, 60%, and >95% MVC) and activation (30%, 60%, and >95% MVA) intensities. Each volunteer will be required to visit the laboratory on three occasions. All participants, prior to the familiarisation and experimental procedures will undertake a standardised 10 min cycle ergometer warm-up. In an attempt to minimise any possible fatigue or learning effects, the testing protocols will be undertaken in a counter balanced fashion based on the two knee joint angles, where participants will only perform tests at one joint angle on each of the two days. Sessions will be separated by at least 48 hours, and a maximum of 72 hours to ensure adequate rest. All testing sessions will be carried out at the exercise physiology laboratories of the School of Health and Human Sciences, Southern Cross University, Australia.

Materials and experimental set up

All trials will be performed using a Biodex Dynamometer (System 4, Biodex Medical Systems, Shirley, NY, USA) to measure torque produced by the knee flexors. Surface electromyography (sEMG) signals of biceps femoris long-head will be recorded using a Trigno Wireless sEMG system with double differentiated surface electrodes (Delsys, Natick, MA, USA) to measure muscular activation.

Torque Measurements

Using the Biodex Dynamometer, torque data will be sampled and recorded at an analogue to digital conversion rate of 2000Hz via a custom written Lab View program (version 8.2 LabView, National Instruments, Austin Texas). During all strength testing sessions, one seat belt will be placed over the participant's hips and consistently fastened to minimise pelvis motion. Participants will be in a seated position with a hip flexion angle of 80°. The dominant leg, selected by the participant, will be fitted into the attachment for knee flexion with the leg strap being approximately 2cm above the medial malleolus of the ankle. The rotational axis of the knee joint will be aligned with the rotational axis of the dynamometer for all testing conditions.

Measurements of Muscle Activation via Surface Electromyography

The sEMG signal will be filtered with a band-pass at a range from 15 to 450Hz, amplified with a gain of 1000 times and sampled at an analogue to digital conversion rate of 2000Hz. A 16-bit A/D converter will be used with the input range of ±5V and resolution of 0.153μV. The sEMG signals will be captured and recorded via the same custom written Lab View program as the data from the Biodex dynamometer allowing for both data sets to be synchronised.

The electrode sensors have three parallel silver bars (99.9% pure silver) of 1mm in diameter, 10mm in length and spaced 10mm apart, resulting in an inter-electrode spacing of 10mm. All electrode placements will be in accordance with the guidelines suggested by SENIAM (Hermens et al., 1999). The electrode placement on the biceps femoris long-head muscle will be placed at 50% of the line between the ischial tuberosity and the lateral epicondyle of the tibia and applied in the direction of the line between the ischial tuberosity and the lateral epicondyle of the tibia. The locations on the skin for recording electrodes will be thoroughly cleaned by first shaving, then wiping the area with alcoholic wipes. A surgical adhesive tape will be used along with double-sided adhesive electrode–skin interface, to secure the electrode to the skin. Electrically conductive gel will be used to enhance conduction between the skin and the surface electrodes.

Data collection and analysis

Maximal Isometric Strength Measurements

Maximal isometric strength will be determined at two separate joint angles (30^0 and 60^0 from full knee extension) for the knee strength assessment. These joint angles, were chosen as they are commonly used by practitioners when assessing strength restoration in early stage hamstring rehabilitation (Schmittt, 2012). The participant will be asked to progressively increase their isometric contraction effort and maintain the maximal isometric contraction for a period of 3 s. The maximal torque value of the three contractions will be selected as the maximal isometric contraction value. The average muscular activation level over the 3 s period will be selected as the maximal isometric activation value.

Experimental Trials

The maximal and submaximal experimental trials will commence at either 60° or 90° from full knee extension. The post-stretch isometric contractions will involve an eccentric phase through a 30° joint excursion for each contraction ending with the final isometric phase at 30° and 60° respectively (Seiberl et al., 2012a) at a velocity of 60°/s. Each contraction will be started and stopped upon the researcher’s verbal instruction and will have a duration of approximately 2 s to 3 s for isometric MVC.

Three sub-maximal post-stretch isometric contractions will be performed using visual feedback control at levels of 30%, 60% and >95% MVA of the biceps femoris long-head, and 30%, 60% and >95% MVC. During stretch contractions, participants will first match the target line visible on the LabView program interface at 60° or 90° knee flexion angle for 3 s. The dynamometer will then be moved 30° at $60°/s^{-1}$ and subjects will be asked to continue to match the target activation line at 30° or 60° knee flexion angle for a further 10 s. All trials will be completed in the order outlined in Table 1. Subjects will receive a minimum of 3 min and maximum of 5 min rest as needed between contractions (Seiberl et al., 2012a).

The best trial for each contraction condition, determined by the lowest standard deviation (SD) from the target level, will be used for analysis. Residual force enhancement and AR will be assessed over intervals of 2 s between 2-4 s after stretch (AS1), 4-6 s (AS2), and 8-10 s (AS3). ‘After stretch’ will be defined as the instant in time when the angular velocity of the dynamometer achieves zero following the eccentric phase of each contraction (Seiberl et al., 2012).

Statistics

Descriptive statistics will be calculated for all variables of interest and expressed as mean ± standard deviation for use in further statistical analyses. Data will be tested for normality via the Kolmogorov-Smirnov test and with visual interpretation of histograms, boxplots and Q-Q Plots. Statistical significance will be set at $p < 0.05$.

Values for residual force enhancement and AR, calculated over each 2 s interval will be submitted to a two factor [angle (30° and 60°) × intensity (30%, 60% and 95%)] repeated measures General Linear Model (GLM) with both angle and intensity as the within-subject factors. If a significant main effect or angle-intensity interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values.

Expected outcomes

It is expected that Experiment 2 will confirm the presence of residual force enhancement and AR in a multi-joint muscle model using maximal and sub-maximal voluntary post-stretch isometric contractions This evidence will inform future investigations (including experiment 3) of sub-maximal post-stretch isometric contraction protocols in an injured multi-joint muscle model such as the hamstrings.

Experiment 3 - Magnitude of activation reduction using pain controlled voluntary post-stretch isometric contractions of injured hamstring muscles

Aim and hypotheses

The primary aim of this experiment is to determine the magnitude of residual force enhancement and AR during the final isometric phase of a voluntary post-stretch isometric contraction undertaken at two different joint angles at a pain controlled (4/10 VAS) contraction intensity in injured hamstring muscle. The secondary aim of this study is to determine whether fascicles lengthen during the eccentric stretch phase of these contractions. The specific hypotheses for experiment 3 are listed and detailed as *H7* and *H8* above in section *"Main hypotheses".*

Participants

The participant recruitment and inclusion and exclusion criteria for experiment 3 are as per *Experiment 1 "Participants "*. The sample size was estimated using G*power 3 (version 3.1.9.3) (Faul, Erdfelder, Lang, & Buchner, 2007). A *priori* estimation was used, and it was found that a minimum of 10 participants would be required to perform a single group, single pain controlled contraction level x 2 joint angle t-test (effect size = 0.80 and power = 0.91).

