Acute neurophysiological responses to resistance-training: An investigation into super-compensation theory

by

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I am the author of the thesis entitled

**Acute neurophysiological responses to resistance-training: An investigation into super-compensation theory**

submitted for the degree of Doctor of Philosophy

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<td>Active motor threshold</td>
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<td>BB</td>
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<td>CSA</td>
<td>Cross sectional area</td>
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<td>Central nervous system</td>
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<td>CP</td>
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<td>CSE</td>
<td>Corticospinal excitability</td>
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<td>CSP</td>
<td>Corticospinal silent period</td>
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<td>DOMS</td>
<td>Delayed onset muscle soreness</td>
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<td>EMG</td>
<td>Electromyography</td>
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<td>GABA</td>
<td>y-amino-butyric-acid</td>
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<td>H-reflex</td>
<td>Hoffman reflex</td>
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<td>HST</td>
<td>Heavy-strength training</td>
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<td>HYT</td>
<td>Hypertrophy training</td>
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<td>ICF</td>
<td>Intra-cortical facilitation</td>
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<td>ISI</td>
<td>Inter-stimulus interval</td>
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<td>LICI</td>
<td>Long interval cortical inhibition</td>
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<td>M1</td>
<td>Primary motor cortex</td>
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<td>MEP</td>
<td>Motor evoked potential</td>
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<td>M_{MAX}</td>
<td>Maximal muscle wave</td>
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<td>MVC</td>
<td>Maximal voluntary contraction</td>
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<td>Abbreviation</td>
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<td>MVIC</td>
<td>Maximal voluntary isometric contraction</td>
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<td>M-wave</td>
<td>Muscle compound wave</td>
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<td>PNS</td>
<td>Peripheral nervous system</td>
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<td>RF</td>
<td>Rectus femoris</td>
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<td>RM</td>
<td>Repetition maximum</td>
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<td>RMT</td>
<td>Resting motor threshold</td>
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<td>RT</td>
<td>Resistance training</td>
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<td>sEMG</td>
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<td>SICI</td>
<td>Short interval cortical inhibition</td>
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<td>SIT</td>
<td>Super imposed twitch</td>
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<td>TMS</td>
<td>Transcranial magnetic stimulation</td>
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<td>TP</td>
<td>Test pulse</td>
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Abstract

Resistance training (RT) induces central and peripheral adaptations which improve neuromuscular performance. Although neural adaptations are known to occur with RT interventions, the time course of neurophysiological fatigue, recovery and adaptation to an acute bout of heavy-strength (HST) or hypertrophic (HYT) training remains less clear. Therefore, the aims of this thesis were to investigate the behaviour of the central and peripheral nervous system in relation to the super-compensation cycle after an acute bout of applied HST or HYT based upon current RT practice. Furthermore, this thesis aims to compare the neurophysiological responses between HST and HYT modalities.

In a series of studies, transcranial magnetic stimulation (TMS) of the primary motor cortex (M1) and peripheral nerve stimulation were used to comprehensively investigate the changes in corticospinal and neuromuscular responses following a single session of applied RT in relation to the super-compensation cycle. In chapter 3, the neurophysiological time course of super-compensation following HST was comprehensively tracked over 72 hrs in the elbow flexors and compared to baseline. Building on the results from chapter 3, chapter 4 directly compared the responses between HST and HYT modalities at specific stages of fatigue (post training – 2hrs), recovery (6, 24 and 48 hrs) and adaptation (72 hrs) in the leg extensors. Lastly, chapter 5 comprehensively tested the adherence of the neurophysiological responses to the suggested super-compensation time course following both HST and HYT over a 96 hr period in the leg extensors. TMS was used to elicit and measure changes in motor
evoked potential (MEP) amplitude, corticospinal silent period (CSP), intra-cortical facilitation (ICF) and short and long intra-cortical inhibition (SICI and LICI), super imposed twitch (SIT) force, while direct current electrical nerve stimulation was used to ascertain changes in peripheral nerve excitability (M_MAX) of the rectus femoris. Finally, isometric dynamometry was used to determine maximal voluntary isometric contraction (MVIC).

Collectively the findings from chapter 3 showed that following HST in the elbow flexors, MVIC, M_MAX and MEP were significantly reduced immediately post training and returned toward baseline by 1 hr. Following which, a super compensatory effect occurred for MVIC and M_MAX at 6 hrs and MEP amplitude at 72 hrs. Following HST and HYT in the leg extensors (chapter 4), an initial decrease in MVIC occurred up until 2 hrs, in M_MAX measures up to 1 and 2 hrs, and CSP of 6 and 24 hrs for HST and HYT respectively. A concomitant increase in MEP up to 2 hrs was observed with the impairments in MVIC, M_MAX and CSP. The SIT force responses were impaired at submaximal (25 and 50% of MVIC) but not during high (75% MVIC) or maximal (100% MVIC) contraction intensities for HST and HYT. Interestingly, intra-cortical facilitation and inhibition appeared to be differentially modulated by training modality. HYT elicited an increase in ICF at 6 hrs, with a release of SICI (less inhibition) up until 24 hrs, while LICI was only greater between 24-96 hrs following HST. No changes were observed for ICF and SICI following HST, whilst no changes in LICI were observed following HYT.
In light of these findings, this thesis provided new evidence for the super-compensation model that is based on acute neurophysiological responses to HST and HYT. Collectively, the results from all three chapters showed that the time course of fatigue and recovery in the elbow flexors and leg extensors was shorter than suggested by the current super-compensation theory. Furthermore, the observed changes in corticospinal and peripheral nerve excitability, and voluntary force generating capacity suggested that fatigue after one session of HST and HYT of the elbow flexors and leg extensors was primarily modulated outside of the M1 that is likely to occur at the peripheral level. Interestingly, the SIT force of the leg extensors revealed that the efficacy of neural drive was impaired during submaximal levels of contraction, but voluntary activation (VA) was maintained during maximal efforts in an attempt to maintain neuromuscular performance in the presence of peripheral fatigue. The other major finding from chapter 4 was that the acute neurophysiological responses did not differ between training modalities during the proposed stages of fatigue, recovery and adaptation. The findings of chapter 4 suggested that the neurophysiological responses to HST and HYT behaved in a similar manner when performed with loads corresponding to maximal effort.

In conclusion, this thesis revealed that 1) the time course of neurophysiological fatigue, recovery and adaptation provide evidence for a shortened super-compensation cycle from applied RT; 2) fatigue following a single session of HYT and HST occurred primarily at the peripheral level with a compensatory increase in corticospinal excitability in an attempt to maintain neuromuscular performance; and 3) the neurophysiological responses following HST and HYT modalities behaved in a similar manner. The evidence provided suggests that shorter recovery periods
between subsequent RT sessions could be implemented for optimal gains in neuromuscular performance. Furthermore, the acute neurophysiological behaviour and responses should be considered as an important factor in understanding the super-compensation cycle following applied RT. The information provided from this thesis holds important implications for strength and conditioning professionals in the design and application of acute and periodised programs to optimise adaptations and improve performance.
CHAPTER ONE: INTRODUCTION
Neural adaptations are known to occur following RT interventions, however less is known about the acute neurophysiological responses from a single applied RT training session. Refined from the general adaptation syndrome (GAS principle) (Seyle 1950), the current super-compensation model by Bompa and Haff (2009), provides a framework of how the body responds following exposure to a training stimulus and has four interconnected stages (refer to section 2.6.1 Super-compensation theory), for a more detailed explanation;

1) *Fatigue*, 2) *Recovery*, 3) *Adaptation* and 4) *Involution*.

The model is frequently used in applied exercise practice, however direct scientific evidence supporting the physiological function of the nervous system in each of the proposed stages remains scarce. Most research in the area has focussed primarily on performance, hormonal responses, metabolites and substrate responses (Howatson et al. 2016; Walker et al. 2012; Walker et al. 2011; Ide et al. 2011) to inform of RT practice (Ratamess et al. 2009), with limited evidence available on the neurophysiological basis of super-compensation.

Recently, non-invasive electrical and magnetic stimulation techniques to measure physiological function of the nervous system have enabled researchers to quantify physiological changes following strength training interventions, greater than 80% of 1 repetition maximum (RM). In particular, TMS has provided insight into the adaptive changes within the M1, (Hendy & Kidgell 2013; Leung et al. 2015; Hendy et al. 2015), corticospinal tract (Griffin & Cafarelli 2007; Carroll et al. 2001; Kidgell & Pearce 2010; Kidgell et al. 2010; Kidgell & Pearce 2011; Latella et al. 2012; Hendy & Kidgell
2013; Carroll et al. 2011) from RT interventions ranging from 2 wks to 2 yrs (del-Olmo et al. 2006). The observed changes have commonly been attributed increases MEP amplitude, and reduction of CSP and SICI (Kidgell et al. 20110; Kidgell & Pearce 2010; Latella et al. 2012; Leung et al. 2015).

In light of the lasting neural adaptations following strength training interventions, research has also investigated the responses to fatiguing, sustained and repetitive motor tasks. Previous studies have investigated the changes in neuro-modulationcortisospinal excitability and intra-cortical inhibition associated with exercise-induced fatigue using sustained voluntary contractions (Sacco et al. 1997), isometric contractions (Nuzzo et al. 2016a; Gruet et al. 2014) and repetitive motor tasks (Teo et al. 2012; Teo et al. 2013; Benwell et al. 2006). Short term increases in cortisospinal excitability (CSE), reduced inhibition, impaired efficacy of neural drive/voluntary activation, motor unit (MU) recruitment and peripheral nerve excitability have commonly been reported in response to these tasks (Goodall et al. 2009; Gruet et al. 2014; Nuzzo et al. 2016a; Nuzzo et al. 2016c; Benwell et al. 2006; Teo et al. 2012; Teo et al. 2013; Sacco et al. 1997).

While previous studies have demonstrated impairments to neuromuscular performance following a single session of RT, little is known about the neurophysiological underpinnings of the super-compensation cycle using applied HST or HYT protocols. Further, the understanding of the neurophysiological basis of super-compensation is limited with most assumptions drawn from knowledge of longer term neural adaptations or short term neural behaviour from fatiguing motor
tasks. Therefore a comprehensive investigation into the neurophysiological basis of super-compensation from applied HST and HYT using validated neuro-stimulation techniques is needed to provide empirical scientific evidence in the field of strength and conditioning. More importantly, the findings on super-compensation will help to inform strength and conditioning professionals to assist in the appropriate design and implementation of RT protocols for athletes aimed at improving neuromuscular performance.
1.1. Thesis aims and hypotheses

The overall aim of this thesis was to assess the acute neurophysiological responses following a single session of HST and HYT to compare the time course of fatigue, recovery, adaptation and involution against the proposed super-compensation cycle.

Specifically, this thesis:

1) Investigated the time course of changes in ICF, SICI and LICI, corticospinal excitability (CSE), $M_{\text{MAX}}$ and MVIC following HST of the upper limb in relation to the 4 phases (fatigue, recovery and adaptation) of the super-compensation cycle (chapter 3).

2) Compared the neurophysiological responses (established in chapter 3), in addition to changes in SIT force responses, VA and CSP, between HST and HYT in the lower limb during the proposed stages of fatigue, recovery, adaptation of the super-compensation cycle (chapter 4).

3) Conducted a separate time-course analysis of the neurophysiological measures to comprehensively track fatigue, recovery and adaptation from either HST or HYT in the leg extensors to provide evidence for the appropriate prescription of RT protocols in an applied setting (chapter 5).
It was hypothesised that:

1) The time course of changes in MVIC, $M_{MAX}$, CSE, SICI, LICI and ICF following HST of the upper limb would differ from the proposed super-compensation cycle.

2) It is hypothesised that HST would impact upon neuromuscular and peripheral (MVIC, $M_{MAX}$) and central neural mechanisms (CSE, SICI, ICF and LICI), whilst the responses observed following HYT would be primarily due to changes at the peripheral level (MVIC and $M_{MAX}$).

3) Thirdly, it was hypothesised HST and HYT in the leg extensors would show an individual time-course of neurophysiological fatigue, recovery when compared to baseline. HST would require a longer recovery period than HST as suggested in current RT guidelines.
CHAPTER 2: REVIEW OF LITERATURE
2.1. Overview

This literature review will critically evaluate the existing knowledge surrounding neurophysiological responses following RT. This will be discussed in relation to the super-compensation model, providing rationale for the basis of HST and HYT training protocols used by strength and conditioning coaches and athletes. The chapter will begin by discussing the structural and mechanistic properties of the human motor system and methods to non-invasively quantify its functional properties. Following this, an overview of current HST and HYT recommendations and guidelines will be presented. A detailed summary of the previously reported neurophysiological adaptations following RT will be provided setting up the rationale for this thesis. Once established, an overview of super-compensation theory from early beginnings to current models will be presented and discussed from a neurophysiological perspective. Finally, the need for an evidence based evaluation of super-compensation theory, and its predicted impact on applied strength and conditioning practice will be discussed.
2.2. Structure and physiology of the human motor system

The nervous system comprises both the central nervous system (CNS; brain and spinal cord) and peripheral nervous system (peripheral nerve fibers incorporating both sensory and motor neurons). Although defined separately, the central and peripheral nervous systems form an intricate network of afferent and efferent connections that serve to facilitate many of the voluntary and involuntary functions of the body (Sherwood 2007). For the purpose of this research the discussion will focus on the M1, corticospinal tract, motor units (MUs), and the neuromuscular junction.

2.2.1. Primary motor cortex

The M1 lies within the pre central cortex, on the anterior border of the central sulcus. The M1 is responsible for planning, controlling and executing voluntary movement (Haines 2006; Rothwell 1994). Outputs from the M1 project to the basal ganglia, cerebellum, red nucleu, reticular formation and the spinal cord. Excitation of areas within the M1 cause localised muscle contractions within specific parts of the body (Latash 2008) as they descend through the spinal cord and synapse onto motor neurons (Haines 2006; Rothwell 1994). The organisation of this motor representation was developed into a motor homunculus from early studies mapping cortical regions (Brodmann 1909), (see figure 2.1.). Large proportions of the representation are dedicated to movement of the fingers, face and tongue which require fine motor control, while less is dedicated to the innervation of large musculature in the lower
limbs. Large cells (Betz cells) are present in the M1 especially in areas projecting to lower limb muscles. It is now known that regions of the M1 are modifiable in response to external stimulus or stressors (Sanes & Donoghue 2000) rather than remaining fixated over the lifespan.
Figure 2.1. A visual map of the motor homunculus representing the musculature innervated along different sites of the M1 (adapted from Poletaev et al. 2012).
The neocortex makes up the most superficial portion of the M1, organised into six different layers that are made up of pyramidal and stellate cells (Fatterpekar et al. 2002; Rothwell 1994, (see figure 2.2.). Pyramidal cells (see section 2.2.2. Corticospinal tract) contain axons which descend out of the cerebral cortex, whilst stellate cells act as interneurons within this area providing both horizontal and vertical connections within the M1 (Rothwell 1994; Nolte 2002). These connections provide a basis for intra and interhemispheric communication and inhibitory and excitatory synapses which can influence the descending drive through pyramidal cells onto the motor neuron pool (Ni & Chen 2008; Rothwell et al. 2009).
Figure 2.2. Visual representation of the layers of the neocortex (Fatterpekary et al. 2002; Haines 2006; Rothwell 1994).

a. The molecular layer is the most superficial, containing few cell bodies.  
b. The external granular layer is densely packed with small pyramidal and stellate cells.

c. The external pyramidal layer is predominantly composed of medium sized pyramidal cells.  
d. The internal granule layer contains densely packed pyramidal and stellate cells.  
e. The ganglionic layer contains the largest pyramidal cells, known as Betz cells.  
f. The multiform layer is relatively thin, with spindle-shaped cells scattered amongst fibre bundles.
2.2.2. Corticospinal tract

Upper motor neurons of the corticospinal tract consist of neuronal projections from the M1 to the spinal cord and onto lower motor neurons (see figure 2.3.). Separate corticospinal tracts originate from the left and right cerebral hemispheres with approximately 85-90% decussating at the level of the medulla (Latash 2008; Rothwell 1994; Haines 2006). Therefore although ipsilateral connections do exist, most corticospinal neurons innervate motor neurons on the contralateral side of the body. The other uncrossed axons form the anterior corticospinal tract and are thought to innervate trunk musculature (Rothwell 1994; Nathan et al. 1990). These corticospinal neurons can be monosynaptic or connect onto interneurons (Enoka 2015). Approximately 1 million neurons in the corticospinal tract originate from the M1 (Latash 2008). The M1 is rich in pyramidal neurons in the lamina (Weber et al. 2002) descending to efferent motor neurons of the spinal cord (Sherwood 2007; Dum & Strick 1996) and relates directly to skeletal muscle innervation. Smaller pyramidal neurons are innervated during maintenance of posture or a constant submaximal force output and are important in small refined movements. Conversely, large pyramidal neurons are innervated when distinct changes in muscular force are needed (Latash 2008), as required in gross movements requiring large muscle contractions.
Figure 2.3. The corticospinal tract comprising of the motor cortex and descending pyramidal neurons innervating skeletal muscle fibres. Adapted from Barrett, Barman, Botano & Brooks (2009).
2.2.3. Motor units

The MU is the basic functional unit of the neuromuscular system (Enoka 2005) (see figure 2.4.). It comprises of the smallest unit of the corticospinal tract and is responsible for the innervation of muscle fibres. Further, they form a final common pathway for the influence of the M1, basal nuclei, cerebellum and brain stem on skeletal muscle fibres (Weber et al. 2002). Almost all motor neurons reside within the ventral horn of the spinal cord with the exception of skeletal muscle supply to the cranial muscles (Sherwood 2007). Alpha motor neurons exist as a single myelinated axon that branch off and innervate corresponding muscle fibres within a muscle (see section 2.2.4. Neuromuscular junction). Each muscle consists of a number of MUs, with less than 100 for small intrinsic muscles to thousands of MUs for large muscles not uncommon (Enoka 2005). The number of muscle fibres innervated by each MU is known as the innervation ratio (MacDougall & Sale 2014).
Figure 2.4. Structure of a motor unit. A representation of motor and reflex nerves comprising of efferent (motor) and afferent (reflex) nerves (adapted from Donaghy et al. 2001).
Three major types of MUs exist, 1) Fast twitch (type IIb/x), 2) Fast Twitch Fatigue Resistant (Type IIa) and 3) Slow twitch fatigue resistant (type I) (MacDougall & Sale 2014) each with a different capacity to generate peak force, time to peak force and magnitude of fatigue properties with sustained isometric contractions (Enoka 2005). Motor neurons can fire repetitively and for sustained periods of time (Heroux et al. 2015) at a frequency dependent upon the amount of synaptic input (Brownstone 2006) and will influence the contractile properties of the muscle fibres (Enoka 2005). Slow twitch MUs innervate less muscle fibres and have a slower conduction velocity and time to peak force. This is in contrast to fast twitch MUs, where the time to peak twitch force ranges from (20-100ms) depending upon the motor unit type. Despite the differing nature of fibre types, recruitment order follows the size principle (Henneman et al. 1957) in which motor units are innervated in order of smallest to largest. Further, high levels of contraction require large MU input, fatigue quickly and are the first to shut off during relaxation, which are directly related to its size and intrinsic properties (Henneman 1965). MU recruitment and changes in firing frequency are the primary mechanisms in the regulation of muscular force output (Milner-Brown & Lee 1975).

2.2.4. Neuromuscular junction

The neuromuscular junction comprises a single efferent MU fibre (part of many axonal fibres) and muscle fibre in close proximity. A descending excitatory action potential from the efferent nerve fibre reaching the junction induces an obligatory effect on the synapse, known as the end plate potential, which always exceeds the threshold to initiate a muscular contraction (Powers & Howley 2007; Latash 2008).
The opening of voltage gated calcium (Ca\textsuperscript{2+}) channels cause a rapid release of Acetylcholine (ACh) from active zones within the presynaptic membrane across the synaptic cleft and re-uptake of the excitatory neurotransmitter (Powers & Howley 2007; Latash 2008), (see figure 2.5.).
Figure 2.5. The neuromuscular junction. A representation of the neuromuscular junction with the motor neuron and skeletal muscle fibre in close proximity (Black & Hawks 2009).
Following the pre synaptic events, high concentrations of Ach specific receptors present on the post synaptic membrane results in changes in ion permeability and depolarising potential (Latash 2008). In turn this post synaptic action potential of the motor end plate (Powers & Howley 2007) travels along the sarcolemma, into T-tubules opening Ca\(^{2+}\) channels. Opening Ca\(^{2+}\) channels results in 100 fold increase in Ca\(^{2+}\) ion concentration within the sarcoplasm and the whole process is quickly reversed (Latash 2008). Ca\(^{2+}\) then act upon contractile filaments (troponin and tropomysosin). Ca\(^{2+}\) makes the myosin binding site available on the actin molecule (Latash 2008). If adenosine triphosphate (ATP) is present the myosin head attaches to actin and uses the energy available from ATP to form cross bridges and the cycle is repeated across actin binding sites. The force of contraction is maintained by a concurrent attachment, re-attachment of molecules along the filaments (Latash 2008) known as the strong binding state whilst at rest the bond although existent is considered to be in the weak state (Powers & Howley 2007). This action is known commonly as the sliding filament theory (Powers & Howley 2007) and the process is reversed once excitation stops.
2.3. Techniques used to measure neuromuscular function and performance

As technology has advanced, so have the techniques used to quantify the nervous system and those occurring with plasticity; the process whereby the nervous system changes and adapts in response to repeated stimuli. Neurological investigations encompass an array of direct and indirect stimulation and measurement techniques in an attempt to further understand the underlying mechanisms. The stimulation of corticospinal neurons via electromagnetic stimulation techniques such as TMS has been routinely used in clinical and training intervention studies (Latella et al. 2012; Hendy & Kidgell 2013; Kidgell et al. 2010; Hendy et al. 2014; Philpott et al. 2016; Ni & Chen 2015). Further, peripheral direct electrical stimulation techniques of spinal and sub spinal regions provide several other evaluations of the nervous system. These include the Hoffman reflex (H-Reflex), maximum compound wave (M-wave) and long latency reflex (see figure 2.6.).
Figure 2.6. Schematic displaying the points of stimulation for TMS and the H-reflex and M-wave along the corticospinal pathway. Force and EMG signals are recorded from the innervated muscle fibres.
Functional Magnetic Resonance Imaging (fMRI) has also been extensively used in neurological investigations (Kamen & Caldwell 1996; Hallett 2000; Perez & Cohen 2008; Kujirai et al. 1993; Pearce et al. 2000; Thickbroom et al. 2009; Aagaard et al. 2002; Palmieri et al. 2004; Hortobaygi et al. 2011) to show areas of activation within the brain due to haemodynamic changes. Maximal voluntary contraction (MVC) or in some cases maximal voluntary isometric contraction (MVIC) is used to assess neuromuscular performance whilst electromyography (EMG) quantifies electrical activity of the muscle. The measures discussed for the purpose of this research are relatively non-invasive, designed at evaluating the nervous system from both central and peripheral aspects.

2.3.1 Maximal voluntary contraction

Maximal voluntary force output has been shown to decrease with exercise induced fatigue and increase rapidly at the onset of a training program (Howatson et al. 2016; Ide et al. 2011; Walker et al. 2012; Cannon & Cafarelli 1987; Griffin & Cafarelli 2003; Lee et al. 2009). It is important to distinguish that MVC in this context will be referred to as the maximal amount of voluntary force that can be produced by the neuromuscular system whilst in some previous literature, measurement of the EMG has been used to evaluate contraction levels (Ng et al. 1997).

Fatigue is often reported as a reduction in performance, voluntary force output or an inability of the neuromuscular system to maintain maximal or desired force (Gandevia 2001). Exercise, high intensity or sustained submaximal isometric in nature can result
in force loss however the underlying processes are the topic of continued debate. Current research has shown acute decreases in maximal force output from intermittent (Howatson et al. 2016; Ide et al. 2011; Walker et al. 2012) and sustained muscular contractions (Taylor & Gandevia 2008).

Overwhelming evidence is available on rapid improvements in MVC with training intervention studies in less than 4 wks (Hortobaygi et al. 2011; Cannon & Cafarelli 1987; Lee et al. 2009). According to Hortobaygi et al. (2011) increases in MVC can be attributed to both spinal and supraspinal mechanisms as a result of both voluntary and electro stimulation strength training. In an early study, Cannon and Cafarelli (1987) reported a 9.5% increase in MVC after 3 days per wk voluntary training of the adductor pollicis muscle for 5 wks. Griffin and Cafarelli, (2003) and Lee et al. (2009) also reported respective 15-18% and 11% increases in MVC force during the first 4 wks of RT, with evidence supporting small adaptations at multiple sites within the neuromuscular system Griffin and Cafarelli (2005). Further, Christie and Kamen (2010) conducted an age related intervention involving 6 training sessions of the ankle dorsiflexors. MVC increased by 17.4 and 19.8% in the young and older groups respectively. MVC provides a gross but important functional outcome evaluation of the neural drive and contractility of the muscle(s), and coupled with other neurological measurement techniques, offers valuable information on neuromuscular function.

2.3.2. Electromyography

Electromyography can be used to provide a representation of the activation of lower motor neurons resulting from muscular effort (Turker 1993). Further, a high inter
individuality often exists in the EMG response which may affect group analysis, however it is still considered reliable in measuring individuals responses to an intervention (Buckthorpe et al. 2012). EMG can be conducted intra musculely and transcutaneously. Surface electromyography (sEMG) where bi-polar electrodes are placed on the skin’s surface directly over the muscle belly is non-invasive yet provides a reliable representation of the electrical activity of the muscle. Surface EMG is considered a valid and useful technique for assessing electrical activity from large superficial MUs up to 35mm deep (Kamen & Caldwell 1996), however there are several limitations that exist with sEMG. Skin thickness, superficiality of the muscle, adjacent musculature, hair and body fat can all influence the signal and careful guidelines for preparation of the skin site is necessary to maintain test/re-test reliability (refer to seniam.org for further information). Changes in neural activation with RT have been consistently shown through sEMG (Remaud et al. 2010; Aagaard, et al. 2003; Jakobsen et al. 2013; Aagaard et al. 2000; Marshall et al. 2011; Oliveira & Goncalves 2009). Changes in sEMG recording following acute exercise have been shown as a result of fatigue in conjunction with a decline in maximal force (Walker et al. 2012). Further studies also support EMG changes in relation to early strength gains from training (Aagaard et al. 2003; Oliveira & Goncalves 2009; Marshall et al. 2011; Jakobsen et al. 2013). Intervention studies using 8 wks of isotonic and isokinetic knee extensor training significantly increased strength by 13.3 and 16.1% respectively, with a significant increase in agonist muscle activity with sEMG (Remaud et al. 2010). Further, Aagaard et al. (2000) demonstrated increases in EMG of between 16 and 32% after 14 wks of heavy concentric and eccentric quadriceps contractions respectively.
Conversely, intramuscular EMG where thin wire electrodes are inserted directly into the muscle belly, minimises the limitations of sEMG (Rajaratnam et al. 2014). With intramuscular EMG techniques recording from single MUs, it is possible and more accurate at detecting signals from small or deep muscles (Turker 1993). However, the invasive nature and difficulty when used in studies investigating human movement deem it insufficient for many exercise studies and hence will not be discussed further for the purpose of this review.

Although the literature has produced consistent findings regarding fatigue and training associated changes in sEMG, as an investigative technique to measure changes in the neuromuscular system, EMG provides a gross estimation of changes in electrical activity throughout the motor system rather than an ability to pinpoint the location of change within neural structures. Despite this, EMG can be useful measurement tool when coupled with other stimulation techniques such as peripheral electrical stimulation and TMS, enabling researchers to determine when and where along the corticospinal-motorneuronal pathway changes have occurred.

2.3.3. Peripheral nerve stimulation

Peripheral nerve stimulation allows for the quantification of sub spinal neural pathways. Direct current electrical stimulation applied to peripheral nerve structures evokes responses that show the excitability between the point of stimulation and the muscle, known as the compound muscle wave (M-wave) and under certain conditions excitability of the spinal reflex pathway known as the Hoffman reflex (H-reflex), (see
figure 2.7). For clarity this section will be divided into discussion of the M-wave and H-reflex.
Figure 2.7. Illustration of the M-wave and H-reflex response in the soleus as recorded by EMG. Note the longer latency period of the H-reflex compared to the M-wave and greater amplitude of the H-reflex when the M-wave response is minimal (adapted from Clark et al. 2006).
The M-wave is commonly reported as the largest evoked response ($M_{\text{MAX}}$) from direct supramaximal electrical stimulation of all motor axons (Perrey 2009). The M-wave has a short latency period in comparison to the H-reflex due to the shorter distance required of the stimulus to travel down the efferent nerve fibre to the muscle. Two components of the M-wave are reported 1) $M_{\text{MAX}}$ amplitude, which is defined as the peak-to-peak values of the waveform, and 2) M-wave latency, recorded as the time difference between stimulation and onset of the waveform (see figure 2.7.). M-wave latency provides useful information on nerve conduction velocity (Kouzaki et al. 2016), and is a valuable measure to normalise intra and inter-individual variability of corticospinal responses which will be discussed further (see section 2.3.4. Transcranial magnetic stimulation). Furthermore, the M-wave has also been used in the normalisation of EMG activity to avoid the possible influence of peripheral mechanisms in the signal (Millet et al. 2011).

The H-reflex reflects the excitability and efficiency of spinal motor neurons in afferent synapses (Aagaard et al. 2002). Due to the absence of supra spinal input inferences about the behaviour of spinal motor neurons can be made from the H-reflex. H-reflex will be detected at lower stimulation intensities than the M-wave (Palmieri et al. 2004) and has a longer latency period (Clark et al. 2006) due to the propagation along afferent fibres, through spinal interneurons and back along efferent fibres. As the stimulus intensity increases the H-reflex will reach a saturation point as the muscle response simultaneously increases eventually diminishing the H-reflex. With this method, it is possible to determine the integrity of the spinal reflex and efficacy of peripheral neural pathways however it may be limited by peripheral nerve accessibility. Hoch and Krause (2009) reported greatest reliability when normalising
the H-reflex response to a ratio of M-max rather than a percentage of stimulus intensity.

Peripheral direct current electrical stimulation techniques provide a quantifiable representation of the efficacy of spinal reflex mechanisms, peripheral nerve excitability and conduction velocity. However, direct current electrical stimulation is limited to detecting excitability changes at and below the spinal level. As will be discussed in the following section, peripheral electrical stimulation is often coupled with supra spinal stimulation techniques to provide evidence for the behaviour of the entire motor system.

2.3.4. Transcranial magnetic stimulation

2.3.4.1. TMS background

Transcranial magnetic stimulation is a useful, valid and safe tool to non-invasively examine the human corticospinal system using single and paired pulse stimulation techniques. Used for over 25 years (Barker et al. 1985), TMS has examined the excitability of the corticospinal tract (Rosler 2001) during movement tasks, and the involvement of cortical regions in various vision, language and motor tasks, and in pathophysiology of brain disorders (Rothwell 1994; Hallett 2000). Due to the nature of stimulation and possible confounding factors that may potentially influence intra and inter-individual reliability of TMS measures, several authors have provided safety and general research recommendations for the use and application of TMS (Rossi et al. 2009; Chipchase et al. 2012). In recent years TMS has been used to assess plasticity
with strength training (Kidgell et al. 2010; Kidgell & Pearce 2010; Latella et al. 2012; Carroll et al. 2011). Single pulse TMS is conducted using a coil (usually circular or figure-of-eight), (Rosler 2001), placed and discharged over the scalp. The discharge of the coil induces a rapidly changing electrical current field in order to evoke a singular magnetic pulse. This pulse, opposite to the current flow can stimulate the neurons underlying the coil (Weber et al. 2002; Rosler 2001). Depending on the orientation and magnitude of stimulation, underlying neurons can be directly or indirectly innervated and is subject to coil shape and size (Carroll et al. 2011). Coil type can influence the depth and focality of the stimulus (Rosler 2001), (see figure 2.8.). Double cone coils generally penetrate deeper than circular coils and activate larger amounts of cortical tissue, whilst figure-of-eight coils may require more precise positioning to target individual muscles (Weber et al. 2002). Orientation angle should also be consistent to minimise variability of the activation response (Weber et al. 2002) and a 45 degree angle in an anterior to posterior direction is used consistently in research (Hendy & Kidgell 2013; Latella et al. 2012). Circular and figure-of-eight coils held tangential to the skull over the vertex of the head and shifted to preferentially activate either M1 to evaluate the central component of exercise investigations (Hendy & Kidgell 2013; Latella et al. 2012).
Figure 2.8. TMS coil innervation field represents the innervation zone of the magnetic field induced by a) circular coil and b) figure-of-eight-coil (taken from Illmoniemi et al. 1999).
If the stimulation intensity is of sufficient amplitude to activate neurons in the motor pathway, a MEP will be generated that is recorded by muscle EMG. The response will be an observable twitch, depending on the placement of the coil over the M1, in the innervated muscle (Rosler 2001). The intensity required to elicit a MEP will vary dependent on whether the muscle is in a resting state or under tonic voluntary contraction and affected by the type of task being performed (Kidgell & Pearce 2011). MEP’s are generally facilitated during an active state with a lower TMS threshold required (Weber et al. 2002) to elicit a response, whilst the amplitude of response will be influenced by the level of excitability between individuals (Rosler 2001). Minimum threshold levels, being the lowest stimulation intensity to evoke a MEP, differ within and between individuals, partly due to variations in scalp thickness, hair and fatigue time of day, training status, and the menstrual cycle (Wassermann 2005). Resting motor threshold is usually defined as a reading of at least 50μV on at least 50% of trials for resting and 200μV for active conditions (Rothwell 1999; Westin et al. 2014; Weber et al. 2002). Likewise, the MEP response for similar stimulus intensities between individuals will differ in amplitude (Wassermann 2005), however when controlled for torque and type of motor task, the MEP can be a reliable measure (Kamen 2004; van Hedel et al. 2007) allowing for confident interpretation of results following acute or chronic interventions. It is also not uncommon to see investigators using a MEP/M-wave ratio to normalise individual MEP variations between participants (Perez & Cohen 2008) and exclude the influence of peripheral fatigue. MEPs from TMS are usually smaller than peripheral electrical nerve stimulation responses, possibly due to less spinal neurons being discharged during magnetic stimulation (Rosler 2001).
Various sub-components of the MEP can be measured such as MEP amplitude, silent period duration and latency (see figure 2.9.). Latency provides a measurement of the neural conduction speed from the stimulus to the beginning of the MEP (Hallett 2000) and is used as for assessing nerve conduction in healthy populations. The MEP latency may have a slight variation between individuals, however significant changes in latencies can be seen in people with neurological disorders (Weber et al. 2002; Kidgell & Pearce 2011). Amplitude is measured as a peak-to-peak value and reflects the level of muscular contraction. The observable twitch is elicited by the summation of descending volleys resulting in motor neuron innervation (Kidgell & Pearce 2011).