Experimental design and protocol

In order to satisfy the aims and test the hypotheses outlined in *"Main Hypotheses"* section above, the following experimental protocol will be used (Table 2). The magnitude of muscular activation will be measured during voluntary post-stretch isometric contractions at knee joint angle, 30° and 60°, during pain-controlled (4/10 VAS) contraction intensities.

Each participant will be required to visit the laboratory on five occasions. Session one, two, three, and four will be separated by at least 48 hours, and a maximum of 72 hours to ensure adequate rest. Session four and five will be separated by at least 24 hours and a maximum of 48 hours to ensure testing occurs during the peak pain period following the eccentric induced muscle damage (EIMD) protocol (Clarkson & Hubal, 2002). All testing sessions will be carried out at the exercise physiology laboratories of the School of Health and Human Sciences, Southern Cross University.

Table 8 Experimental protocol experiment 2

Day 1	• Informed consent and familiarization. As per table 1
Rest Period	• 48-72 hours rest period
Day 2	• Baseline testing of healthy muscle. As per table 1
Rest Period	• 48-72 hours rest period
Day 3	• Experimental testing of healthy muscle. As per table 1
Rest Period	• 48-72 hours rest period
Day 4 **Eccentric Induced Muscle Damage protocol**	• Cycle ergometer warm-up protocol (10mins) • Familiarisation of all experimental procedures including the practice of all testing conditions • 6 x 12 maximal eccentric contraction baseline assessment trials at 30° knee flexion • Isometric MVC performed at 60° knee flexion at the completion of each 12 repetition set. Torque will be measured at the completion of each set.
Rest Period	• 24-48 hours rest period
Day 5 **Post EIMD tests**	• Cycle ergometer warm-up protocol (10mins) • Familiarisation of all experimental procedures including the practice of all testing conditions • 3 x pain controlled (4/10 VAS) isometric contraction baseline assessment trials at 60° knee flexion • 3 x pain controlled (4/10 VAS) isometric contraction baseline assessment trials at 30° knee flexion • 3 x pain controlled (4/10 VAS) trials at 90° knee flexion • 3 x pain controlled (4/10 VAS) trials at 60° knee flexion

Materials and experimental set up

The materials and experimental set up for experiment 3 are the same as those outlined for experiment 2 in *“Materials and experimental set up”*.

Data collection and analysis

Aside from the eccentric induced muscle damage protocol (day 4) and the pain assessments and pain-matching aspects of the post-injury tests (day 5) data collection and analyses for experiment 3 are the same as those outlined in *Experiment 2 “Data collection and analysis”*. The following details for data collection and analysis are unique to experiment 3:

Eccentric Induced Muscle Damage Protocol

The EIMD protocol scheduled on day four as outlined below will be adopted from (Hicks et al., 2016). Prior to eccentric exercise, a warm-up of 10 isokinetic knee extensions and flexions will be carried out through the full test range of motion (60°-30° from full knee extension, at 60°/s^{-1}), ensuring a progressive increase in effort (with the last contraction being maximal). For the eccentric exercise, the knee extension range of motion will be set at 60°-30° from full knee extension. Participants will be asked to perform six sets of 12 maximal voluntary eccentric knee extensions, which has previously been reported to induce significant EIMD (Jamurtas et al., 2005). The eccentric phase of the contractions will be performed at an angular velocity of 60°/s^{-1}. Two minutes rest will be provided between each set. Participants will remain seated in the isokinetic dynamometer throughout the entire exercise protocol, including the rest period. Visual feedback and verbal encouragement will be provided throughout the protocol. Maximal voluntary eccentric knee extension torque will be recorded throughout each contraction and displayed via the torque acquisition system. For each set, peak maximal voluntary eccentric knee extension torque will be determined as the highest torque out of the 12 repetitions. Average peak maximal voluntary eccentric knee extension torque will be calculated as an average of peak maximal voluntary eccentric knee extensions across six sets.

Muscle Soreness Rating

Following a rest period of 24 to 48 hours, participants will return to the laboratory for day four experimental testing. Muscle soreness will be measured using a VAS. The visual analogue scale will consist of a line which is 100 mm long, with 0 mm labelled and denoting "No pain at all" and 100 mm labelled and denoting "Unbearable pain". Seated in the isokinetic dynamometer the dominant leg will be passively moved through a full range of motion at $60°/s^{-1}$. Participants will be asked to mark the visual analogue scale, between 0 mm-100 mm, to denote the level of pain they experienced during the passive movement. The visual analogue scale has been reported to be a valid and reliable measure of muscle soreness (Inter class correlation > 0.96 (Bijur et al., 2001).

Pain Controlled Isometric Strength Measurements

Pain controlled (4/10 VAS) isometric strength will be determined at two separate joint angles (30^0 and 60^0 from full knee extension) for the knee strength assessment. These joint angles, were chosen as they are commonly used by practitioners when assessing strength restoration in early stage hamstring rehabilitation (Schmittt, 2012). The participant will be asked to progressively increase their isometric contraction effort and maintain the pain controlled isometric contraction for a period of 3 s. The maximal torque value of the three contractions will be selected as the maximal pain controlled isometric contraction value.

Experimental Trials

Prior to experimental testing on day 5, a standardised 10 min cycle ergometer warm-up and familiarisation will be undertaken by all participants.

Three pain-controlled post-stretch isometric contractions will be commenced at 90° and 60° from full knee extension. Torque and activation outputs will be blinded to the participant. During stretch contractions, participants will gradually increase the intensity of the isometric contraction. The participant will be instructed to maintain the contraction intensity at a pain level of 4/10 (VAS) at 90° or 60° knee flexion angle for 3 s. The dynamometer will then be moved 30° at 60°/s^{-1} (Seiberl et al., 2012a) and subjects will be asked to continue to maintain the contraction intensity at 60° or 30° knee flexion angle for a further 10 s. All trials will be completed in the order outlined in table 2. Subjects will receive as much rest as needed between contractions, but a minimum of 3 min will be enforced (Seiberl et al., 2012a).

All data will be captured at 2000Hz and processed using a customised Lab View program (version 8.2 LabView, National Instruments, Austin Texas). Each trial will be used for analysis. Residual force enhancement and AR will be assessed over intervals of 2 s between 2-4 s after stretch (AS1), 4-6 s (AS2), and 8-10 s (AS3). ‘After stretch’ will be defined as the instant in time when the angular velocity of the dynamometer achieves zero following the eccentric phase of each contraction.

Statistics

Descriptive statistics will be calculated for all variables of interest and expressed as mean ± standard deviation for use in further statistical analyses. Data will be tested for normality via the Kolmogorov-Smirnov test and with visual interpretation of histograms, boxplots and Q-Q Plots. Statistical significance will be set at $p < 0.05$.

Day 2 data, values for residual force enhancement and AR, calculated over each 2 s interval will be submitted to a two factor [angle (30° and 60°) × intensity (30%, 60% and 95%)] repeated measures GLM with both angle and intensity as the within-subject factors. If a significant main effect or angle-intensity interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values. Fascicle length data will be submitted to a two factor [angle (30° and 60°) × intensity (30%, 60% and 95%)] repeated measures GLM with both angle and intensity as the within-subject factors. If a significant main effect or angle-intensity interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values.

Day 5 data, AR will be assessed over each 2 s interval will be submitted to a two factor [angle (60° and 30°) × contraction intensity] paired t-test with angle as the within-subject factors. If a significant main effect or interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values. If a significant main effect or interaction is found, a post-hoc analysis with Bonferroni adjustment will be conducted to identify the significant difference between mean values.

Expected outcomes

It is expected that experiment 3 will confirm the presence of AR in an in injured multi-joint muscle model using pain controlled voluntary post-stretch isometric contractions. This evidence will inform future investigations of sub-maximal post-stretch isometric contraction protocols in an injured multi-joint muscle model such as the hamstrings.

Impact and Importance

Current rehabilitation methods for hamstring strain injuries are only recently starting to incorporate scientifically sound and evidence based eccentric training to better prevent re-injury. Nonetheless, these emerging practices still avoid utilising eccentric contractions until later stages of rehabilitation. Due to substantial evidence regarding mechanisms involved in post-stretch isometric contractions, muscle remodelling and scarring it is hypothesized that a new paradigm for early stage rehabilitation may be warranted. Making use of a brief and highly controlled post-stretch isometric contraction in acute and sub-acute stage rehabilitation may assist in promoting sarcogenesis and aid in more efficiently transitioning through rehabilitation progression. It is expected that the use of a submaximal, highly controlled post-stretch isometric contraction, may benefit the injured athlete due to three factors: i) optimizing the alignment of collagen fibres around the trauma site at the earliest time post injury, resulting in smaller scar tissue size; ii) an increase in fascicle length; and iii) earlier implementation of an eccentric component to rehabilitation protocols, potentially resulting in faster transition through rehabilitation phases. However, prior to the implementation of such an approach in rehabilitation it is essential to further understand the phenomena behind the post-stretch isometric contraction; residual force enhancement and AR. The aforementioned studies will provide vital information, which will underpin future research on developing and optimising the use of residual force enhancement and AR in rehabilitation of muscle strain injuries.

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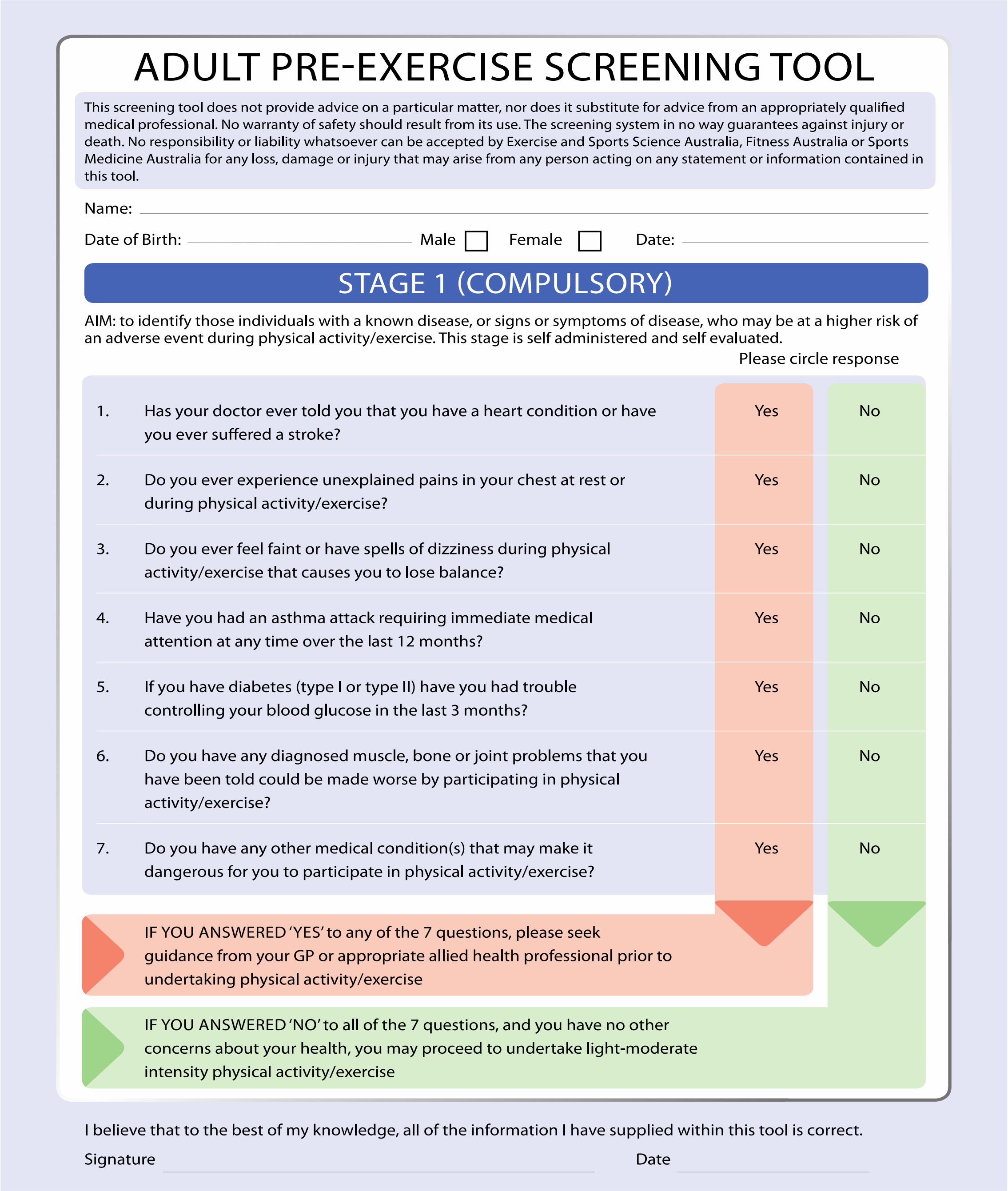
Exercise and Sports Science Australia Adult Pre-exercise Screening tool



ADULT PRE-EXERCISE SCREENING TOOL

This screening tool does not provide advice on a particular matter, nor does it substitute for advice from an appropriately qualified medical professional. No warranty of safety should result from its use. The screening system in no way guarantees against injury or death. No responsibility or liability whatsoever can be accepted by Exercise and Sports Science Australia, Fitness Australia or Sports Medicine Australia for any loss, damage or injury that may arise from any person acting on any statement or information contained in this tool.