MEP amplitude responses can be variable and difficult to control for at low stimulus intensities, but becomes more consistent with increasing intensity (Weber et al. 2002) and during active conditions which increases corticospinal excitability and reduces variability (O’Leary et al. 2015; Darling et al. 2006; Jubeau et al. 2014). The CSP duration is a notable absence of sEMG activity following an MEP collected during an active muscle contraction. CSP duration relates to the level of inhibition within the corticospinal pathway (Weber et al. 2002; Chen et al. 1999, Wilson et al. 1993) that is measured from the beginning of the MEP to return of EMG activity (Weber et al. 2002). It is generally longest in intrinsic hand muscles and shortest in proximal arm and leg muscles (Weber et al. 2002). CSP can be present before a MEP is detected, indicating that the inhibition stimulus is less than the stimulus requirement for excitatory responses (Weber et al. 2002). CSP duration is influenced by Gaba Amino Butyric Acid (GABAa or GABAb) inhibition and is a result of spinal (group III and IV muscle afferents), and cortical inhibitory mechanisms (Rotenberg et al. 2014; Chen et al. 1999; Jubeau et al. 2014). The first 50 ms is attributed to spinal processes (GABAa,
inhibition), also known as Renshaw inhibition (Weber et al. 2002), while the later portion is due to inhibition (GABA_b), within cortical areas (Inghilleri et al. 1993).
**Figure 2.9.** MEP recorded from the biceps brachii (BB). Latency duration is measured from stimulus artefact to MEP onset and is shown at (a), peak to peak MEP amplitude, representing corticospinal excitability, is shown at (b). Silent Period duration (c), representing corticospinal inhibition, is measured from onset of the MEP to return of EMG. Return of EMG activity is shown at (d) (taken from Kidgell & Pearce 2011).
2.3.4.2. TMS compared to other neuro-investigative techniques

A major difference between TMS and other neuroimaging techniques such as fMRI is that TMS has the ability to investigate the intrinsic functions of intra-cortical inhibitory (i.e. SICI and LICI) and facilitatory (i.e. ICF) neural networks (Weber et al. 2002; Abbruzzese et al. 1999; Hanajima and Ugawa, 2008; Di Lazzaro et al. 2002; Nakamura et al. 1997). There are a number of studies that have directly shown increased excitability (Pascaul-Leone et al. 1995; Chen & Hallett 1999) in a cortical motor area during task activation or, conversely, using TMS to transiently suppress regions of the cerebral cortex, providing stronger evidence of motor regions directly involved in a task (Rothwell 1994). It is for this reason that TMS has been pivotal in a variety of research areas within clinical neurophysiology (Jameson 2012) and motor control (Petersen et al. 2003). Furthermore, many studies now combine both spatial imaging techniques such as fMRI with temporally sensitive techniques such as TMS to investigate areas of the brain directly involved with motor function (Bohning et al. 1999; Kuhtz-Buschbeck et al. 2003).

TMS also has the ability to be used as a neuroimaging tool, illustrating topographical representation of muscles on the motor cortex in healthy (Wilson et al. 1993), athletic (Pearce et al. 2000), or conversely in people with neurological deficits (Byrnes et al. 1999; Thickbroom et al. 2006). Using a latitude-longitude grid system, TMS can be systematically employed to stimulate a number of areas overlying the M1. Averaging the MEP waveforms collected over each site, a topographical matrix of MEP versus stimulus site can be generated to provide a representation of the muscle targeted.
during stimulation. For an in depth discussion on the technique and methodology of TMS mapping, please see either Wilson et al. (1993) or Thickbroom and Mastaglia (1998).

2.3.4.3. Paired pulse TMS

Recently, paired pulse TMS techniques have allowed for the evaluation of intracortical inhibition and excitation using doublets of pulses at pre-selected inter-stimulus intervals. Unlike single pulse TMS which cannot distinguish between changes in cortical and subcortical responses, paired pulse measures assess the modulation of intra-cortical excitability and inhibition (Weber et al. 2002; Abbruzzese et al. 1999; Hanajima and Ugawa, 2008; Di Lazzaro et al. 2002; Nakamura et al. 1997) and has been used to study cortico-cortical interactions with a host of neurological disorders (Ridding et al. 1995; Ziemann 1996). Cortical inhibition and facilitation are thought to stem from two separate mechanisms which synapse on to a common motor neuron (Ziemann 1996). To quantify cortical inhibition and facilitation, paired pulse TMS using an initial (conditioning) stimulus and a second (test) stimulus (Chen 2000; Kujirai et al. 1993) allows for the measurement cortico-cortical interactions. Changes in cortical motor excitability produced by the conditioning pulse (CP) are estimated by changes in the size of the conditioned MEP, compared to the test pulse (TP) elicited by the test stimulus alone (Hanajima & Ugawa, 2008). Thus the magnitude of facilitation or inhibition can be determined within supraspinal levels. The intensity of these paired pulses, and the time interval by which they are separated, are the factors that are manipulated in order to test different populations of neurons within the motor cortex (Kujirai et al. 1993). At sub-threshold CP intensities, a stimulus can
preferentially activate inhibitory neurons, whereas a supra-threshold CP can increase cortical excitability due to greater activation of excitatory neurons (Hanajima & Ugawa 2008).

Several paired pulse techniques exist and for the purpose of this thesis will be discussed in detail. These include SICI, ICF and LICI. SICI and ICF utilise a sub-threshold conditioning stimulus (approximately 70-90% of motor threshold) (Abbruzzese et al. 1999; Boroojerdi et al. 2000) followed by a test stimulus (120-130% of motor threshold), (Abbruzzese et al. 1999; Boroojerdi et al. 2000). An inter-stimulus interval of between 2-5ms (Boroojerdi et al. 2000) and 7-25ms (Abbruzzese et al. 1999; Boroojerdi et al. 2000) is recommended to induce SICI and ICF respectively (see figure 2.10.). Assessment of LICI requires two supra threshold stimuli (Hammond & Garvey 2006) separated by an ISI of 50-200ms with commonly used intervals of 100 and 150ms (Sanger et al. 2001; valls-Sole et al. 1992; Wassermann et al. 1996). LICI is expressed as a ratio of the test stimulus MEP to the conditioning stimulus (LICI conditioning: LICI test).

SICI and ICF are analysed as a ratio of the unconditioned single-pulse MEP amplitude. ICF is prevalent in proximal arm muscles where progressive force modulation is generally required for synergistic movements and tonic postural control (Abbruzzese et al. 1999). SICI reflects GABA$_a$ inhibition (Hanajima et al. 1998) and reflects inhibition of high threshold outputs (Sanger et al. 2001). SICI is easily observable in intrinsic muscles requiring quick force modulation for complex tasks (Abbruzzese et al. 1999) while LICI reflects GABA$_b$ inhibition (Rogasch et al. 2012; Werhahn et al. 1999) of low threshold outputs (Sanger et al. 2001) within the cortex.
and can be overcome with strong excitation (Connors et al. 1988). Intra-cortical measures can display abnormal traits in several neurological conditions (Chen et al. 1997; Priori et al. 1994) including stroke (Classen et al. 1997).
Figure 2.10. Paired pulse inhibition and facilitation. The effect of inter-stimulus interval on the test MEP response. At each inter-stimulus interval, the size of the paired pulse responses is expressed as a percentage of the size of the single pulse MEP response. The y-axis represents the conditioned MEP size in relation to the test pulse. Taken from, Kujirai et al. (1993).
2.3.4.4. Voluntary activation and twitch force

To achieve maximal force the CNS must be able to drive all motor neurons at a sufficient frequency and intensity. If MVC is less than the maximal force generating capacity of the muscle, voluntary activation (VA) is said to be incomplete (Sindhu et al. 2009). Whilst some research has shown an ability of the nervous system to completely activate muscle fibres during isometric contractions in healthy individuals (Gandevia 2001), others have shown that skeletal musculature may not fully activate under voluntary conditions (Gibala et al. 1995; Shield & Zhou 2004). Similarly, muscle specific activation differences have been observed in muscle groups of the upper and lower limbs. The elbow flexors are generally thought to achieve a higher percentage of VA than the quadriceps group (Behm et al. 2002) which are only capable of producing 85-95% of VA (Shima et al. 2002; Norregaard et al. 1994; Roos et al. 1999). Further, VA can be affected by fatigue, age, muscle damage and other neurological conditions (Taylor & Gandevia 2011; Khan et al. 2016; Kennedy et al. 2015; Kennedy et al. 2014; Molenaar et al. 2013). At present, several techniques exist to quantify the magnitude of VA and fatigue. The most common method to assess VA and central drive is via a super imposed electrical stimulus (Sindhu et al. 2009) to the muscle or nerve root (Gandevia et al. 1996), however several technical and methodological issues have arisen regarding the application of technique (Folland & Williams 2006). The twitch interpolation technique uses a direct electric current applied superficially to the muscle or motor nerve root under resting or active conditions (Gandevia et al. 1996; Belanger & McComas 1981). The corresponding increase in evoked force from the stimulus is recorded as the ‘twitch force’. The ratio of the super imposed twitch during activation relative to the resting twitch can indicate
the level of VA; 100% indicative of full activation. The second technique uses a paired pulse stimulus applied to the resting muscle (10ms apart) or thirdly, a train of low frequency (20Hz) or high frequency (80Hz) direct electrical stimulation to assess low frequency depression of force (Enoka 2015).

Alternatively, super imposed TMS of the M1 at various contraction intensities has been used as a technique to assess VA (Urbach & Awiszus 2000) and fatigue. Super imposed TMS offers a quantifiable representation of the efficacy of corticospinal drive along the motor pathway and has shown good correlation with electrical stimulation protocols in the assessment of maximal VA and supraspinal fatigue of the knee extensors (Lampropoulou et al. 2012). The TMS induced super imposed twitch response (SIT) has a linear force relationship at various contraction intensities, whilst PNS is considered to be curvilinear (Goodall et al. 2009; Sindu et al. 2009). Goodall et al. (2009) conducted supra maximal stimulation at 130% of motor threshold to estimate the twitch force responses during contraction strength of 25, 50, 75 and 100% MVC and showed decreased responsiveness between 50-100% MVC, (see figure 2.11.).
Figure 2.11. SIT force response. Depicts the relationship between the decrease in twitch force response to super imposed TMS stimulation with increasing contraction intensity in the leg extensors at a) 25%, b) 50%, c) 75% and d) 100% of MVC.
However, a limitation of the super imposed TMS twitch response is that it must be estimated under resting conditions due to lower cortical and motor neuron excitability. Coupled with stimulation at the cervico-medullary region, nerve root and muscle site, multifocal stimulation can gauge the contribution of descending drive from either cortical, subcortical or spinal regions.

Current electrical and magnetic methods of assessing VA can provide quantifiable evidence for the efficacy of neural drive. The existence of magnetic and electrical stimulation methods have shown good correlations and reliability (Clark et al. 2007) for quantifying VA in different muscle groups, with exercise induced fatigue that will be discussed further in (section 2.6.1.1. Fatigue).
2.4. Current Resistance Training Recommendations

The following sections on strength and hypertrophic training recommendations will be based upon current literature surrounding the exercise principles of intensity, repetitions, rest periods, volume and frequency. It is acknowledged that there are other factors; specificity and movement velocity that are also considered important in the development of strength or hypertrophic adaptations (see figure 2.12.). However, for the purpose of this review these factors will not be discussed with the reader directed to the appropriate references (Ratamess et al. 2009; Crewther et al. 2005; Folland & Williams 2007; Rhea et al. 2016; Carpinelli et al. 2004; Fisher et al. 2016; Schoenfield 2010; Schoenfield 2014; Wernbom et al. 2007; Schuenke et al. 2012).
Figure 2.12. Resistance exercise prescription flow chart. Proper program design incorporates structured acute program variables leading to specific training outcomes, adapted from Bird et al. (2005).
2.4.1. Strength Training Recommendations

Strength training is centred on priming the neuromuscular system to generate the most amount of force possible against a given resistance. As noted in previous sections, the development of strength is governed by several physiological and neural characteristics (Bloomer & Ives 2000) with the appropriate planning and prescription of training variables required to induce strength changes (Souza et al. 2014; Bird et al. 2005). Although a large body of evidence is available on the influence of strength training on the acute hormonal (Walker et al. 2012), metabolic (Brandon et al. 2015), architectural (Aagaard et al. 2001; Matta et al. 2011), fibre composition (Campos et al. 2002; Tesch 1988) and contractile changes (Aagaard et al. 2001), less is understood about the underlying neurophysiological processes (Enoka 2007). The following sections will discuss the literature regarding the influence of strength training program variables and the recommendations for the development of strength and performance outcomes (Ratamess et al. 2009; Carpinelli et al. 2004).

2.4.1.1. Intensity

Although strength improvements have been shown with training intensities of as little as 15% (Moss et al. 1997), 45-50% (Ratamess et al. 2009) and 60% (Rhea et al. 2003) of 1RM in novice individuals (Ratamess et al. 2009), it is generally accepted that training intensities equal to or greater than 80% and up to 100% 1RM (Latella et al. 2012; Crewther et al. 2005; Van Roie et al. 2013; Bompa 1999; Ratamess et al. 2009; Peterson et al. 2004; Hakkinen et al. 1985; Lee et al. 2009) are optimal for strength
and neural adaptations, especially in experienced lifters (Baechle & Earle 2008). It is thought that training at mean intensity of 85% of 1 RM and above has a greater magnitude of effect on strength adaptations (Ratamess et al. 2009; Mangine et al. 2016). The magnitude of strength adaptation is highly correlated with the direction of the training stimulus, therefore training with higher training intensities usually resulting in greater improvements in maximal strength (Campos et al. 2002; Mangine et al. 2016). One such study in experienced powerlifting athletes showed that a linear periodised low volume training program working up toward 95% of 1 RM significantly improved the squat by 30.3%, bench press 33.5%, and deadlift 76.9%, over a 16 wk cycle (Joao et al. 2014) providing evidence for the superiority of high intensity training in advanced individuals. This concept was also shown with maximal or explosive strength training whereby late force development showed greater improvements with maximal strength training (Anderson et al. 2009) whilst early rate of force development associated with explosive training (Tillin & Folland 2014) showed lesser change. Therefore heavy loads greater than 80% of 1 RM are considered superior in development of strength whilst lower loads may be sufficient for novice or recreationally trained individuals.

2.4.1.2. Repetitions

Correlating with the intensity/volume relationship (Verkoshansky 1998), low individual set repetitions are considered optimal for the development of strength (Bompa & Haff 2009; Haff & Triplett 2016), (see figure 2.13.). Set repetitions of between 1-6 RM are considered effective at increasing dynamic strength (Crewther et
al. 2005; Berger 1962; Campos et al. 2002; Ratamess et al. 2009), with a range of 5-6 RM considered optimal (Ratamess 2009). Heggelund et al. (2013) showed that 4-5 RM strength training improved maximal strength in the leg after knee extension training and was beneficial over 10 RM. Interestingly, loads of 2-3, 5-6 and 9-10 RM (O’Shea 1966), 10 repetitions at 50-75% of maximal strength (Cannon & Marino 2010) and 9-15 RM (Weiss et al. 1988) have also been shown to increase strength in novice individuals (O’Shea 1966) suggesting that specificity of the repetition range is not necessarily essential regardless of training experience (Carpinelli et al. 2004). While training loads are usually prescribed as a percentage of 1 RM, an important consideration is that training to mechanical failure may not be necessarily required for strength adaptation (Folland et al. 2002; Sampson & Groeller 2016; Davies et al. 2016; Nobrega & Libardi 2016) and in some cases may be superior to performing sets to failure (Sanborn et al. 2000). Furthermore, minimisation of training to failure may reduce the likelihood of injuries. Despite these suggestions, recent evidence has also supported the superiority of training to momentary failure on strength gains (Fisher et al. 2015; Fisher et al. 2016), although the repetition range for optimal strength development is still a topic of recent debates.

2.4.1.3. Rest Periods

It has been well established that strength training requires considerable rest periods between sets to optimise performance (Baechle & Earle 2008). Intrinsic session performance may be affected by shorter rest periods less than 1 min (Scudese et al. 2015) and negate overall strength gains (Ratamess 2009; Robinson et al. 1995).
Longer rest periods 2-6 mins are considered superior to shorter rest periods for in
session performance and adaptation depending on exercise complexity (Ratamess et
al. 2009; Bompa 1999; Robinson et al. 1995; Schoenfield et al. 2016; De Salles et al.
2009; Bird et al. 2005). Robinson et al. (1995) showed that 180 sec was beneficial
over 30 sec recovery for 1 RM squat performance and also been recommended by
Kraemer et al. (1991). Similarly, Schoenfield et al. (2016) reported that resistance
trained men significantly improved their maximal bench press and back squat after 8
wks of RT with 3 mins compared to 1 min recovery. A review by De Salles et al.
(2009) showed that 3-5 minutes rest between sets produced greater increases in
absolute strength. Given that intensity is important in the development of strength for
advanced lifters, fatigue causing a reduction in lifting intensity may impact upon
strength adaptations. However this concept has not always been shown with Folland
et al. (2002) demonstrating that the acute fatigue induced by strength training with 30
sec recovery between sets versus 30 sec rest between individual repetitions sets was
not any more beneficial for strength adaptation. In light of the research and current
recommendations (Ratamess et al. 2009; Folland et al. 2002; Robinson et al. 1995)
longer rest periods of more than 2 mins, are currently considered beneficial for in
session performance and strength adaptations over time.

2.4.1.4. Volume

For the purpose of this discussion volume will be defined as the number of sets performed during a session. Strength training volume is typically characterised by low repetitions (see section 2.4.1.2. Repetitions) and multiple sets although the
recommended number of sets is ambiguous (Ratamess et al. 2009). Reports of strength increases in novice (Berger 1962), recreationally trained (Baker et al. 2013), and elderly populations (Radaelli et al. 2013) has been presented with single set programs, with some evidence suggesting single-set training to be as effective as multi-set training across most populations (Carpinelli & Otto et al. 1998; Carpinelli et al. 2004). Despite these reports, a large body of evidence exists for the superiority of multi-set regimes. Reviews by Frohlich et al. (2010) and Galvao and Taaffe (2004) have shown that multi-set programs are superior at increasing strength during short and long term training interventions. According to a number of authors, sets of between 2 and 8 are considered superior in most circumstances, especially for experienced individuals (Fleck & Kraemer 1997; Kraemer & Fleck 1988; Kraemer et al. 1988; Humburg et al. 2007; Kraemer et al. 2000; Kraemer & Ratamess 2004; Kelly et al. 2007; Marshall et al. 2011). A meta-analysis by Rhea et al. (2003) showed that 4 sets was ideal for strength gains in trained and untrained individuals, however this value may need to be doubled for experienced and athletic populations (Marshall et al. 2011). Other research supports these findings in novice (Sanborn et al. 2000) and athletic populations (Kraemer et al. 1997).