Name: ____________________

Date of Birth: ____________ Male ☐ Female ☐ Date: ____________

STAGE 1 (COMPULSORY)

AIM: to identify those individuals with a known disease, or signs or symptoms of disease, who may be at a higher risk of an adverse event during physical activity/exercise. This stage is self administered and self evaluated.

Please circle response

1.	Has your doctor ever told you that you have a heart condition or have you ever suffered a stroke?	Yes	No
2.	Do you ever experience unexplained pains in your chest at rest or during physical activity/exercise?	Yes	No
3.	Do you ever feel faint or have spells of dizziness during physical activity/exercise that causes you to lose balance?	Yes	No
4.	Have you had an asthma attack requiring immediate medical attention at any time over the last 12 months?	Yes	No
5.	If you have diabetes (type I or type II) have you had trouble controlling your blood glucose in the last 3 months?	Yes	No
6.	Do you have any diagnosed muscle, bone or joint problems that you have been told could be made worse by participating in physical activity/exercise?	Yes	No
7.	Do you have any other medical condition(s) that may make it dangerous for you to participate in physical activity/exercise?	Yes	No

IF YOU ANSWERED 'YES' to any of the 7 questions, please seek guidance from your GP or appropriate allied health professional prior to undertaking physical activity/exercise

IF YOU ANSWERED 'NO' to all of the 7 questions, and you have no other concerns about your health, you may proceed to undertake light-moderate intensity physical activity/exercise

I believe that to the best of my knowledge, all of the information I have supplied within this tool is correct.

Signature ____________________ Date ____________

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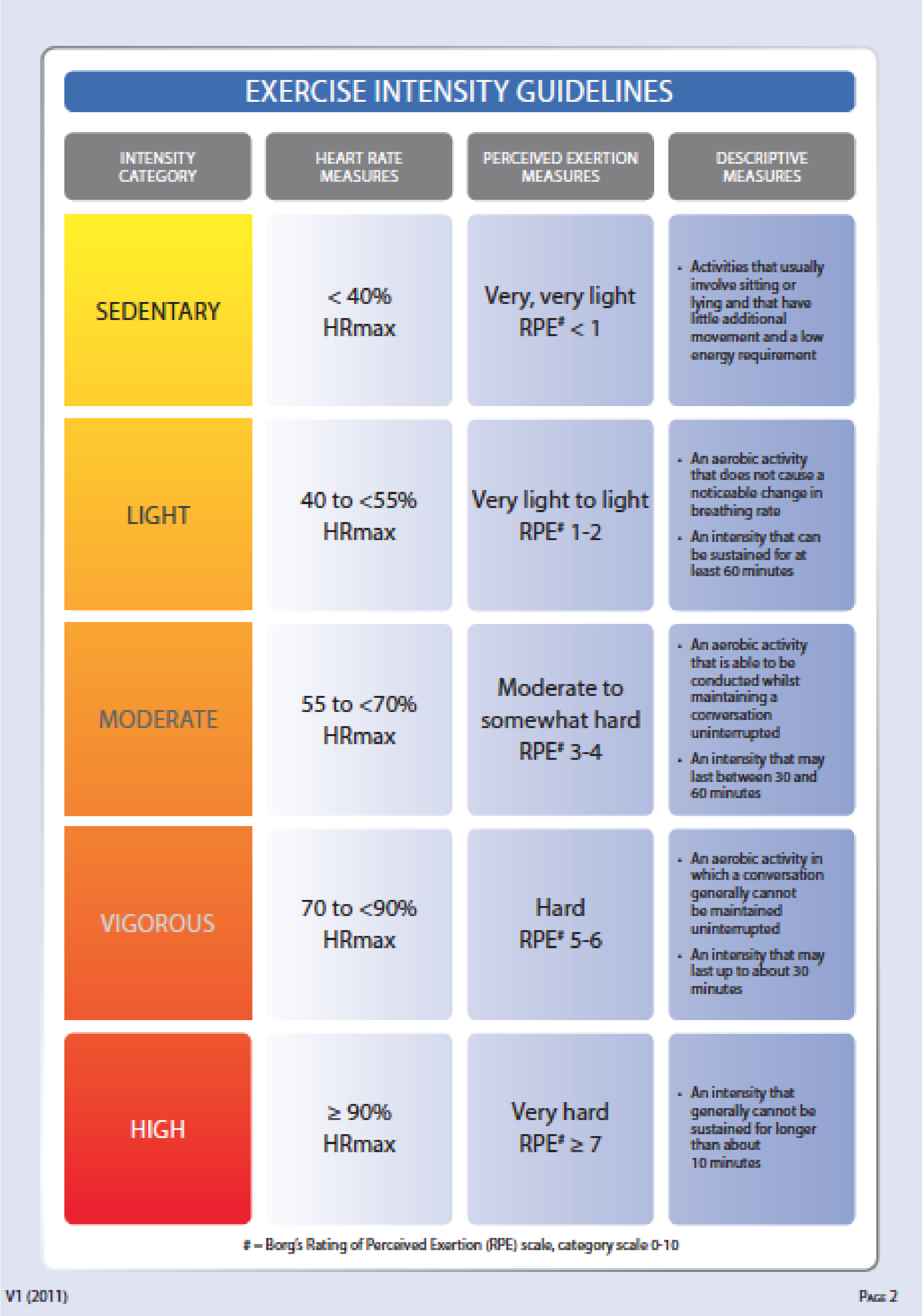
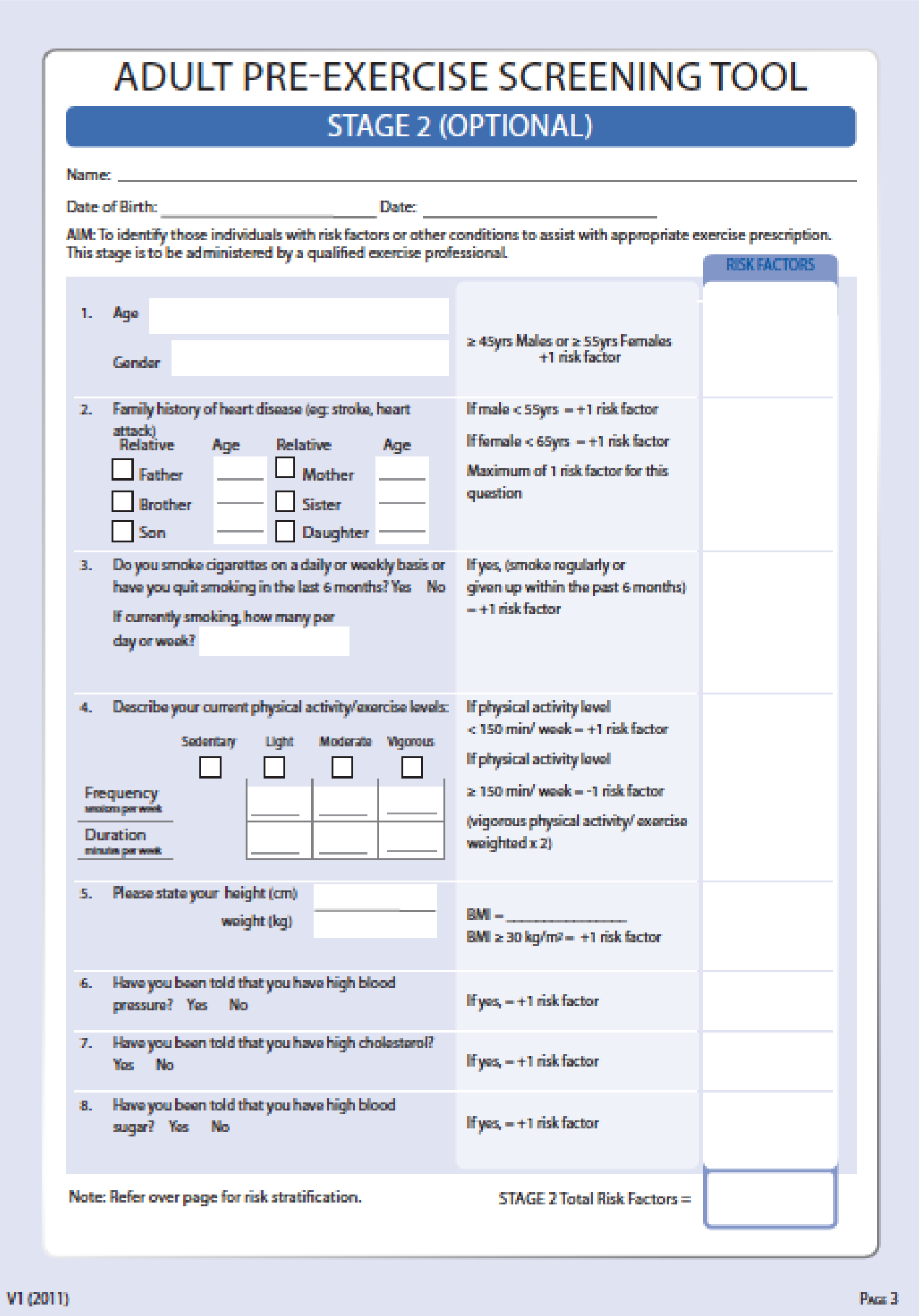


EXERCISE INTENSITY GUIDELINES

INTENSITY CATEGORY	HEART RATE MEASURES	PERCEIVED EXERTION MEASURES	DESCRIPTIVE MEASURES
SEDENTARY	< 40% HRmax	Very, very light RPE# < 1	- Activities that usually involve sitting or lying and that have little additional movement and a low energy requirement
LIGHT	40 to <55% HRmax	Very light to light RPE# 1-2	- An aerobic activity that does not cause a noticeable change in breathing rate - An intensity that can be sustained for at least 60 minutes
MODERATE	55 to <70% HRmax	Moderate to somewhat hard RPE# 3-4	- An aerobic activity that is able to be conducted whilst maintaining a conversation uninterrupted - An intensity that may last between 30 and 60 minutes
VIGOROUS	70 to <90% HRmax	Hard RPE# 5-6	- An aerobic activity in which a conversation generally cannot be maintained uninterrupted - An intensity that may last up to about 30 minutes
HIGH	≥ 90% HRmax	Very hard RPE# ≥ 7	- An intensity that generally cannot be sustained for longer than about 10 minutes

– Borg's Rating of Perceived Exertion (RPE) scale, category scale 0-10



ADULT PRE-EXERCISE SCREENING TOOL

STAGE 2 (OPTIONAL)

Name: ______________________________

Date of Birth: ____________________ Date: ____________________

AIM: To identify those individuals with risk factors or other conditions to assist with appropriate exercise prescription. This stage is to be administered by a qualified exercise professional.