Research comparing single vs multi-set regimes has produced conflicting results (Galvao & Taaffe 2004; Carpinelli & Otto et al. 1998; Carpinelli et al. 2004). A review by Carpinelli & Otto (1998) found no significant differences between 1 vs 2 and 1 vs 3 sets protocols on the magnitude of strength gained, however the difference in volume in this study may not accurately depict different training volumes (Radaelli et al. 2015). Conversely, Carpinelli et al. (2004) reviewed evidence of single vs multi-set regimes for novice individuals, and did not show any difference of improvement...
between either training volumes. Only one study has shown similar improvements in strength for previously resistance trained individuals using single versus multi-set regimes (Hass et al. 2000). Although there is some evidence to suggest that single set programs do offer some strength improvement, greater improvements in strength are still observed with multi set training regimes (Krieger 2009). Therefore single set programs seem inferior to multi-set programs however the consensus on the optimal number of sets in a multi-set program has not been reached.

2.4.1.5. Frequency

Training frequency is considered as an important variable in the development of strength (Raastad et al. 2012; Hartman et al. 2007; Hakkinen & Kallinen 1994) with recommended guidelines established to identify optimal spatiality between training sessions (Ratamess et al. 2009). It is generally accepted that strength training should be scheduled no sooner than 72 hrs for optimal recovery (Bompa & Haff 2009; Baechle & Earle 2009). However, training status may play a critical role in influences recovery, with more experienced individuals capable of higher training frequencies than novice populations (Ratamess et al. 2009; Raastaad et al. 2012; Fleck & Kraemer 1997; Zatsiorsky 1995). Previously, it has been shown that as little as 1 training session per wk can maintain or even improve strength in previously untrained and recreational populations (Tan 1999; Ohmori et al. 2010; McLester et al. 2000). Despite these findings, it is suggested that 2-3 days per wk training is suitable for novice individuals, with 3 days per wk ideal for strength improvement (Ratamess et al. 2009). According to Ratamess et al. (2009), intermediate individuals are capable of training
3-4 days per wk, 4 days if using a muscle groups split routine so that frequency of the same muscle group equates to 2 days per wk (Ratamess et al. 2009). Athletic populations are capable of training most days of the wk with 4-6 days per wk with each muscle group trained approximately 2 times per wk (Peterson et al. 2004) considered optimal for hypertrophic adaptations. Serra et al. (2015) further supported the need for multiple sessions per wk, with 2-4 days suggested to produce significant strength gains even in untrained individuals. Specific strength sports utilising ultra-high frequency, double split routines daily with as high as 18 sessions per wk have shown to be beneficial over other protocols in Olympic level lifters (Fleck & Kraemer 1997; Zatsiorsky 1995). Recently, Cook et al. (2014) showed that scheduling RT early in the day can positively impact strength performance that same afternoon, whilst Ekstrand et al. (2013) also showed that resistance exercise can improve athletic power performance 4-6 hrs later. Despite the recommendations, optimal training frequencies in the development of strength remain the subject of continuing debate with multiple training frequencies per wk considered superior in the development of strength.
Table 2.1 shows a summary of resistance training variables recommended for strength and hypertrophy training in novice and experienced individuals.

<table>
<thead>
<tr>
<th></th>
<th>Strength</th>
<th>Hypertrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intensity</strong></td>
<td>45-60% Novice 80-100% Experienced</td>
<td>65-85% Novice/Experienced</td>
</tr>
<tr>
<td><strong>Repetitions</strong></td>
<td>12-10 RM Novice 1-6 RM Experienced</td>
<td>6-15 RM Novice/Experienced</td>
</tr>
<tr>
<td><strong>Rest Periods</strong></td>
<td>2-6 minutes</td>
<td>30 sec – 2 min</td>
</tr>
<tr>
<td><strong>Volume</strong></td>
<td>1 set Novice/Recreational/Elderly 2-8 Experienced</td>
<td>1 – 3 sets Novice 3 – 6 sets Experienced</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>1-3 p/w Novice 4-6 p/w Advanced 6+ p/w Olympic Athletes</td>
<td>2 – 3 full body Novice 4-6 split routine Experienced</td>
</tr>
</tbody>
</table>
2.4.2. Hypertrophic Training Recommendations

Hypertrophy from RT occurs via mechanical tension, muscle damage and metabolic stress (Schoenfield 2011). In turn, these factors trigger a variety of metabolic, morphological, hormonal and mechanical processes (Kraemer et al. 2000; Goldspink 1999; Viru 1995; Folland & Williams 2007; Borst et al. 2001; Walker et al. 2012; Kraemer et al. 1991; Schoenfield et al. 2011) via neuromuscular fatigue (Ogborn et al. 2014; Schoenfield et al. 2013; Schott et al. 1995). These processes result in muscle protein synthesis, degradation, changes in fibre composition and cross sectional area (CSA) (Fowles et al. 2000; Lieber & Friden 1993; Souza et al. 2014; Campos et al. 2002; Folland & Williams 2007). Despite the known impact of muscle hypertrophy on force generating ability and performance (Ikai & Fukunaga 1968; Maughan et al. 1983) the potential neural underpinnings are often overshadowed. Increases in CSA in the order of 10-15% are known to occur after 10-14 wks of dynamic RT (McCall et al. 2012; Ronnestad et al. 2007) yet absent in the early stages of training (Moritani 1979) for up to 8 wks (Latella et al. 2012). The following section will highlight the current recommendations for applied HYT practice.

2.4.2.1. Intensity

Intensity is an important training variable in the development of muscular hypertrophy (Fry 2004). Commonly, submaximal loads of 67-75% of 1 RM are employed, with shorter rest periods and a higher overall volume (Crewther et al. 2005). Despite the use of these workloads, higher intensities up to 80-85% of 1 RM have also been shown
to be effective in promoting hypertrophic adaptations (MacDougall 1992; Kraemer et al. 2002 Holm et al. 2008; Wernbom et al. 2007; Mitchell at al. 2012). Overall, workload-matched studies have provided evidence that high intensity exercise produces more hypertrophic adaptations over low intensity protocols (Campos et al. 2002; Holm et al. 2008) with loads of up to 100% of 1 RM having been shown effective for advanced lifters when used in conjunction with submaximal intensities (Ratamess et al. 2009). Interestingly, low intensity loads of 30% of 1 RM have also shown some promise and in some instances a similar response in comparison to higher intensities (Mitchell et al. 2012; Lerger et al. 2006; Lamon et al. 2009; Ogasawara et al. 2013). However, loads lesser than 65% of 1RM have not always been reported as an effective method of inducing hypertrophy of muscle fibres (Schuenke et al. 2012; McDonagh & Davies 1984).

Further, hypertrophy may not be uniform across a muscle with different intensity loading reflective of proximal or distal changes in CSA (Earp et al. 2015) and between fibre types (Ogborn et al. 2014). Higher intensity loading is preferential for inducing hypertrophic changes in fast twitch (Type II) muscle fibres (Fry et al. 2004). Conversely, lower intensity loading to concentric failure is thought to induce hypertrophy in slow twitch (Type 1) muscle fibres (Mitchell et al. 2012) however research using low loading schemes is scarce (Fry et al. 2004; Wernboom et al. 2009). This mixed intensity model for HYT is supported by Ogborn et al. (2014) who propose that a range of intensities should be incorporated to ensure continuing hypertrophic adaptations within the muscle.
2.4.2.2. Repetitions

Individual HYT set repetitions are aimed at inducing high levels of metabolic stress to induce adaptations (Fry et al. 2004). Current recommendations suggest the optimal repetition range to be between 6-15 RM to induce HYT adaptations (Bird et al. 2005; Crewther et al. 2005; Ratamess et al. 2009; Schoenfield 2010; Campos et al. 2002; Schuenke et al. 2012) and has been widely accepted in general and applied practice (see figure 2.13.). Despite these recommendations, reports of repetitions as low as 1-5 RM (Campos et al. 2002; Ratamess et al. 2009) and as high as 25-35 RM (Goto et al. 2004) have been shown to be effective at inducing muscular hypertrophy. However, training with higher repetition ranges of 15-20RM have not always been shown to be effective (Campos et al. 2002; Schuenke et al. 2012). Ratamess et al. (2009) propose that to maximise overall muscle mass, training should be conducted across a wide repetition range with more time spent in the 6-12RM zone rather than 1-6 RM loading schemes.

2.4.2.3. Rest Periods

Rest period durations aimed at inducing hypertrophic adaptations require large amounts of metabolic stress to be induced. A range of rest period durations have been suggested to effectively induce HYT adaptations with short rest intervals of 30 sec, 1 min (Kraemer et al. 1991), and up to 2 mins recommended (Ratamess et al. 2009). Shorter rest periods induce a high amount of metabolic stress and hormonal responses, however may impair muscular performance in subsequent sets (Schoenfeld 2010;
Ratamess et al. 2007; Pincivero et al. 1997). Although long rest periods may improve force generating capabilities, the associated reduction in anabolic and metabolic responses may impair the HYT response (Schoenfield 2010; Kraemer et al. 1991).

In light of the varied consensus, rest period duration may depend upon exercise selection and complexity (Ratamess et al. 2009). Given the current evidence, moderate rest intervals (60-90 secs) appear to offer the best approach for HYT adaptations (Schoenfield 2010). Importantly, the hormonal and metabolic response appears to be important in adaptive hypertrophic processes such as changes in fibre composition muscle protein synthesis (Fowles et al. 2000; Lieber & Friden 1993; Souza et al. 2014; Campos et al. 2002; Folland & Williams 2007).

2.4.2.4. Volume

Typical HYT regimes employ high within session training volumes. Evidence suggests that total session volume (Candow & Burke 2007) and force production plays an integral role in endocrine activity (Walker et al. 2012), which mediate muscle hypertrophic responses (Crewther et al. 2005; Marx et al. 2001; Mulligan et al. 1996). Given the presented evidence on repetition range, there has subsequently been a multitude of research to further investigate the effect of single- versus multi-set programs on hypertrophy (Galvao & Taaffe 2004), with recommendations suggesting as few as 1-3 sets for novice and 3-6 sets for advanced individuals (Kraemer & Ratmess 2004; Ratamess et al. 2009). In support of these findings, most research has shown multiple set training to be more beneficial than single set protocols (Krieger
2009; Galvao & Taaffe 2004; Aguir et al. 2015; Wolfe et al. 2004). Conversely, Mitchell et al. (2012) showed that hypertrophic changes can occur with as little as 1 set of exercise over a 10 wk period. Recently, Aguir et al. (2015) investigated the effects of a standard RT protocol using 3 sets of 8-12 RM at 75% of 1 RM versus 3 sets of 8-12 RM 2 days per wk over 8 wks. A single set of exhaustive exercise at 20% of 1RM was performed prior to the main session. The findings showed that prior exhaustive exercise had a significant benefit in increasing CSA, indicating that fatigue of physiological and metabolic associated mechanisms may be superior over standard RT protocols. To further highlight the discrepancies in the literature, Fisher (2012) conducted a meta-analysis to compare the hypertrophic gains between single and multi-set training programs. The result of the analysis suggest that due to the differences in training experience, gender, intervention duration, repetition duration and the method for assessing hypertrophy, a confident conclusion cannot be drawn regarding optimal volume for HYT.

2.4.2.5. Frequency

Optimal HYT frequency can depend on the experience level of the individual. Here it is important to distinguish that HYT frequency refers to the number of total RT sessions per wk and requires differentiation between the frequencies that the same muscle group is trained. Recommendations state that 48 hrs is required between subsequent HYT session (Bompa & Haff 2009; Ratamess et al. 2009). Further, novice individuals are recommended to train 2-3 times per wk incorporating full body workouts (Coburn et al. 2006; Cureton et al. 1988), whilst intermediate participants 4
days per wk with the frequency of each muscle group 2 days per wk and advanced participants 4-6 days per wk. Split routines placing emphasis on specific muscle groups are though to increase the hypertrophic response (Kerksick et al. 2009). Wernbom et al. (2007) indicate that 2-3 sessions per muscle group per wk are achievable however the frequency may be affected by the volume and intensity and should be adjusted accordingly (Ratamess et al. 2009). In further support of Ratamess et al. (2009), long term training interventions with HYT have seldom been investigated and thus longer recovery periods require consideration due to the typically higher volume workloads (Naclerio et al. 2013). Supporting longer recovery periods, Candow and Burke (2007) demonstrated no difference in muscle mass between individuals who performed 2 or 3 days per wk HYT. Given the varying nature of frequency recommendations further research is required to investigate the effect of session frequency on muscle hypertrophy to provide clarification for the effect on physiological and neural mechanisms.
Figure 2.13. Repetition flow chart. Represents the effect of RM on the development of strength, power, hypertrophy and muscular endurance. Yellow areas indicate optimal repetition zones for the development of each trait (Baechle et al. 2008).
2.5. Neurophysiological adaptations to resistance training

2.5.1. Neuroplasticity

Neuro-plasticity refers to the nature of lasting adaptations in numerous sites within CNS. Plasticity is evident in early years of growth and development (Sherwood 2007) and continues to occur in response to user specific demands and experiences (Weber et al. 2002; Thickbroom & Mastaglia 2009; Sanes & Donoghue 2000; Carroll et al. 2001). The proposed mechanisms are thought to be via the generation of neuronal synapses, enhanced synaptic efficiency, innervation of latent synapses and changes in representational patterns (Donoghue et al. 1996; Carroll et al. 2001; Kleim et al. 2002; Ziemann et al. 1998; Sherwood 2007). Jacobson (1991) defines plasticity as a consequence of one of two circumstances:

1) Due to normal changes resulting from sensory input (visual, auditory, somatosensory, olfactory and autonomic); or

2) Those that occur after brain or other forms of injury (Pascual-Leone et al. 1996).

Plasticity is commonly seen after longitudinal RT interventions (Griffin & Cafarelli 2007; Kidgell & Pearce 2010; Kidgell et al. 2010; Weier et al. 2012) at multiple sites within the CNS and PNS. The known mechanisms will be discussed in the following section.
2.5.2. Known neurophysiological strength training adaptations

Improvements in the force generating capacity of a muscle and functional movement patterns are directly related to several neural and physiological factors (Bloomer & Ives 2000). Moritani and deVries (1979) were one of the first to report adaptations in the nervous system in the early stages of strength development. Neural adaptations show a strong relationship with early strength gains in the absence of peripheral changes (Moritani & deVries 1979; Sale 1988), (see figure 2.14.), which may account for as high as 60% of the adaptations observed during the first 60 days of training (Narici et al. 1989). These adaptations are thought to continue to occur even in highly trained athletes (Judge et al. 2003).
Figure 2.14. Time course of neural, hypertrophic and strength adaptations. Neural adaptations dominant in the initial stages, with hypertrophic mechanisms becoming prevalent in the later stages. Progress becomes limited in advanced trainers (taken from Sale (1988)).
It has since been well established that the adaptations from RT are highly specific (Beck et al. 2007). Changes in central motor control include increased prime mover activation/co-ordination, reduced antagonist activation and motor unit firing frequency/synchronisation have been demonstrated in earlier research (Milner-Brown & Lee 1975). EMG changes have also been shown in relation to early strength gains from training (Aagaard et al. 2003; Oliveira & Goncalves 2009; Marshall et al. 2011; Jakobsen et al. 2013). Training intervention studies using 8 wks of isotonic and isokinetic knee extensor training significantly increased strength by 13.3 and 16.1% respectively, coinciding with a significant increase in agonist sEMG activity (Remaud et al. 2010). Further, Aagaard et al. (2000) demonstrated increases in the EMG of between 16 and 32% after 14 wks of heavy concentric and eccentric quadriceps contractions.

More comprehensive neurophysiological investigations have shown changes within the M1 (Hendy et al. 2014; Weier et al. 2012) and corticospinal drive from strength (Kidgell et al. 2010; Weier et al. 2012; Goodwill et al. 2012; Griffin & Cafarelli 2007; Latella et al. 2012; Lee et al. 2009) and ballistic strength training (Beck et al. 2007). Furthermore, changes in spinal (Peacey et al. 2014) and spinal reflex excitability (Vila-Cha et al. 2012), increased agonist activity (Hakkinen & Hakkinen 1995) reduced antagonist co-activation (Griffin & Cafarelli 2005), motor unit firing frequency (Behm 1995) and synchronisation (Folland & Williams 2007) are also known to occur. Semmler and Enoka (2000) outlined the sites of adaptation within the nervous system (see figure 2.15.), however these adaptations do not appear to be a universal response (Griffin & Cafarelli 2005; del Olmo et al. 2006; Jensen et al. 2005; Kidgell & Peace 2010; Tallent et al. 2013; Iglesias-Soler 2016; Beck et al. 2007).
Duchateau et al. (2006) speculates that most adaptations from RT occur outside of the M1 with further research required to identify specific sites of adaptation (Folland & Williams 2007; Del Balso & Cafarelli 2007; Carroll et al. 2011).

Despite the magnitude of research regarding neural adaptations from RT, the exact mechanisms underlying these changes remain unclear. The discrepancies in the findings may be due to non-uniform training and testing methodologies. To further complicate the issue, the basis for the initiation of these adaptations (the acute training responses from applied RT), are poorly understood.
Figure 2.15. Potential sites of adaptation in the nervous system. Following strength training these may include: (1) cortical reorganisation, (2) reduced co-contraction of antagonists, (3) increased descending drive from supraspinal centres, (4) cross-education (spinal interneuronal coupling), (5) changes in the bilateral deficit, (6) changes in motor unit behaviour, (7) increased muscle activation, and (8) increased motoneuron excitability. IN indicates interneurons and MN indicates motor neurons. Taken from Semmler and Enoka (2000).
2.6. Neurophysiological responses to an acute training session

While the exposure to repeated RT stimuli results in physiological and neural adaptation (Carroll et al. 2011; Selvanayagam et al. 2011; Griffin & Cafarelli 2005) the responses to an acute session remain unclear. Exercise has the potential to disrupt the body’s normal homeostatic control (Powers & Howley 2007) causing perturbations in physiological systems. Post exercise, the physiological systems of the body undergo several key phases in an attempt to recover from and protect against future stress. However, continued exposure to the same stimuli over time with inadequate recovery will eventually lead to a state known as “staleness” describing a state of possible overtraining, resulting in no further adaptation or “prolonged maladaptation” (Meeusen et al. 2013). Other factors can also affect the adaptation to stimuli. Highly trained individuals encounter difficulty achieving the same magnitude of gains as a novice trainee. This is known as the ‘ceiling effect’ where an athlete has advanced to a point where a plateau begins to occur due to genetic potential (Bompa & Haff 2009). The following section will discuss in detail the development of the super-compensation model, the stages of fatigue, recovery, adaptation and involution and the current lack of understanding of the acute responses to a RT session.

2.6.1. Super-compensation theory

First termed *super-compensation* by Folbrot in 1941, (Siff & Verkhoshansky 1999), and as Weigert’s law, the phenomenon was used to describe the body’s physiological response and adaptation to a heavy exercise stimulus. Seyle (1950) further discussed
this phenomenon, known as the General Adaptation Syndrome (GAS), to examine the nature in which a typical pattern emerges when an organism is exposed to a stressor. In turn, adaptive mechanisms occur in order to avoid an endangerment to life. The stages were known as the “shock/alarm”, “resistance” and “exhaustion” phases. The initial alarm phase constitutes the recognition of the stressor, which then initiates an autonomic sympathetic response (known as the fight or flight response). During the resistance phase compensatory changes in metabolic, endocrine and immune responses dominate until biochemical substrates have been depleted (Fry et al. 2000; Hakkinen 1989; Bompa & Haff 2009). Seyle (1950) deduced that the ability to adapt to a stress requires energy, however this energy is limited and if the stress is not alleviated exhaustion occurs and defence of the organism to the stressor is no longer adequate in meeting the demands. Therefore the adaptation or ‘defence’ to the stress that occurred during the resistance phase would be over run during in the exhaustion phase. These physiological concepts were later applied to exercise conditioning by Garhammer in 1979.

This GAS model remained relatively unchanged until refinement in the 1990’s. The model was further developed (Bompa & Haff 2009) to consist of four distinct phases; fatigue, recovery, adaptation and involution across neural, psychological and performance domains in response to exercise (see figure 2.16.). In current literature, super-compensation theory forms an integral part of our current understanding of exercise prescription, planning and periodisation. Thus, several similar models have been conceptualised such as the stimulus-fatigue-recovery-adaptation theory (Verkhoshansky 1986) and the fitness-fatigue paradigm (Plisk & Stone 2003; Chiu & Barnes 2003) aimed at explaining general responses to exercise. Bompa and Haff’s
(2009) super-compensation model is divided into 4 stages, described by a series of distinguishable yet interconnected events.
Figure 2.16. The super-compensation model (taken from Bompa & Haff 2009). Comprises of 4 stages; I) Fatigue, II) Compensation, III) Super-compensation, IV) Involution
I) Fatigue: Exposure to training stimuli results in central and peripheral fatigue associated with metabolite accumulation, changes in substrate usage and hormonal levels and reductions in neural activation.

II) Compensation: This phase (24-48 hrs) consists of a rapid replenishment of muscle ATP and PCR stores, gradual return of muscle glycogen to base levels, and increased resting energy expenditure and an increase in protein synthesis.

III) Super-compensation: Can be considered the ‘adaptation’ phase with a reduction in muscle soreness, improved psychological state of mind and full replenishment of glycogen stores. The proposed time frame for this stage is 36-72 hrs.

IV) Involution: Occurs if the athlete is not exposed to repeated stimuli within the super-compensation period. Results in a decrease in physiological performance obtained from the previous stimulus leading to mal adaptation or overtraining (MacDougall & Sale 2014). May also occur if the stimulus is too great with continued inadequate recovery.

It is widely accepted that training stress is vital for improved performance (Silva 1990). Recently, Naclerio et al. (2013) derived the super-compensation model to further explain the relationship between exercise intensity and volume (see figure 2.17.) on fatigue and recovery. It was proposed that the greater the stress (intensity and load) the longer the time course of the cycle (Naclerio et al. 2013). Further, Zatsiorsky and Kraemer (2006) have proposed that the positive training effect (super-compensation phase duration) is three times longer than the recovery period. However, limited neural and neuromuscular research has investigated such responses (Brandon et al. 2015) and renders these claims somewhat unconvincing. Current super-
compensation theory requires more conclusive, empirical evidence to support the proposed time course of fatigue, recovery and adaption in response to exercise. Specifically, the acute neurophysiological responses have not been comprehensively tracked post-training up until 96 hrs. Based upon the lack of supporting evidence, further investigation into these mechanisms is required for optimal implementation into applied strength and conditioning settings.
Figure 2.17. Effect of intensity and volume on super-compensation. Depicts the theoretical relationship of low, moderate, high and maximum volume and intensity exercise on the super-compensation cycle time-course adapted from Nacleiro et al. (2013).
2.6.1.1. Fatigue

Fatigue, is usually categorised as central (neural fatigue) or peripheral (muscular fatigue) in origin (Gandevia 2001). Fatigue is associated with a period of decreased force output (Froyd et al. 2016), performance, subjective motivation and/or feelings of tiredness (Gandevia et al. 2008; Enoka & Duchateau 2016; Enoka 2012). Fatigue is often reported as a reduction in performance, voluntary force output or an inability of the neuromuscular system to maintain maximal or desired force (Gandevia 2001) due to feedforward and feedback mechanisms (Enoka et al. 2011). To date, research has presented mixed findings on the mechanisms of central and peripheral fatigue, with voluntary and evoked muscular conditions (Gandevia et al. 1996; Gandevia et al. 2001; Noakes 2010; Noakes 2011; Matkowski et al. 2009) and the mechanisms that result in fatigue are specific to the task being performed (Enoka & Duchateau 2008). Bompa and Haff (2009) propose that post exercise fatigue accumulates and occurs maximally between 1-2 hrs. The authors suggest that fatigue is multidimensional, encompassing reductions in neural activation, changes in endocrine secretion, substrate depletion, lactic acid accumulation. Further, Chiu and Barnes (2003), and Tillin and Bishop (2009) agree that fatigue from maximal intensity and strength exercise can be delayed due to a potentiation effect. This has recently been supported by Thomas et al. (2015), showing an increase in explosive muscular performance 8 mins post heavy RT in in male athletes.

To date a multitude of research has also presented findings on performance decrements with fatigue (Brandon et al. 2015) with different contraction types
(Babault et al. 2006; Marshall et al. 2015) and contributing neuromuscular (Tran et al. 2006) and neural mechanisms (Gruet 2014). Research investigating outcome measures of neuromuscular strength and force production has been extensively covered during fatigue from different RT protocols (Howatson et al. 2016; Ide et al. 2011; Brandon et al. 2015; Nicholson et al. 2014).

Despite fatigue manifesting as impaired neuromuscular performance, the physiological basis is often attributed to both peripheral (physiological) and central (supra spinal) factors, (Vollestad 1997). Noakes (2011) suggested that the entire process involves a complex regulation of human performance, rather than single perspective studies of fatigue commonly seen in literature. For further discussion on the regulation of fatigue, the reader is directed to the work of Noakes (2011) and Noakes (2010). From a functional standpoint, a decrease in neuromuscular performance has been well documented. Chiu et al. (2004) showed a decrease of lower limb peak force as measured through isokinetic dynamometry by 9.5% following 10 sets of 5 speed squats and a further 8.9% following a second bout of training the same day. Tran et al. (2006) also showed reductions in MVIC with both time under tension controlled or short concentric exercise of the elbow flexors. Further evidence from Babault et al. (2006) and Marshall et al. (2015) has reported decreases in torque following isometric and concentric contractions and similarly with fatiguing contractions (Plautard et al. 2015) of the knee extensors and eccentric contractions of the plantar flexors (Racinais et al. 2008). More recently, applied training protocols have provided further insight into strength decrements during fatigue. Walker et al. (2012) investigated neuromuscular fatigue following either a 15 x 1 RM HST or 5 x 10 RM HYT protocol. The results showed large reductions in maximal isometric force...
for HST and HYT and EMG following HST post training. Brandon et al. (2015) showed that 10 sets of 5 heavy squat repetitions caused more residual peripheral fatigue over moderate load repetitions at 75% and concluded that moderate stimulation may be beneficial for athletic populations to maintain neuromuscular stimulus whilst minimising fatigue.

From a neural standpoint, changes in neural activation with RT have been consistently shown through sEMG (Remaud et al. 2010; Aagaard et al. 2003; Jakobsen et al. 2013; Aagaard et al. 2000; Marshall et al. 2011; Oliveira & Goncalves 2009; Walker et al. 2012), however is limited as an assessment of neuromuscular function. Investigations into cortical and corticospinal excitability during fatigue have also been investigated (McNeil et al. 2011; Brasil-Neto 1992; Benwell et al. 2006; Gandevia et al. 1999; Gruet et al. 2014; Ruotsalainen et al. 2014; Thomas et al. 2015; O’Leary et al. 2016). However the findings must be compared to the state of the muscle at the time of stimulation (contracted versus relaxed), (Gruet et al. 2013) and thus the literature has reported mixed findings (Ruotsalainen 2014; McNeil et al. 2011; Brasil-Neto 1992; Gruet et al. 2014).

During resting conditions, McNeil et al. (2011) showed a decrease in MEP amplitude after sustained muscular contractions at 25% of MVC over 10 mins. Brasil-Neto (1992) also showed a 60% decrease in MEP amplitude immediately following a bout of repetitive wrist flexion movements. In line with these findings Benwell et al. (2006) also reported a 35-44% decrease in MEP amplitude following MVC. Similarly reductions have also been shown by Gandevia et al. (1999) in the elbow flexors during
isometric contractions, Brasil-Neto (1993) and Zanette et al. (1995) in intrinsic hand muscles and by McKay et al. (1995) and Lentz and Nielsen (2002) in the lower leg. Further evidence has been shown by Gruet et al. (2014) who tracked corticospinal changes in the lower limb up to 6 mins following a fatiguing isometric exercise of the quadriceps. Corticospinal inhibition was shown to increase up to 2 mins post exercise. Conversely no change in cortical and corticospinal measures have been reported after heavy resistance exercise (Thomas et al. 2015).

Less evidence has been presented during active muscular contractions. The MEP during fatigue conducted with voluntary contraction has been shown to remain above baseline values, which is suggested to be due to the voluntary effort of contraction inadvertently overcoming the decreased motor cortex excitability observed in a relaxed state (Sogaard et al. 2006; Smith et al. 2007; Iguchi & Shields 2011; Keller et al. 2011). Ruotsalainen et al. (2014) found an increase in CSE between each set of HYT session, concomitant with a decrease in force generating capacity of the elbow flexors. Similarly, an increase in MEP amplitude has been shown at start of a sustained sub maximal task, and after exercise-induced fatigue Ruotsalainen et al. (2014) and after ballistic isometric elbow flexor contractions (Nuzzo et al. 2016). Secondly, CSP duration has been found to increase during sustained high intensity dynamic contractions resulting in fatigue in the hands (Szubski et al. 2007), upper limb (Hunter et al. 2006; Roustralainen 2014), and lower limbs (Iguchi & Shields 2011; Gruet et al. 2014). Conversely, evidence of a shortened CSP has been presented following exhaustive cycling exercise (O’Leary et al. 2016).
While there is evidence to support changes in CSE following RT, only limited evidence has been presented on acute changes in intra-cortical modulation with fatiguing tasks (Benwell et al. 2006; McNeil et al. 2009; Butler et al. 2003; Hunter et al. 2016). Benwell et al. (2006) reported decreases in SICI following repeated MVCs of the first dorsal interosseous (FDI) muscle and may represent a functional resetting of inhibition or increase recruitment of the motor neuron pool as fatigue develops. The same decreases in LICI were also observed in a similar subsequent study (Benwell et al. 2007). However an increase in LICI was observed by McNeil et al. (2009) following a 2 min MVC of the elbow flexors and recently by Hunter et al. (2016) who showed decreased excitability of ICF networks during a sustained submaximal contraction of the biceps brachii and subsequent increased SICI at 2 mins post activity. The findings suggest lower excitability and changes in intrinsic properties of the motorneurons (Butler et al. 2003).

Investigations into VA following acute exercise have produced conflicting results. VA can provide an assessment of supraspinal efficiency and central fatigue (Gandevia et al. 2013). Although VA is relatively stable in healthy individuals in a non-fatigued state (Hunter et al. 2006; Behm et al. 2002; Shima et al. 2002; Norregaard et al. 1994; Roos et al. 1999), changes in VA following exercise can provide information on acute supra-spinal fatigue and longer lasting muscle damage (Taylor & Gandevia 2011; Khan et al. 2016; Kennedy et al. 2015; Kennedy et al. 2014; Molenaar et al. 2013). A fatigue related increase in the super imposed twitch force (SIT) may result from increased motor unit activation or firing frequency (Cheng et al. 2013). However, investigations into VA following acute exercise bouts have produced conflicting results. Previously, reductions in VA have been established with exhaustive whole
body (Goodall et al. 2012; Temesi et al. 2014), endurance (Goodall et al. 2012; Thomas et al. 2015) and resistance type exercise (Gandevia et al. 1996). Specifically, following resistance activity, reduced VA has been shown with fatiguing sustained submaximal, maximal and isometric contractions in the upper and lower limbs using peripheral (Gandevia et al. 1996; Taylor & Gandevia 2008; Gandevia et al. 1996) and cortical stimulation techniques (Urbach & Awiszus 2000; Gruet et al. 2014; Nuzzo et al. 2016). Gandevia et al. (1996) reported that VA can be impaired by as much as 9.8% percent following a 2 min sustained maximal contraction of the elbow flexors and both twitch amplitude and the muscle compound wave (MMAX) impaired after a 1 min isometric contraction (Gandevia et al. 2013). Interestingly, Gandevia (1996) reported a reduction in VA of 20 percent despite a 70 percent decrease in force (Gandevia 1996). Another study by Sogaard et al. (2006) used TMS and brachial plexus electrical stimulation to assess VA during a sustained submaximal contraction. The authors concluded that approximately 40 percent of the decline in force was associated with an impairment in drive from the M1. Reductions in VA of the leg extensors following resistive exercise (Gruet et al. 2014) and fatiguing endurance exercise (Jubeau et al. 2014; O’Leary et al. 2015) of between 13.4% and 5-14% respectively have also been shown. Contrary to other reports, no change in the quadriceps peripheral VA has been shown following dynamic leg extension exercise despite reductions in muscular contractility (Bigland 1986), and an even an increase in the elbow flexor cortical twitch response reported following acute concentric or isometric strength training (Nuzzo et al. 2016). However, differences in VA between isometric and dynamic exercises (Perrey 2009; Millet & Lepers 2004; Place et al. 2009; Burnley et al. 2012) and the influence of group III and IV muscle afferents on different motor neuron pools (Martin et al. 2006) and impaired action potential
propagation (Place et al. 2008; Clausen & Nielsen 2007) may have contributed to these disparate findings. Therefore a complex relationship may exist between supraspinal fatigue and cortical excitability (Gruet et al. 2013). To further complicate the issue, previous research has either purposefully induced a fatigued neuromuscular state or used ‘resistive exercise’ protocols dissimilar to ‘real-world’ resistance training practice. Although the findings provide useful mechanistic information in the study of VA, the translation into strength and conditioning practice may not be feasible.

However, differences in VA between isometric and dynamic exercises appear to exist (Perrey 2009) and the influence of group III and IV muscle afferents on different motor neuron pools (Martin et al. 2006). TMS to force ratio increased in the last quarter of the task and immediately post exercise. The authors concluded that high intensity quadriceps exercise induced late supraspinal fatigue. In further support of the findings, Babault et al. (2006) showed impairment of the twitch force in the lower limbs. Although strong support for changes in VA, several authors have suggested that the fatigue response is attributed to both central and peripheral mechanisms (Babault et al. 2006; Tran et al. 2006). In support of this notion, Bigland-Ritchie (1986) suggested that the central motor system was capable of fully activating the motor neuron pool during fatigue of the quadriceps muscle group and the loss of force results from failure of the muscle contractile apparatus. Therefore a complex relationship may exist between the notion of central fatigue and cortical excitability (Gruet et al. 2013). However, the varied nature of fatiguing tasks and disparity between peripheral and cortical stimulation protocols used in the research makes comparison difficult. To further complicate the issue, the exercise employed by the current body of research has either purposefully induced a fatigued neuromuscular
state or used ‘resistive exercise’ protocols dissimilar to ‘real-world’ resistance training practice. Although the findings provide useful mechanistic information in the study of VA activation the translation of these findings into strength and conditioning practice may not be feasible. Hence it is unclear whether impaired VA contributes to neuromuscular fatigue following applied resistance training and whether these changes are a global response to ‘resistive exercise’ or are modulated according to resistance training modality.