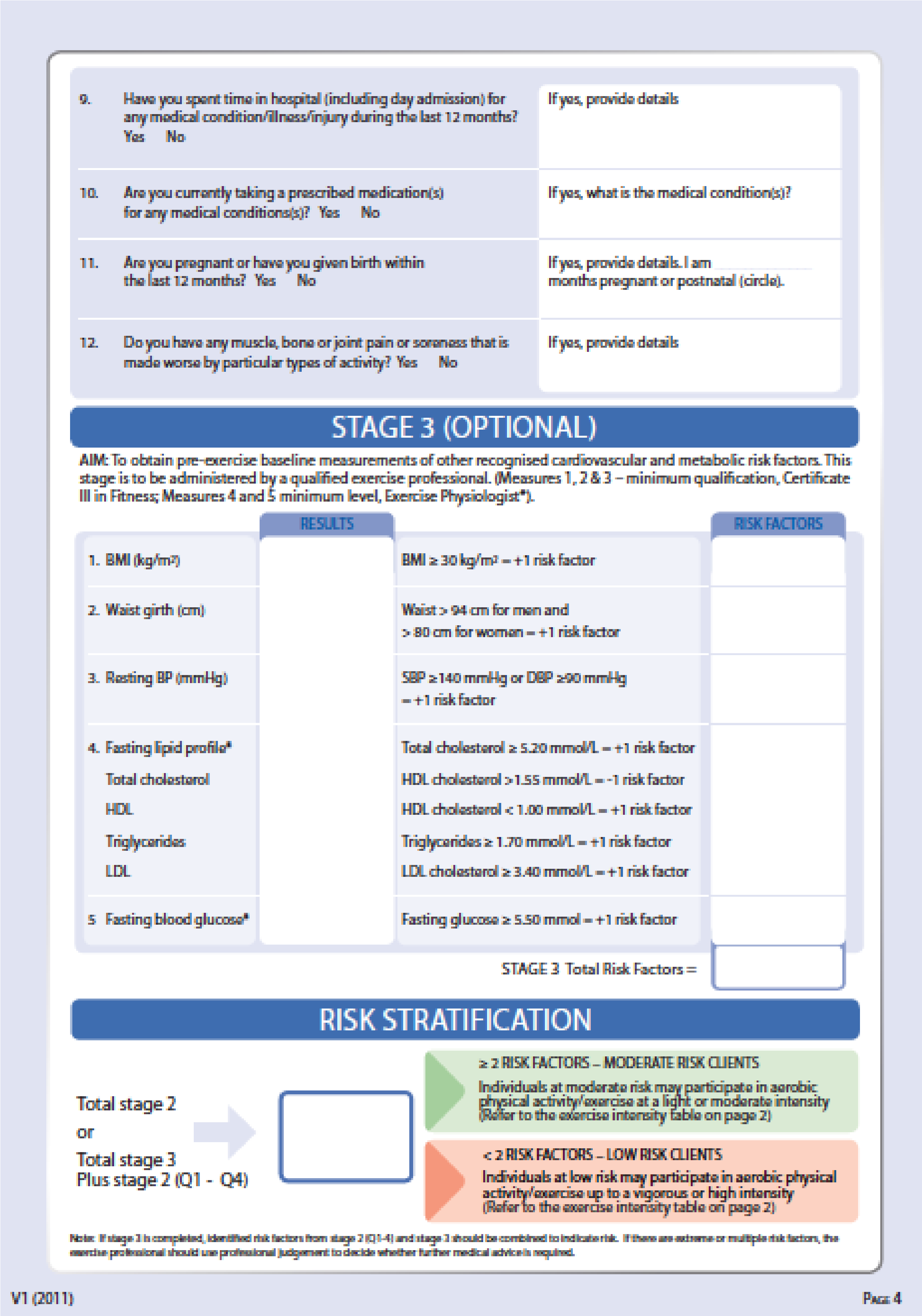
		RISK FACTORS
1. Age ____ Gender ____	≥ 45yrs Males or ≥ 55yrs Females +1 risk factor	
2. Family history of heart disease (eg: stroke, heart attack) Relative / Age / Relative / Age ☐ Father ____ ☐ Mother ____ ☐ Brother ____ ☐ Sister ____ ☐ Son ____ ☐ Daughter ____	If male < 55yrs = +1 risk factor If female < 65yrs = +1 risk factor Maximum of 1 risk factor for this question	
3. Do you smoke cigarettes on a daily or weekly basis or have you quit smoking in the last 6 months? Yes No If currently smoking, how many per day or week? ____	If yes, (smoke regularly or given up within the past 6 months) = +1 risk factor	
4. Describe your current physical activity/exercise levels: Sedentary ☐ Light ☐ Moderate ☐ Vigorous ☐ Frequency (sessions per week): Light ____ Moderate ____ Vigorous ____ Duration (minutes per week): Light ____ Moderate ____ Vigorous ____	If physical activity level < 150 min/ week = +1 risk factor If physical activity level ≥ 150 min/ week = -1 risk factor (vigorous physical activity/ exercise weighted x 2)	
5. Please state your height (cm) ____ weight (kg) ____	BMI = ____________ BMI ≥ 30 kg/m² = +1 risk factor	
6. Have you been told that you have high blood pressure? Yes No	If yes, = +1 risk factor	
7. Have you been told that you have high cholesterol? Yes No	If yes, = +1 risk factor	
8. Have you been told that you have high blood sugar? Yes No	If yes, = +1 risk factor	

Note: Refer over page for risk stratification.

STAGE 2 Total Risk Factors = ____

V1 (2011)

PAGE 3



9. Have you spent time in hospital (including day admission) for any medical condition/illness/injury during the last 12 months? Yes No	If yes, provide details
10. Are you currently taking a prescribed medication(s) for any medical conditions(s)? Yes No	If yes, what is the medical condition(s)?
11. Are you pregnant or have you given birth within the last 12 months? Yes No	If yes, provide details. I am ________ months pregnant or postnatal (circle).
12. Do you have any muscle, bone or joint pain or soreness that is made worse by particular types of activity? Yes No	If yes, provide details

STAGE 3 (OPTIONAL)

AIM: To obtain pre-exercise baseline measurements of other recognised cardiovascular and metabolic risk factors. This stage is to be administered by a qualified exercise professional. (Measures 1, 2 & 3 – minimum qualification, Certificate III in Fitness; Measures 4 and 5 minimum level, Exercise Physiologist*).

	RESULTS		RISK FACTORS
1. BMI (kg/m²)		BMI ≥ 30 kg/m² = +1 risk factor	
2. Waist girth (cm)		Waist > 94 cm for men and > 80 cm for women = +1 risk factor	
3. Resting BP (mmHg)		SBP ≥140 mmHg or DBP ≥90 mmHg = +1 risk factor	
4. Fasting lipid profile*		Total cholesterol ≥ 5.20 mmol/L = +1 risk factor	
Total cholesterol		HDL cholesterol >1.55 mmol/L = -1 risk factor	
HDL		HDL cholesterol < 1.00 mmol/L = +1 risk factor	
Triglycerides		Triglycerides ≥ 1.70 mmol/L = +1 risk factor	
LDL		LDL cholesterol ≥ 3.40 mmol/L = +1 risk factor	
5. Fasting blood glucose*		Fasting glucose ≥ 5.50 mmol = +1 risk factor	

STAGE 3 Total Risk Factors =

RISK STRATIFICATION

Total stage 2
or
Total stage 3
Plus stage 2 (Q1 - Q4)

≥ 2 RISK FACTORS – MODERATE RISK CLIENTS
Individuals at moderate risk may participate in aerobic physical activity/exercise at a light or moderate intensity
(Refer to the exercise intensity table on page 2)

< 2 RISK FACTORS – LOW RISK CLIENTS
Individuals at low risk may participate in aerobic physical activity/exercise up to a vigorous or high intensity
(Refer to the exercise intensity table on page 2)

Note: If stage 3 is completed, identified risk factors from stage 2 (Q1-4) and stage 3 should be combined to indicate risk. If there are extreme or multiple risk factors, the exercise professional should use professional judgement to decide whether further medical advice is required.