Similar to other neural studies, no consensus has been reached on peripheral nerve excitability with fatigue. Changes in $M_{\text{MAX}}$ following exercise reflect excitation of the entire motor pool (Iglesias-Soler et al. 2016). Decreased $M_{\text{MAX}}$ amplitude following exercise in the upper limb has been associated with fatigue (Sacco et al. 1997; Fuglevand et al. 1993). It has been suggested that the changes observed in peripheral nerve excitability may directly result from changes in Na+/K+ ion gated channels at the sarcolemma (Sacco et al. 2000; Pensini et al. 2002). Despite these reports, several authors have reported no change (Thomas et al. 2015; Benwell et al. 2006) and in some cases a potentiation effect of $M_{\text{MAX}}$ with shorter duration exercise (Rodriguez-Falces et al. 2015; Behm & St Pierre 1997), during this period

Whilst current literature provides insight into the initial cortical, corticospinal, peripheral and neuromuscular responses to fatiguing exercise, the relatively non-typical and non-standard fatiguing strategies used in interventions, may not accurately reflect responses to applied RT. Furthermore, the differences observed in CSE observed between single-joint and whole-body exercise may reflect the specificity in
the task on neuro-modulatory responses (Gruet et al. 2013; Jubeau et al. 2014). Secondly, the variability of testing methodology, regarding exercise and muscle selection and neural quantification techniques makes comparison difficult. Although neuromuscular fatigue and decreased performance is a known product of fatigue, the neurophysiological mechanisms remain poorly understood. The existence of different neural activation patterns, firing frequencies and strength of corticospinal projections between upper and lower limbs warrants further methodological investigation and may alter the proposed time course of neurophysiological fatigue from RT.

2.6.1.2. Recovery

Exercise recovery and its importance in exercise training has been the centre of much debate. Understanding recovery is pivotal to performance, particularly in applied settings. However, the knowledge of the behaviour of neurophysiological mechanisms pertaining recovery are also poorly understood. It has been proposed that the recovery period may differ depending on the level of neural and mechanical stress placed on the body’s physiological systems (Naclerio et al. 2013) and although feasible, it has seldom been tested with evidence disparate to performance outcome or strength measures. The characteristics of the training session may significantly alter the recovery process (Platonov 2001). An increase in training volume is thought to increase recovery time (Naclerio et al. 2013; Platonov 2001) with maximal efforts or competitions thought to require up to 96 hrs (McLean et al. 2010; Naclerio et al. 2013). Recovery from speed, maximal strength and HYT is thought to require longer than other forms of training (Platonov 2001). The recommendations have been
theoretically modelled for corresponding training load and intensity (see figure 2.14.) by Naclerio et al. (2013). A properly designed training program should facilitate the recovery process and adaptation (Graham 2002). The super-compensation model (Bompa & Haff 2009) suggests an impairment in performance lasting 24-48 hrs. Studies investigating neuromuscular recovery from RT have shown a recovery period of between 24 to 48 hrs (Ide et al. 2011; Howatson et al. 2016), whilst Michaut et al (2003) demonstrated that recovery may occur within 24 hrs following 10 sets of 10 maximal knee extensions. However the use of non-standardised exercise protocols and outcome measures once again has made it difficult to standardise this recovery period across typical strength and hypertrophic training paradigms.

Despite the large body of evidence surrounding neuromuscular force following RT, the neurophysiological behaviour has usually been investigated with repetitive or fatiguing skill related motor tasks (Zanette et al. 1995; Teo et al. 2012a). Zannette et al. (1995) used finger abduction/adduction at maximal frequency for total of 1 min and measured neural recovery, via TMS, every 5th minute up to 30 mins post training. MEP amplitude was suppressed immediately post training with a gradual return to base levels by 30 mins. Although a valuable insight into possible corticospinal behaviour, it may provide a different representation to applied RT. In particular, strength training is thought to be highly demanding on neural systems (Adamson et al. 2008) and thus may alter the neurophysiological behaviour differently than local muscular endurance activities, particularly in a small intrinsic hand muscle is likely to yield different results to that of a high intensity strength protocol in a gross motor movement, due to different motor unit recruitment and corticospinal projections to the hand (Brouwer and Ashby 1990). To investigate CSE, Gruet et al. (2014), used a high
intensity knee extension protocol tracking responses up to 6 mins post exercise. The authors found that changes in CSP and VA recovered within 2 mins which although provides some insight into the nature of acute post exercise responses does not provide further insight into the super-compensation cycle. It is suggested that traditional RT protocols be employed in neurophysiological investigations of recovery to thoroughly understand its behaviour in response to exercise. This will in turn inform exercise science practice on the principles of recovery fundamental for program design and performance.

2.6.1.3. Adaptation

The third stage of the super-compensation cycle encompasses the primary training aim of facilitating an adaptation that improves performance. The upregulation in performance above pre training levels is thought to occur between 36-72 hrs (Bompa & Haff 2009). Although research has quantified the performance changes over time (Serra et al. 2015; Raastad et al. 2012), limited evidence is available on the acute super-compensation response. Recent research has found support for improved performance within an acute time frame (Cook et al 2014, Ekstrand et al. 2013). Cook et al. (2014) found that an early morning strength session results in improved in performance in a later session that day. This effect has similarly been found by Ekstrand et al. (2013) on explosive power. However, time of day training (Teo et al. 2011) plus the addition of a neuromuscular priming effect (Cook et al. 2014) may more accurately depict the performance improvements observed rather than the occurrence of super-compensation itself. Therefore, further neurophysiological investigations are required to tease out these findings.
Previous methodological approaches have generally investigated repeated training stimuli to detect neural adaptations (Latella et al. 2012; Kidgell et al. 2010; Hendy & Kidgell 2013; Carroll et al. 2011; Semmler & Enoka 2000). Changes in corticospinal excitability in the upper limbs (Kidgell et al. 2010), corticospinal inhibition in the lower limbs (Latella et al. 2012) and skill related intra-cortical changes (Hendy & Kidgell 2013) have all been demonstrated with training interventions, yet has not been well established in the proposed adaptation phase from an acute exercise session. Jessop et al. (2013) showed no change in spinal inhibition as measured via H-reflex activity of the ankle flexors after a single training session of 250 isotonic body weight ankle flexion or extension movements or 100 isometric ankle extensions. Despite these findings it is possible that acute responses to more typical HST or HYT may induce adaptive changes within this time frame.

Further, consideration needs to be held that neural control between upper and lower limbs, gross and fine motor patterns and task complexity all require different neuro-modulation (O’Leary et al. 2016). Therefore, a one-model fits all approach is unlikely to give an accurate representation of neurophysiological super-compensation. There are numerous physiological factors that have the ability to influence performance adaptation. Changes in hormonal secretion (Teo et al. 2011a; Teo et al. 2011b), protein synthesis (Schoenfield 2013) and structural properties can all influence performance and facilitate adaptations. However, considering the established importance of neural adaptation with RT and the lack of evidence for acute exercise responses investigation into this area is necessary to understand the fundamental properties of adaptation.
2.6.1.4. Involution

Involution can occur via two mechanisms. Firstly de-adaptations begin to occur when training ceases or is intermitted, or when the spatiality between stimuli is too long; ≥ 120 hrs (Bompa & Haff 2009). Secondly, repeated and excessive stimuli not allowing for adequate recovery can lead to staleness, over training or prolonged periods of overreaching causing maladaptation (Halson & Jeukendrup 2004; Meeusen et al. 2013) and a chronic decrease in performance ability (Bompa & Haff 2009). The effect known as ‘burnout’ dates back to the GAS principle as proposed by Seyle (1950) and can be an accumulation of repetitive trauma to the musculoskeletal system resulting from excessive loading and volume (Smith 2000; Smith 2004). Although it is known that declines in performance will occur during a period of no training or unloading, the underlying mechanisms remain unclear following periods of non-exercise or limb unloading (Clark et al. 2006a; Clark et al. 2006b; Narici et al. 1989; deBoer et al. 2007). An early study by Narici et al. (1989) showed that the time course of CSA and quadriceps torque during de-adaptation was similar to that of training adaptations after 60 days of isokinetic leg extension training. Shorter duration physiological studies have shown that deterioration of tendon mechanical properties can occur within 2 wks and decreased maximum torque caused by unspecific tissue factors in the lower limbs (Berg & Tesch 1996). Further, physiological mechanisms are though to occur through quantitative changes (atrophy) and qualitative changes (protein expression) following 3 wks muscular disuse in the lower limbs (Brocca et al. 2015). It is suggested that the length of the training period causes adaptive effects and therefore influences involution time (Stone et al. 2007; Zatsiorsky & Kraemer 2006).
The neurological theory has been supported by reductions in EMG in the knee extensors observed after 4-6 wks of unloading or bed rest (Deschenes et al. 2002; Berg et al. 1997). However, changes in EMG amplitude only give a vague representation of neural mechanisms. Further neurological evidence has arisen from Clark et al. (2006a) and Clark et al. (2006b) who showed that changes in contractile properties involved in the excitation-contraction coupling process and reductions in central activation explained up to 48% of the strength loss observed after 4 wks of lower limb suspension. Cook et al. (2014) reported a 6% decrease in central activation and 12% reduction in evoked force after 30 days of lower limb suspension on the knee extensors. Despite these findings, Seynnes et al. (2010) concluded that changes in muscle strength after 24 days of unloading of the plantar flexor muscles was not attributed to changes in voluntary activation or efferent motor output.

In applied exercise settings, recommendations suggest that 2 sessions per wk are generally required to maintain performance (Ratamess et al. 2009), whilst as infrequent as 1 session per wk can maintain if not enhance performance in untrained individuals (Ohmori et al. 2010; Serra et al. 2015; McLester et al. 2000). Further it has been shown that protective benefits of exercise on subsequent session may last several wks to several months (McHugh et al. 1999; McHugh et al. 2003; Nosaka et al. 2005).

Ultimately there lies a trade-off between optimal stimuli and performance. Skewness to the side of too little or too much can negatively affect performance in the short and long term. Despite a broad consensus on this area, a comprehensive understanding of the neurophysiological processes associated with involution have once again seldom been investigated.
2.8. Summary

Despite the multitude of research on RT adaptations, the acute neurophysiological responses to during fatigue, recovery and adaptation from a single session remains unclear. Current non-invasive brain and neural stimulation techniques have provided evidence for the adaptive nature of the nervous system to RT and neural responses during fatigue from repetitive, isometric, submaximal and sustained motor tasks. However, understanding the neurophysiological basis of super-compensation theory with applied RT is an important concept in strength and conditioning settings.

Despite the generalised decrease in neuromuscular performance from fatiguing exercise, there have been no attempts to comprehensively investigate the neurophysiological responses to a single bout of applied RT over the super-compensation period. This thesis addressed the gaps in the literature by examining the neurophysiological stages of super-compensation in relation to fatigue, recovery and adaptation from applied RT (HST or HYT) paradigms in both the upper and lower limb. The findings from this thesis would help to inform strength and conditioning professionals on the time course and neurophysiological underpinning of super-compensation. In turn this would allow for the optimisation of periodised RT programs aimed at increasing performance.
CHAPTER THREE: STUDY ONE

The time-course of acute changes in corticospinal excitability, intra-cortical inhibition and facilitation following a single-session heavy strength training of the biceps brachii

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3.1. Introduction

It is well-documented that repeated sessions of heavy strength training (HST) induces lasting adaptations at many levels of the neuromuscular system (Aagaard et al. 2002; Carroll et al. 2011; Sale 1988) resulting in overall strength gains (for review, see Zatsiorsky 2008). In particular, adaptations to the central nervous system such as an increase in corticospinal excitability and release of short-interval intra-cortical inhibition (SICI) following 2- to 8-wk strength training programs have been commonly observed (Deschenes et al. 1994; Hendy & Kidgell 2013; Kidgell et al. 2010; Latella et al. 2012; Weier et al. 2012). While there is strong evidence to suggest that significant neural adaptations occur following multiple resistance training sessions (Kidgell et al. 2010; Latella et al. 2012), and acute changes in corticospinal excitability with sustained submaximal isometric exercise (Nuzzo et al. 2016), few studies have systematically investigated the acute central and peripheral neural responses associated with a single HST session.

Previously, acute corticospinal responses following a single-session of exercise is thought to reflect central fatigue or acute neuroplastic responses to exercise (Smith et al. 2007; Teo et al. 2012b). These studies have commonly showed a reduction in corticospinal excitability, as measured by a decrease in motor-evoked potential (MEP) amplitude, and an increase in SICI following maximal and submaximal exercise. Further, peripheral changes such as a reduction in motorneurone excitability and maximal strength production have also been reported (Todd et al. 2003). While these studies provide some insights into the initial corticospinal and
peripheral responses to exercise, they only provide a short “window” of observation to the neural responses, most only up to 60 mins post exercise, which limits our understanding of the time-course and recovery of neuromuscular system following HST.

To better understand the time-course and body’s physiological responses to exercise, Bompa and Haff (2009) previously proposed the super-compensation model that consists of four distinct phases; 1) fatigue (0-2 hrs); 2) compensation back to baseline (24-48 hrs); 3) super-compensation beyond baseline (48-72 hrs); and 4) involution (> 72 hrs). They suggested that while the recovery period (i.e. fatigue and compensation phase) may differ depending on the type of exercise and intensity, more neurally-demanding exercises, one such as HST, may require up to 24 to 48 hrs to recover back to baseline and for super-compensation to occur. However, to the best of our knowledge, no studies to date have investigated the time-course of corticospinal responses following HST and compared it to the current super-compensation model.

Therefore, the purpose of this study was to map the acute time-course of corticospinal excitability, intra-cortical inhibition and facilitation, peripheral nerve excitability of the biceps brachii (BB) and maximal force production of the elbow flexors up to 72 hrs following HST. Specifically, we aim to determine if the changes in corticospinal and peripheral responses would coincide with the four stages of the super-compensation model proposed by Bompa and Haff (2009). Based upon evidence that strength improvements may still be observed even if HST was
performed with less than 48 hrs rest in between HST sessions (Raastaad et al. 2012; Cook et al. 2014), we hypothesised that the fatigue, compensation and super-compensation phases of the cycle would be shorter than current suggestions of a 24-48hr recovery period back to basal levels.
3.2. Methods

3.2.1. Participants

Fourteen healthy (7 M, 7 F) right-handed participants (age 26.2 ± 5.8 y, height 179.2 ± 3.8 cm, body mass 79.1 ± 15.9 kg) participated in the study. Prior to TMS all participants were screened using a TMS safety questionnaire (see appendix a) to exclude participants with potential contraindications, such as implants in the skull, previous history or head trauma, concussion or seizures, use of prescribed medications or the presence of any neurological disorders prior to testing (Rossi et al. 2009). To rule out a further confounding variable of age-related response to TMS, criteria of 18-35 years of age had to be met. All participants were tested at the same time-of-day and were asked to refrain from consuming caffeine 24hrs prior to and during the study.

All participants were recreationally resistance-trained (at least 6 months experience) with no reported incidence of neuromuscular injury to the upper limb and reported training at least twice per wk (average 3 hrs weekly total), (see appendix b & c). A recreationally trained population was chosen to rule out possible lasting effects of excessive delayed onset muscle soreness; novice populations, or a ceiling effect; experienced populations and therefore deemed to provide a more accurate representation of a typical super-compensation paradigm. Informed written consent was obtained for each participant prior to the start of testing session. Test of limb dominance was conducted using the Edinburgh handedness test
(Oldfield 1971), (see appendix d) and the dominant limb was used for all testing conditions. This study was carried out in accordance with the recommendations of Deakin University Human Research Ethics Committee with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Deakin University Human Research Ethics Committee (Project ID: 2013-198), (see appendix f).

3.2.2. Experimental protocol

All participants completed the study, performing HST and control (CON, no training) sessions in a randomised, counter-balanced order. Participants completed a familiarisation session to introduce the single-arm dumbbell curl exercise of the elbow flexors and transcranial magnetic stimulation (TMS) procedures to reduce any potential effect of learning. HST was performed using a standard preacher curl bench (Life Fitness, Australia) and weight adjustable dumbbell (Australian Barbell Company, Australia). TMS was conducted with the participant seated in a standard desk chair. Each participant’s 1 RM was also determined during the familiarisation session. A one-week washout period was implemented after familiarisation and between conditions (HST vs. CON). The contraction tempo for the BB contractions was set at 3 s eccentric phase, 0 s pause, 3 s concentric phase and has been previously used in other strength training studies investigating neurophysiological outcomes (Hendy & Kidgell 2013; Latella et al. 2012; Weier et al. 2012).
Participants were asked to refrain from exercise 72 hrs prior to and during the course of each condition.

Prior to the training session, all participants performed a 5min warm up on a cycle ergometer at 60% estimated maximum heart rate, and two warm up sets of 12 and 10 repetitions with increasing weight. The training load for the HST was set at the participants’ estimated 3 RM, calculated as a percentage (90-95%) of the 1RM obtained in the familiarisation session (Bompa 1999). Working sets consisted of 5 sets of 3 RM with 180s recovery between each set. The training load was increased if the researcher (a certified strength and conditioning practitioner) deemed that extra repetitions could be performed, and likewise, lowered if failure to complete the repetitions with proper form was observed. For CON, all participants performed the pre training measures, then sat quietly for 20 mins, corresponding to the exercise duration in the strength condition, then performed post measures at the same time points- baseline, immediately post, 10, 20, and 30 mins, and again at 1, 2, 6, 24, 48 and 72 hrs (see figure 3.1.).
Figure 3.1. Schematic overview of chapter three protocol. Arrows indicate testing time points in mins or hrs post-training.
3.2.3 Maximal voluntary isometric contraction of the elbow flexors

MVIC of the elbow flexors was measured using a hand-held force transducer (Powerlab, USA) at each time point following the HST protocol. Participants performed three slow ramp MVIC trials against an immovable resistance with the arm resting on a platform while maintaining 90° of elbow flexion, as measured by a goniometer (Biometrics, USA). Verbal encouragement and visual feedback were given for each maximal effort until no further increase in force was observed and the highest recorded force of the 3 trials was reported.

3.2.4 Transcranial magnetic stimulation measurements

All TMS measurements pre- and post-training were taken with the participant seated with their arm resting at a 90° angle. Surface electromyography (sEMG) was recorded from the BB muscle in the right arm using Ag-AgCL electrodes. Two electrodes were placed 20 mm apart on the midpoint of the belly of BB, with the ground electrode placed over the lateral epicondyle of the right radius. The skin was prepared by removing any hairs and cleaned with 70% isopro alcohol swabs prior to the placement of the electrodes. sEMG signals were amplified (1000x) with bandpass filtering between 20 Hz and 1 kHz and digitised at 10 kHz for 500 ms, recorded and analysed using PowerLab 4/35 (ADinstruments, Australia).

To ensure consistent delivery of TMS stimuli within and between testing sessions, all participants wore a snug-fitted cap (EasyCap, Germany), positioned in relation
to nasion-inion and inter-aural lines and re-fitted each session in line with these measurements to ensure consistency across all time points. The cap was marked with points at 1cm intervals in a longitude-latitude matrix, to allow repeated stimuli to be performed at the same point over the motor cortex each time. The cap was checked regularly (after every 20 stimulus) to ensure that no changes in position occurred.

Single and paired-pulse TMS was applied over the motor representation of the BB on the primary motor cortex (M1), using a 70 mm figure-of-eight coil attached via a BiStim unit (Magstim 200⁴ Magstim, Dyfed, UK). Sites near the estimated centre of the BB area were explored to determine the spot at which the largest and most consistent (at least 5 out of 10 trials) MEP amplitude was evoked. This site was defined as the ‘optimal’ site. The TMS coil was placed tangential to the skull (Latella et al. 2012) with the handle tilted 45° away from the midline while delivering TMS (Di Lazzaro et al. 2004).

All TMS measures were recorded from the BB at rest with background sEMG 100ms before stimulation analysed to ensure no activation. Resting motor threshold was first determined by delivering 10 TMS pulses that elicited a peak-to-peak MEP amplitude of 0.05 to 0.1 mV in 5 out of 10 pulses. Ten single-pulse TMS were then applied at 20% above RMT (120% RMT) with a random inter-stimulus interval of 5-8 s. All single-pulse MEP amplitude was normalised to the maximum compound wave (M\text{MAX}) and reported as a ratio of M\text{MAX} (MEP amplitude/M\text{MAX}). Paired-pulse TMS consisting of a conditioning (CS) and test stimulus (TS) separated by
individual interstimulus intervals (ISI) used to analyse SICI, intra-cortical facilitation (ICF) and long-interval intra-cortical inhibition (LICI). The paired-pulse TMS configuration for SICI, ICF and LICI were as follows; SICI (CS = 90% RMT, TS = 120% RMT, ISI = 3 ms) (Kujirai et al. 1993), ICF (CS = 90% RMT, TS = 120% RMT, ISI = 12 ms) (Kobayashi & Pascual-Leone 2003; Kujirai et al. 1993) and LICI (CS = 120% RMT, TS = 120% RMT, ISI = 100 ms) (Du et al. 2014; McNeil et al. 2011b). Both SICI and ICF were expressed as a percentage of the unconditioned single-pulse MEP amplitude, while LICI was calculated and expressed as a percentage of the test to conditioning MEP amplitude for each individual paired stimuli.

3.2.5. $M_{\text{MAX}}$ measurements

$M_{\text{MAX}}$ was obtained from the right BB muscle by direct supramaximal electrical stimulation (pulse duration 100 ms) of the musculocutaneous nerve under resting conditions using a high-voltage constant current stimulator (Nihon Khoden, Japan). Stimulation was delivered by positioning bipolar electrodes over the right brachial plexus (Hendy et al. 2015) at Erb’s point. An increase in current strength was increased progressively until there was no further increase in sEMG amplitude. To ensure maximal responses, the current was increased an additional 20% and the average $M_{\text{MAX}}$ obtained from 5 stimuli was recorded.
3.2.6. Statistical Analyses

All data analysed using IBM SPSS Statistics (IBM, USA). Data was screened with a Shapiro-Wilk test and found to be normally distributed prior to further analysis. One-way repeated measures (1x11) analysis of variance (ANOVA) was used to compare changes in outcome measures (MVIC, MMAX, MEP, SICI, ICF and LICI) across time points (Pre x Post, Pre x 10 min, Pre x 20 min, Pre x 30 min, Pre x 1 hr, Pre x 2 hrs, Pre x 6 hrs, Pre x 24 hrs, Pre x 48 hrs, Pre x 72 hrs) for HST and CON separately. This approach, of using a one-way ANOVA was used as the main aim of the study was to map the time-course of neurophysiological changes post-HST and not a between-group comparison and is similar to other acute (Kumar et al. 2012) and physiological studies tracking responses over time (DeFreitas et al. 2011). Where statistical significance was detected, post hoc t–tests with a Bonferroni correction were conducted to test for changes to baseline measures (Field 2013). Alpha level was set at $P < 0.05$, and all results are displayed as MEANS ± SD. Where significance was not met, but approached the alpha level ($p \geq 0.05 \leq 0.07$), effect size was calculated using Cohen’s $d$ formula:

$$\text{Cohen's } d = \frac{M_1 - M_2}{SD_{pooled}}$$

Calculations were grouped into moderate $d \geq 0.5 < 0.79$ or large $d \geq 0.80$. Only interactions with a moderate or large effect sizes were reported in the analysis.
3.3. Results

3.3.1. Maximal voluntary isometric contraction

Figure 3.2. shows the change in MVIC for HST and CON across all time points. One-way ANOVA showed a main effect of time for HST ($F_{10,120} = 10.185$, $P < 0.001$). Post-hoc analyses revealed a significantly lower MVIC immediately post training compared to baseline (-19.5%, $p = 0.001$). Moderate and large effects were detected at 10 mins post (-13.7%, $d = 1.30$), 20 mins post (-8.1%, $d = 1.14$) and 30 mins post (-5.7%, $d = 0.71$). A significant increase in force was observed at 24 hrs (8.5%, $p = 0.003$), and large effect sizes were also detected at 6 hrs (5.6%, $d = 0.89$) and 48 hrs (10.0%, $d = 1.34$). Changes in maximal force for the control condition are shown in Figure 3.2. No main effect was detected for CON ($F_{10,130} = 1.746$, $P = 0.154$).
Figure 3.2. Changes in MVIC as a percentage of baseline for (a) HST and (b) CON. MVIC gradually returned to baseline values by 1 hr and super-compensation took place as soon as 6 hrs post-training, which was earlier than the current super-compensation model (Bompa and Haff 2009). No significant main effects were observed across time for CON ($P = 0.154$). (*) indicates a significant main effect over time while (#) indicates a moderate to large effect size.
3.3.2. Peripheral nerve excitability

Figure 3.3. shows the change in $M_{\text{MAX}}$ in HST and CON across all time points. One way ANOVA showed a main effect of time for the strength condition ($F_{2.475, 29.705} = 3.179, P = 0.047$). Post-hoc analysis revealed $M_{\text{MAX}}$ was significantly lower compared to baseline immediately post training (-21.4%, $p = 0.004$). Moderate and large effects were detected at 10 mins post (-20.4, $d = 0.84$), 20 mins post (-15.9, $d = 0.88$) and 30 mins post (-13.3%, $d = 0.66$). $M_{\text{MAX}}$ returned to baseline at 1 hr with moderate and large effects detected at 6hrs (27.9%, $d = 0.94$) and 72hrs (-3.9%, $d = 0.69$). Changes in $M_{\text{MAX}}$ for the control condition are shown in Figure 3.3. No main effect was detected for CON ($F_{10,120} = 0.443, P = 0.623$).
Figure 3.3. Changes in $M_{\text{MAX}}$ as a percentage of baseline values for (a) HST and (b) CON. Similar to MVIC, $M_{\text{MAX}}$ gradually returned to baseline values by 1 hr with a super-compensation effect taking place at 6 hrs post-training. No significant main effects were observed across time for CON ($P = 0.623$). (*) indicates a significant main effect for training over time while (#) indicates a moderate to large effect size.
3.3.3. Single pulse MEP

Figure 3.4. shows the change in normalised MEP amplitude for HST and CON across all time point. One way ANOVA showed a main effect of time for the strength condition ($F_{10,110} = 3.336, P = 0.001$). Post-hoc analysis revealed a large decrease in MEP compared to baseline immediately post training ($-46.1\%, p < 0.001$) returning to pre training levels at 1 hr and a large increase ($181.3\%, d = 1.04$) at 72 hrs. Changes in MEP for the control condition are shown in Figure 3.4. No main effect was detected for the control condition ($F_{10,110} = 0.739, P = 0.661$).
**Figure 3.4.** Changes in normalised single-pulse MEP for (a) HST and (b) CON. Reductions in the training group MEP immediately post-training indicate initial changes in corticospinal drive followed by an increase in corticospinal drive in the later stages of the super-compensation cycle. (#) indicates a moderate to large effect size. No significant main effects were observed across time for CON ($P = 0.627$).
3.3.4. Intra-cortical facilitation and inhibition

Figure 3.5. shows the time-course of ICF, LICI and SICI following HST and CON. One-way ANOVA showed no main effect of time for the ICF ($F_{10,110} = 0.750, P = 0.676$), LICI ($F_{10,110} = 0.838, P = 0.497$) and SICI ($F_{10,110} = 0.716, P = 0.582$) in the HST group. No main effect was detected for the ICF ($F_{10,110} = 1.193, P = 0.328$), LICI ($F_{10,110} = 0.688, P = 0.586$) and SICI ($F_{10,110} = 0.482, P = 0.709$) for CON as well.
Figure 3.5. A comparison of post-training TMS measures for ICF, LICI and SICI in HST and CON. No significant main effects were observed for ICF (a and b), LICI (c and d) and SICI (e and f) were observed in both groups over time.
3.4. Discussion

The aim of the study was to map the time-course of corticospinal adaptations and maximal force output, up to 72 hrs post-training, following a single session of HST of the elbow flexors. The results indicated an immediate reduction in MVIC, followed by a super-compensatory increase at 6 hrs post-training. $M_{\text{MAX}}$ showed a reduction immediately post-training that lasted for 30 mins, before increasing at 6 hrs. A reduction in MEP amplitude was observed immediately post-training up to 20 mins, which was followed by an increase at the 48 and 72 hr mark. Collectively, our results suggest that changes in corticospinal excitability, intra-cortical inhibition and facilitation, peripheral nerve excitability and maximal force production following HST of the BB may follow a shorter time-course of fatigue, recover and super-compensation as previously suggested by Bompa and Haff (2009).

The main finding from this study showed that MVIC returned to baseline levels within 1 hr, with an increase at 6 hrs post-training indicative of a super-compensation effect. This pattern of recovery within 1 hr and super-compensation by 6hrs post-training suggests a significantly shorter time-course of recovery and super-compensation compared to the current proposed model. A possible explanation for this effect may be that training in the morning may improve performance measures later in the day. A study by Cook et al. (2014) found that when a 3 RM back squat protocol was performed in the morning, strength was improved when tested in the afternoon. Similarly, Ekstrand et al. (2013) showed
that resistance exercise in the morning improved explosive power 4-6 hrs later. However afternoon and evening strength training can be positively influenced by the body's natural circadian rhythm and optimal core temperature (Teo et al. 2011a; Teo et al. 2011b) and thus may contribute at least in part to these findings. Previously, the super-compensation model has suggested a significant reduction in force output observed immediately post-training, remaining impaired up until 1hr (Routsalainen et al. 2014), followed by a proposed return to baseline between 24 to 48 hrs (Ide et al. 2011). It is therefore recommended that a 72 hr rest period between HST sessions to prevent overtraining. This concept is in line with work by Howatson et al. (2016) suggesting force is impaired until at least 24 hrs after strength exercise. However, studies prescribing strength training frequencies as high as 5 times per wk have also shown greater increases maximum bench press than those who trained 4 or less times per wk (McKenzie 1981; Serra et al. 2015). Other high frequency protocols (Raastaad et al. 2012) have also supported the idea of increased training frequency. The current inconsistencies on performance recovery, improvement and training frequency is likely due to the differing protocols used in previous literature thus making comparison between studies difficult. The findings of the current study suggests a shortened time course of recovery with strength training in the arm and supports previous research (McKenzie 1981; Serra et al. 2015; Raastaad et al. 2012) applying high frequency training for optimal strength gains.

Similarly, the observed changes in $M_{\text{MAX}}$ post-training do not adhere to the time-course as shown in previous super-compensation models (Bompa & Haff 2009). When analysed over time, there was a significant suppression of $M_{\text{MAX}}$ post-
training lasting up until 30 mins. $M_{\text{MAX}}$ has previously been shown to decline with muscle fatigue in the elbow flexors with maximal contractions (Todd et al. 2003). A likely reason for the suppression of $M_{\text{MAX}}$ may be explained by a reduction in sodium-potassium pump efficiency of the sarcolemma following heavy strength training (Kirkendall 1990; Mileva et al. 2012; Tucker et al. 2005). Other mechanisms have also been implicated, such as fatigue-related changes in neurotransmitter release at the neuromuscular junction that may affect electrical nerve conduction (Deschenes et al. 1994; Kirkendall 1990). Following this, increases in $M_{\text{MAX}}$ showed an excitatory increase above baseline as early as 6 hrs whereby increased peripheral drive may reflect alterations in motor neuron recruitment and firing rate (Aagaard 2003). Similar to force production, the time-course of $M_{\text{MAX}}$ fatigue, recovery and super-compensation was much shorter than proposed by previous literature (Bompa & Haff 2009) and coincides with an increase in force generating capacity. The super-compensation window appears to begin earlier than the proposed time line in this model. The efficacy of peripheral nerve excitability recovery may contribute, at least in part, to the shortened time-course for super compensatory effects after a single strength training session.

In this study, normalised MEP responses from TMS showed an immediate decrease in corticospinal excitability that lasted up to 30 mins post-training. Previous studies have showed mixed evidence on the changes in MEP amplitude following heavy strength training (Hendy & Kidgell 2013; Kidgell et al 2010; Routsalainen et al. 2014; Weier et al. 2012). Ruotsalainen et al. (2014) reported an increase in MEP amplitude at the start of a task, while McNeil et al. (2011a) showed a decrease in MEP amplitude after sustained muscular effort at 25% of MVC over 10 mins. Our
study showed a significant reduction in MEP amplitude immediately post-training, followed by an increase at 72 hrs. Our findings are in agreement with previous studies (McNeil et al. 2011a; Todd et al. 2003) where a reduction in MEP amplitude following sustained submaximal muscular contractions in the elbow flexors was observed (Todd et al. 2003), and has similarly been found in other muscle groups after isometric voluntary contractions (McNeil et al. 2011a).

An interesting finding from our study was the lack of intra-cortical changes after a single session HST. This is dissimilar to studies reporting an increase in corticospinal excitability and a reduction in SICI after 2 and 4 wks of strength training in the upper and lower limb (Hendy & Kidgell 2013; Weier et al. 2012). Our findings suggest that, with no evident change in intra-cortical facilitation or inhibition and a concurrent decrease in peripheral neural excitability the reductions in MEP amplitude appear to be primarily driven by mechanisms downstream of the M1. It is possible that spinal inhibitory mechanisms contribute to this finding (McNeil et al. 2011a). Further, changes in excitability have commonly been found to occur at sub-cortical spinal levels with acute and early strength training (Aagaard 2003; Nuzzo et al. 2016). Therefore the acute responses may reflect perturbations at subcortical levels.

In light of our findings that differ to previous studies, we acknowledge that several limitations in our study that may have contributed to disparate findings. Firstly, one strength session may not be sufficient stimulus to induce long-lasting changes, but rather, changes downstream of the M1 may primarily drive super-compensatory
responses after training. Secondly, maximal force production has been shown to increase with training, without any apparent increases in sEMG (Cannon & Cafarelli et al. 1987; McNeil et al. 2011a) and that maximal voluntary activation increases may not be reflected in sEMG signals (Latella et al. 2012). This would imply that any increase could not be completely attributed to changes in central nervous system. Thirdly, heavy strength training recruits small and large motor units and testing the corticospinal tract at rest with TMS may target different neurons in the motor neuron pool and not be a direct representation of activated motor units (McNeil et al. 2011a). Likewise, the difference between gross movement employing large muscle groups, synergists and stabilisers in comparison to simple or isolated tasks is not known, and it is possible that exercise complexity may influence the output from the central nervous system. Although the primary aim of this study was to investigate acute neurophysiological responses, other factors outside the scope of this study such as mechanical, metabolite and hormonal responses may also contribute to the super-compensation cycle.Fourthly, it is believed that alteration of the LICI inter stimulus interval from 100 ms to 150 ms may influence the activation of pre and post synaptic GABA$_b$ receptors and thus should be considered to clarify the locus of GABA$_b$ mediated inhibition (Vallence et al. 2014). Lastly, we acknowledge that the findings support a shortened super-compensation cycle in only recreationally trained populations and may not translate to other populations such as older adults or even in athletes of different training status. Future studies should compare different population groups; novice, or elite, and within training factors such as the effects of increased volume, which may present a different fatigue and recovery response profile due to physiological factors outside the scope of this study.
3.5. Conclusion

In conclusion, our findings reveal that after a single strength training stimulus, the time-course of fatigue and recovery and possible super-compensation from an acute HST session in the BB appears to be shorter than that proposed in the current super-compensation model for recreationally trained populations. We acknowledge that other factors may also contribute to the super-compensation cycle, however, the observed neurophysiological changes appear to be primarily driven by peripheral neural mechanisms downstream of the M1. Our results from this study may have significant implications for coaches and strength and power athletes who may program their training based on the current super-compensation model. Based on our current findings, it may be that optimal frequency of strength training can be scheduled sooner than 72 hrs to enhance strength and neuromuscular adaptations associated with HST. We believe that investigating the basic of post-training neurophysiological changes and comparing it to the super-compensation model may provide evidence for better exercise prescription in future.
CHAPTER FOUR: STUDY TWO

Effects of resistance training modality on acute intra-cortical, corticospinal and neuromuscular responses
4.1. Introduction

Different modes of resistance training (RT) are applied in athletic conditioning, rehabilitation and general RT practice in order to promote targeted gains in neuromuscular performance (Ratamess et al. 2009). HYT is characterised by higher volumes of moderate intensity loads (67-75% of 1 RM, 6-15 repetitions) commonly employed during the early phase of a training to increase muscle mass (Bompa & Haff 2009; Haff & Triplett 2016). On the other hand, HST is characterised by high intensity loads (≥ 80% of 1 RM, 1-6 repetitions) intended to increase maximal strength (Ratamess et al. 2009), and is often introduced after the hypertrophy phase or where specific strength adaptations are required (Bompa & Haff 2009).