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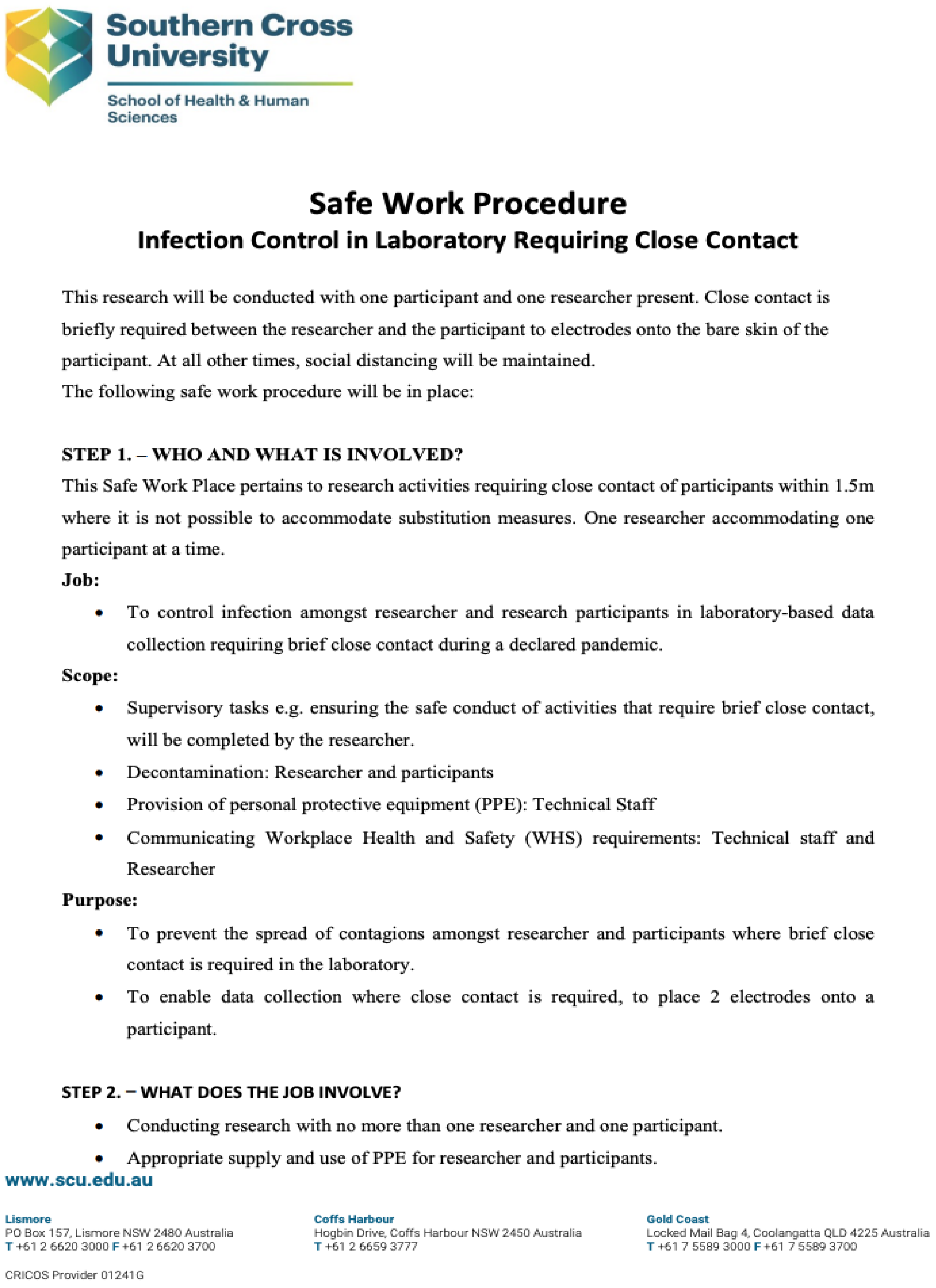
Appendix F Ethics Amendment



Southern Cross University
School of Health & Human Sciences

Safe Work Procedure

Infection Control in Laboratory Requiring Close Contact

This research will be conducted with one participant and one researcher present. Close contact is briefly required between the researcher and the participant to electrodes onto the bare skin of the participant. At all other times, social distancing will be maintained.
The following safe work procedure will be in place:

STEP 1. – WHO AND WHAT IS INVOLVED?

This Safe Work Place pertains to research activities requiring close contact of participants within 1.5m where it is not possible to accommodate substitution measures. One researcher accommodating one participant at a time.

Job:

- To control infection amongst researcher and research participants in laboratory-based data collection requiring brief close contact during a declared pandemic.

Scope:

- Supervisory tasks e.g. ensuring the safe conduct of activities that require brief close contact, will be completed by the researcher.
- Decontamination: Researcher and participants
- Provision of personal protective equipment (PPE): Technical Staff
- Communicating Workplace Health and Safety (WHS) requirements: Technical staff and Researcher

Purpose:

- To prevent the spread of contagions amongst researcher and participants where brief close contact is required in the laboratory.
- To enable data collection where close contact is required, to place 2 electrodes onto a participant.

STEP 2. – WHAT DOES THE JOB INVOLVE?

- Conducting research with no more than one researcher and one participant.
- Appropriate supply and use of PPE for researcher and participants.

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- Provision of appropriate hand washing facilities, hand sanitiser, 2-in-1 cleaner-disinfectant, and plastic bags for containment of personal items.
- Regular cleaning and disinfection of work surfaces, tools and equipment.
- Disposal of consumables used by researcher and participants.
- Disposal of paper towel used to decontaminate.

STEP 3. – WHAT IS THE WORK ENVIRONMENT?

- Biologicals: Researcher or participants may carry the contagion responsible for the pandemic, and are closer than 1.5m from another person during specific activities.
- Psychological: Participants may experience anxiety associated with being closer than 1.5m from another person during specific activities.

STEP 4. ASSESSING THE INHERENT WHS RISKS

- Exposure to contagion by body contact, causing immediate or long-term health issues.
- Exposure to contagion by inhaling aerosols causing immediate or long-term health issues.
- Researcher/Participants who would identify as a vulnerable person (Aboriginal and Torres Strait Islander people 50 years and older with one or more chronic medical conditions, people 65 years and older with one or more chronic medical conditions, people 70 years and older, and people with compromised immune systems) **are not eligible for this research**.
- The researcher or participant being anxious about the current situation.

STEP 5. FINDING SOLUTIONS TO THE WH&S

- No more than one researcher and one participant will be involved at any one time throughout the data collection period to minimize cross-contact whilst practicing exercise science data collection techniques.
- The participant will have to complete and sign a waiver for safe participation, and to communicate any flu-like symptoms that may appear within 14 days after the testing protocols
- The only time social distancing cannot be maintained is during electrode placement. During this time, both the researchers and participant will be required to wear a mask.
- Following the initial placement of electrodes, the researcher will **NOT** be required to come within 3m of the participant.

- The participant will be asked to remove the electrodes themselves. If this cannot be done, both researcher and participant will wear a mask.
- All disposable equipment will be discarded into a waste bin immediately after use.
- All reusable equipment will be sanitised immediately prior and immediately following personal contact.

Equipment to be handled:

For exercise protocol:

- Electrodes *
- Tape (to stick electrodes and markers on the participant)
- Sand Paper
- Razor
- Alcohol swabs
- Laboratory computer*
- Biodex*
- Powerlab*

* to be reused between participants

PPE and Hygiene:

For all data collection activities where 1.5m social distancing cannot be maintained:

- Level 1 disposable surgical masks fitted correctly for a maximum of 4h or prior to 4h if the masks become moist due to excessive mouth breathing, coughing, or sneezing.
- Alcohol-based hand sanitiser available to perform hand hygiene prior to touching another person, and at regular intervals during an activity.
- TGA approved 2-in-1 cleaner-disinfectant spray / wipes available at every station.
- Gloves available for use as per standard precautions.
- Gloves must be decontaminated at regular intervals with hand sanitiser or an ethanol spray.
- Researcher must decontaminate all work surfaces, tools, and equipment before and after each and every use with a TGA approved 2-in-1 cleaner-disinfectant provided by Technical staff.
- Discard all other used disposable items into general waste bins immediately after use.

- Researcher and Participants must wash hands (20sec) with laboratory / hospital hand wash and thoroughly dry with paper towel or perform hand hygiene using an alcohol-based hand sanitiser containing 60-80% alcohol:
    - On entry to the laboratory
    - Before and after touching their face
    - Immediately before applying and immediately after removing gloves
    - Immediately after removing PPE (including face mask)
    - Immediately after cough or sneeze
    - Immediately after using a tissue
    - Immediately before and after using any shared equipment
    - After Touching any work surface
    - Immediately prior to exiting the laboratory

STEP 6. RESOURCES: PPE, materials needed.

- PPE (nitrile gloves, disposable P1 level facemasks).
- General Waste bins.
- TGA approved 2-in-1 cleaner-disinfectant.
- Laboratory / hospital hand wash.
- Paper towel.
- Alcohol-based hand sanitiser containing 60-80% alcohol.

STEP 7. FIRST AID

- First Aid kit in the laboratory.
- First Aid Officer on duty.

Southern Cross University
School of Health & Human Sciences

COVID-19 Safe Information Sheet:

This information sheet is yours to keep

Residual Force Enhancement Study

This information sheet is in addition to the Information Sheet explaining the research study being completed. This COVID-19 Safe information sheet explains what the research will involve in order to mitigate the risks involved with close contact participation. It explains the precautions that will be taken by the researchers and what will be expected from you as a participant.

What this research project involves: The research project requires brief close contact between a researcher and the participant. Therefore, this project includes a Safe Work procedure designed for infection control within the laboratory during close contact data acquisition. Safety precautions taken include but not limited to:

- No more than one researcher and one participant will be present throughout testing.
- The proper supply and use of Personal Protection Equipment (PPE). Including the use of a mask when social distancing cannot be maintained.
- The provision and regular use of hand sanitiser and disinfectant.
- Completion of a Covid-19 safe consent form, whereby the participant consents to inform the researchers if they have experienced any flu-like symptoms before participation, and of any flu-like symptoms within 14-days after their participation.

Risks involved: With the global COVID-19 pandemic, participation in research that involves human to human contact is inherently higher in risk, as the contagion can be easily spread in close contact situations without proper safety guidelines in place. Exposure to the contagion causes immediate and possibly long-term health issues. The contagion can be spread through the air by inhaling it, or by touching surfaces infected by the contagion and then touching your eyes or mouth.

What will be expected of you to reduce the risks involved:

1. Carefully read, complete, and sign the additional consent form during COVID-19 prior to your participation in the study.
2. Inform the researcher if you experienced any flu-like symptoms in the 14-days prior to your participation date.
3. During your participation, please wash your hands (20 sec) with the hand wash supplied at the washing stations:
    - On entry to the laboratory facilities
    - Before and after touching your face
    - Immediately before applying and immediately after removing gloves
    - Immediately after removing PPE (including face mask)
    - Immediately after cough or sneeze

  - Immediately after using a tissue
  - Immediately before and after using any shared equipment
  - After touching any work surface
  - Immediately prior to exiting the laboratory

4. Proper use of the PPE supplied as instructed by the researcher.
5. Maintain social distancing (1.5m) where possible
6. Refrain from touching any equipment or surroundings, unless requested by the researcher.
7. **Immediately inform the researcher of any flu-like symptoms experienced 14-days after your participation, and if being tested positive for the COVID-19 virus.**

If you still wish to participate after you have carefully read and understood the COVID-19 Safe Information Sheet, please complete and sign the attached Consent Form and return it to the researcher at: **alec.mckenzie@scu.edu.au**

For further details regarding the study or to participate please contact Neil Chapman at:
neil.chapman@scu.edu.au or 0413 993 511
If you have any concerns about this study, please contact Dr John Whitting at:
john.whitting@scu.edu.au or 02 6620 3305

This project has been approved by the Human Research Ethics Committee of Southern Cross University (Approval Number ECN-19-090).

Complaints about the research/researchers:

If you have concerns about the ethical conduct of this research or the researchers, write to the following:
The Ethics Complaints Officer Southern Cross University PO Box 157, Lismore NSW 2480
Email: ethics.lismore@scu.edu.au
All information is confidential and will be handled as soon as possible.

Southern Cross University
School of Health & Human Sciences

Residual Force Enhancement Study

Additional Consent Form for use during COVID-19

Participant's name: ____

Contact information (phone number and email address):

____

I am up to date with all the latest COVID-19 information from the NSW Government?	Yes ☐	No ☐
I have been unwell with flu-like symptoms in the past 14 days? If yes, I am not allowed to participate.	Yes ☐	No ☐
I will wash and sanitise my hands regularly during participation?	Yes ☐	No ☐
I will maintain social distancing (1.5 m) where possible? (researchers will make physical contact while applying and removing the electrodes and markers)	Yes ☐	No ☐
I will avoid spitting, and if and when I need to blow my nose, I will do so using a tissue?	Yes ☐	No ☐
I will avoid any physical contact where possible? (researchers will make physical contact while applying and removing the electrodes and markers)	Yes ☐	No ☐
I will sanitise upon arrival, before I leave and when directed to?	Yes ☐	No ☐
I will allow researchers to come within social distancing parameters and make physical contact as needed while applying and removing electrodes.	Yes ☐	No ☐
I will not make contact with any other equipment or object around me, and will stay within the designated area?	Yes ☐	No ☐
I will contact and advise the lead researcher if I started to show any flu-like symptoms or tested positive for COVID-19 within 14 days after participation.	Yes ☐	No ☐

I have read, understood, and truthfully answered all the questions above, and will immediately contact the lead researcher if any flu-like symptoms appear within 14 days after participation.

Participant's Signature: ______________________________**Date:** ________________

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