From a neuromuscular standpoint, acute impairments in force production have been investigated extensively following strength, hypertrophy and power training (Walker et al. 2012; Howatson et al. 2016; Brandon et al. 2015; Nicholson et al. 2014), however due to differences in exercise selection and training parameters (i.e. load and volume), the literature has produced conflicting results. Nicholson et al. (2014) showed no difference in peak force following HST or HYT squat training when the load was equal between conditions. Similar reductions in MVIC have also been reported by Howatson et al. (2016) in the knee extensors following strength (4 x 5 RM) or power training (5 x 5 repetitions at 30% of the strength condition), and Brandon et al. (2015) following heavy (85% of 1 RM), moderate (75% of heavy condition), and light (50% of heavy condition) back squats to repetition maximum. Conversely, Walker et al. (2012) showed impairment of the MVIC to be greater
following (5 x 10 RM) compared to (15 x 1 RM) leg presses. The discrepancies in force production following different modes of RT are likely due to varied testing methodologies, rendering the translation of these findings into applied practice difficult. Given the importance of applied HST and HYT in strength and conditioning settings, further investigations between modalities are required.

While the neuromuscular adaptations from repeated HST are well-established (Latella et al. 2012; Hendy et al. 2013; Kidgell & Pearce 2010; Carroll et al. 2011; Selvanayagam et al. 2011), the acute neurophysiological responses have seldom been directly compared with other RT modes such as HYT. In chapter 3, the results indicated a reduction in CSE in the absence of changes in SICI following HST of the BB muscle. However, previous studies have demonstrated disparate findings with some studies indicating an increase is CSE (Nuzzo et al. 2016a; Ruotsalainen et al. 2014) while others showing a reduction in SICI (Leung et al. 2015) following various contraction types (ballistic and slow-ramp isometric, dynamic and metronome-paced) of the elbow flexors. At the peripheral level, changes in peripheral nerve excitability are also known to occur with fatiguing exercises such that both reductions (Behm and St-Pierre 1997; Sacco et al. 1997; Nuzzo et al. 2016c) and increases (Behm and St-Pierre 1997; Nuzzo et al. 2016b) in $M_{\text{MAX}}$ have been shown following resistance exercise. While there has been no direct comparison between applied HST and HYT paradigms, previous studies have suggested that dynamic RT duration may have a differential effect on peripheral nerve excitability (Behm & St Pierre 1997), while others have showed no differences between 2 and 12 sets of isometric training (Nuzzo et al. 2016b). As such, it is unclear whether RT training modality would cause a different effect in
measures of corticospinal excitability, cortical inhibition and peripheral nerve excitability.

In this chapter, the primary aim was to directly compare the acute changes in intracortical, corticospinal and peripheral nerve responses between the modalities of HST and HYT in the leg extensor muscles. Based on the findings from chapter 3, this chapter extends the investigations into the leg extensor muscles to provide a greater overview of central and peripheral responses of different musculature commonly used in applied HST and HYT modalities. Given the different structure and function between the elbow flexors and leg extensors (Behm et al. 2002; Bortoluci et al. 2014; Staron et al. 2000; Krustrup et al. 2004), understanding the acute neurophysiological behaviour holds important implications for applied practice. Given that the lower limbs are important in gross movements requiring large amounts of force production, the optimal implementation of HST and HYT in the lower limbs is critical in many athletic disciplines. It was hypothesised that the behaviour of neurophysiological responses would differ between modalities due to the different demands placed on the central and peripheral nervous system. Furthermore, it was hypothesised that HST would induce a greater decrement in neuromuscular function compared to HYT.
4.2. Methods

4.2.1. Participants

Fourteen (9 M, 5 F) healthy right dominant individuals (26.2 ±3.1 years, 81.3 ± 9.6 kg, 174.2 ±10.5 cm) with no reported incidence of neuromuscular injury to the lower limb completed a randomised, counterbalanced crossover study comparing; HST, HYT and CON conditions. All participants were recreationally trained (6-12 months experience) in resistance training and reported training at least twice per wk, (see appendix b & c). Informed written consent was obtained for each participant prior to the start of testing session. Test of limb dominance was conducted using the Waterloo Footedness Questionnaire (Elias et al. 1998), (see appendix e). Prior to TMS all participants were screened using a TMS safety questionnaire (see appendix a) to exclude potential participants with contraindications to TMS, such as; metallic implants in the skull, aneurysm clips, previous history or head trauma, concussion or seizures. In addition, methodological factors which may influence TMS outcomes were screened for; age, use of prescribed medications or the presence of any neurological disorders prior to testing (Chipchase et al. 2012). All procedures used in this study were approved by the Deakin University Human Research Ethics Committee (Project ID: 2013-198), (see appendix f) and conducted to the standards set by the Declaration of Helsinki.
4.2.2. Experimental protocol

Figure 4.1. shows the setup and timeline for each testing session. Prior to testing, all participants completed a familiarisation session to reduce the potential of any learning effects on the outcome measures of the study. The outcome measures included leg extension (Nautilus Pin Loaded Leg Extension, Canada), voluntary maximal isometric contraction on dynamometer (Cybex Humac Norm, USA), single- and paired-pulse TMS (Bistim 200\textsuperscript{2}, Wales) and peripheral nerve stimulation (Nihon Koden, Japan). Each participant’s 1RM single leg extension strength was also measured and recorded. A one-week washout period was implemented between each of the four visits (familiarisation, HST, HYT and CON). The contraction tempo for the leg extension exercise was set at 3 sec eccentric phase, 0 sec pause, 3 sec concentric phase (Ackerley et al. 2013, Latella et al. 2012; Hendy et al. 2013).

The resistance for the strength session was set at the participant’s calculated 3 RM (94% of 1 RM), and 12 RM (67% of 1 RM) derived from the 1 RM obtained in the familiarisation session using the formula developed by Brzycki (1993). The HST protocol consisted of 5 working sets consisting of 3 RM leg extensions using a range of 90 degrees of flexion to full extension with 180 sec recovery in between (total volume 15 repetitions). The HYT protocol consisted of 3 working sets consisting of 12 RM with 60 sec recovery in between (total volume 36 repetitions). The training load was increased if the researcher (a certified strength and
conditioning practitioner) deemed that extra repetitions could be performed, and likewise, lowered if there was failure to complete the repetitions with proper form. Prior to exercise, all participants performed a 5 min warm up on a cycle ergometer at 60% estimated maximum predicted heart rate, and 2 warm up sets at 12 and 10 repetitions at an increasing weight. During the control session, all participants’ sat quietly for 15 min (average training time of HST and HYT conditions) between pre and post neurophysiological measures. All outcome measures were assessed at specified time points corresponding to the fatigue (post-training - 2 hrs), recovery (6, 24 and 48 hrs) and adaptation (72 hrs) phases as reported by the super-compensation theory (Bompa & Haff 2009). The post-training time point was conducted as soon as the participant finished the last set and was positioned on the dynamometer (approximately 2-3 mins).
Figure 4.1. Schematic overview of chapter four protocol. Depicts HST, HYT and CON protocols and neurophysiological testing measures at proposed stages of the super-compensation cycle over a 72 hr period.
4.2.3. Maximal voluntary isometric contraction of the leg extensors

Maximal voluntary isometric contraction of the knee extensors was measured using a 5 sec isometric contraction (2 sec ramp up, 3 sec maximal effort). The 3 trials were conducted with the knee flexed at 45 degrees off full extension (0 degrees) against an immovable resistance (Cybex Dynamometer, USA) and separated by 30 sec rest (see figure 4.2.). Verbal encouragement and real-time visual force feedback were provided for each effort and the maximal recorded torque (in Newton meters [Nm]) of the 3 trials was reported as MVIC.

4.2.4. Transcranial magnetic stimulation measurements

Testing for each session began at the same time of day with participants asked to refrain from consuming caffeine 48 hrs prior to and during the study. Measurements were taken with the participant seated upright with their leg at a 45 degree angle (maximal voluntary isometric contraction of the leg extensors) for positioning. Surface electromyography (sEMG) was recorded from the RF muscle in the dominant leg using Ag-AgCL electrodes. Two electrodes were placed 20mm apart on the midpoint of the belly of RF, with the ground electrode placed over the patella according to SENIAM guidelines (SENIAM, Netherlands). The skin was prepared by removing any hair and cleaned with 70% isopro alcohol swabs prior to the placement of the electrodes. SEMG signals were amplified (1000x) with bandpass filtering between 20 Hz and 1 kHz and digitised at 10 kHz for 500 ms, recorded and analysed using PowerLab 4/35 (ADinstruments, Australia).
To ensure consistent delivery of TMS stimuli within and between testing sessions, all participants wore a snug-fitted cap (EasyCap, Germany), positioned in relation to nasion-inion and inter-aural lines (see figure 4.2.). The cap was marked with points at 1cm intervals in a longitude-latitude matrix, to allow repeated stimuli to be performed at the same point over the motor cortex each time. The cap was checked regularly (approx. every 20 stimuli delivered) to ensure that no changes in position occurred. Single and paired-pulse TMS were applied over the cortical motor representation of the RF on the M1, using a double cone 110mm coil (maximal output 1.4 tesla), attached via a BiStim unit (Magstim 200\textsuperscript{2} Magstim, Dyfed, UK). Coil placements near the estimated centre of the RF area were explored to determine the ‘optimal site’ at which the largest and most consistent MEPs were evoked during a low-level contraction of 10% of MVIC (Rothwell 1999). The handle of the TMS coil was placed over the vertex of the head and tangential to the skull and positioned to preferentially activate the left motor cortex, contralateral to the right leg (Jubeau et al. 2014). Establishing resting motor threshold (RMT) required the minimisation of background EMG activity and defined as the lowest TMS intensity at which a MEP could be obtained with at least 5 of the 10 stimuli with peak-to-peak amplitude being greater than 50 µV at rest (Rothwell 1999; Westin et al. 2014). Active motor threshold (AMT) required the participant to hold a steady contraction at 10% MVIC and defined as the lowest TMS intensity at which a MEP could be obtained with at least 5 of the 10 stimuli with peak-to-peak amplitude being greater than 200 µV (Rothwell 1999).
Initially five single-pulse TMS were applied at 20% above AMT and were administered with a randomly chosen 5-8s intervals between stimuli. MEP amplitude was calculated using peak-to-peak difference of the response and were normalised to $M_{\text{MAX}}$ ($\text{MEP amplitude}/M_{\text{MAX}} = \text{Normalised MEP}$). Paired-pulse TMS was conducted with the muscle at rest using RMT for the calculation of stimulation intensities following single-pulse stimulation. SICI, ICF and LICI were conducted in respective order. For paired pulse protocols (SICI, ICF and LICI) including inter-stimulus intervals and stimulation intensities as a percentage of motor threshold please refer to section 3.2.4. Paired-pulse TMS consisting of a conditioning (CS) and test stimulus (TS) separated by individual interstimulus intervals (ISI) used to analyse SICI, intra-cortical facilitation (ICF) and long-interval intra-cortical inhibition (LICI). The paired-pulse TMS configuration for SICI, ICF and LICI were as follows; SICI (CS = 90% RMT, TS = 120% RMT, ISI = 3 ms) (Kujirai et al. 1993), ICF (CS = 90% RMT, TS = 120% RMT, ISI = 12 ms) (Kobayashi & Pascual-Leone 2003; Kujirai et al. 1993) and LICI (CS =120% RMT, TS = 120% RMT, ISI = 100 ms) (Du et al. 2014; McNeil et al. 2011b). Both SICI and ICF were expressed as a percentage of the unconditioned single-pulse MEP amplitude, while LICI was calculated and expressed as a percentage of the test to conditioning MEP amplitude for each individual paired stimuli.
Figure 4.2. Experimental set-up of chapter four. Picture of one participant seated on the cybex dynamometer, with knee at 45 degrees. Note TMS cap placement and electrodes over the RF, BF and patella (ground).
4.2.5. Transcranial magnetic stimulation super imposed twitch force

Super imposed twitch (SIT) force responses were conducted using the same TMS preparation as stated in (section 4.2.4. Transcranial magnetic stimulation measurements) following paired-pulse stimulation. The TMS stimulator output was set to produce the largest possible MEP in the RF during knee extension at 50% MVIC (Sidhu et al. 2009; Rupp et al. 2012). A single TMS pulse was delivered during a contraction at 25, 50, 75 or 100% of MVIC (Jubeau et al. 2014) at each time point once a steady force level was achieved. Any additional increments in force were recorded in real time and analysed off-line (HUMAC NORM software 2015, USA). The SIT force response was reported as the difference between the peak voluntary contraction force (taken 0-100ms prior to stimulation [Marshall et al. 2014]) and maximal force achieved as a result of TMS during each contraction level.

Linear regression using the twitch responses (25-100% of MVIC) was then used to calculate the estimated resting twitch (ERT) for individual participants at each time point for HST, HYT and CON. The value of the y-axis intercept at rest (0% MVIC) was defined as the ERT. VA was then calculated using the method developed by (Todd et al. 2003) and similarly used by (Todd et al. 2004, Sidhu et al. 2009) by applying the equation; [1 – (superimposed twitch/ERT)] x 100.

4.2.6. Maximal M-wave measurements

Maximal M-waves were obtained from the dominant RF muscle by direct supramaximal electrical stimulation (pulse duration 100ms) of the femoral nerve
under resting conditions using a high-voltage constant current stimulator (Nihon Khoden, Japan). Stimulation was delivered prior to TMS stimulation at each time point by positioning bipolar electrodes over the right femoral nerve in the femoral triangle (3-5cm below the inguinal ligament) (Doguet & Jubeau 2014). Stimulation was delivered by positioning bipolar electrodes over the right inguinal fold. An increase in current strength was applied until there was no further increase in sEMG amplitude ($M_{MAX}$). To ensure maximal responses, the current was increased an additional 20% and the highest $M_{MAX}$ obtained from 5 stimuli was recorded.

4.2.7. Statistical analysis

All data was analysed using IBM SPSS Statistics (IBM, USA). Data was screened with a Shapiro-Wilk test and found to be normally distributed prior to further analysis. A (3 x 7) repeated measures analysis of variance (ANOVA) with factors CONDITION (HST, HYT and CON) and TIME (Pre, post, 2 hrs, 6 hrs, 24 hrs, 48 hr and 72 hrs) was used to compare changes in MVIC, $M_{MAX}$, MEP amplitude, CSP, SICI, ICF, LICI and SIT at 25, 50, 75 and 100% of MVIC between conditions and across time. Alpha level was set at $P < 0.05$, and all results are displayed as means ± SE. Where statistical significance was detected between conditions, post hoc $t$-tests with a Bonferroni correction were conducted to test for differences between individual groups (Field 2013). For all tests, the Greenhouse-Geisser correction was applied if the assumption of sphericity was violated.

Within participant reliability data was calculated for MVIC, $M_{MAX}$, MEP, CSP, ICF, SICI and LICI using intra-class correlation coefficients (ICCs) and Pearson’s
product-moment coefficient (r) at baseline for each condition and across time for the CON condition. ICCs were classified as poor (< 0.40), fair (0.40-0.59), good (0.60-0.74) and excellent (≥ 0.75) as used in previous TMS research (Temesi et al. 2017). In addition the within participant coefficient of variation (CV) was expressed as a percentage derived from the formula (poolSD/poolMean) x 100 where the SD and mean is a pooled value of the sample. Absolute reliability was calculated to establish the variability of repeated measurements (Atkinson & Nevill 1998) using the standard error of the mean (SEM) = SD √(1-ICC) and the minimal detectable change at the 95% confidence interval (MDC_{95}) = SEM x √(2) x 1.96 was also calculated as similarly displayed in other physical research studies (Overend et al. 2010). All reliability data has been reported in (Table 4.1 and 4.2).
4.3. Results

4.3.1. Maximal voluntary isometric contraction

Figure 4.3.1. shows the percentage change in MVIC for HST, HYT and CON conditions from baseline to 72 hrs post-training. A 3x7 repeated measures ANOVA showed a significant group x time interaction (F_{12,132} = 3.188, P < 0.001). Post-hoc analyses revealed MVIC was significantly reduced immediately post-training for HST (p = 0.004) and HYT (p < 0.001), and at 2 hrs for HST (p = 0.024), when compared to CON. No differences were observed between HST and HYT immediately post-training (p = 0.086) or at 2 hrs (p = 0.242).
Figure 4.3.1. MVIC as a percentage of baseline values for HST, HYT and CON. (*) indicates a significant interaction between HST and CON while (#) indicates a significant interaction between HYT and CON. No differences were observed between HST and HYT immediately post-training (p = 0.086) or 2 hrs (p = 0.242).
4.3.2. Peripheral nerve excitability

Figure 4.3.2. shows the percentage change in $M_{\text{MAX}}$ for HST, HYT and CON conditions from baseline to 72 hrs post-training. A 3x7 repeated measures ANOVA showed a significant group x time interaction ($F_{12,132} = 2.684$, $P = 0.003$). Post-hoc analyses revealed $M_{\text{MAX}}$ was significantly reduced immediately post-training for HST ($p = 0.001$) and HYT ($p = 0.004$), and 2 hrs for HYT ($p = 0.010$), when compared to CON. No differences were observed between HST and HYT immediately post-training ($p = 0.831$).
Figure 4.3.2. $M_{\text{MAX}}$ as a percentage of baseline values for HST, HYT and CON. (*) indicates a significant interaction between HST and CON while (#) indicates a significant interaction between HYT and CON. No differences were observed between HST and HYT immediately post-training ($p = 0.831$).
Figure 4.3.2.1. provides a visual representation of the raw $M_{\text{MAX}}$ for HST, HYT and CON conditions at pre, immediately post training and 2 hrs.
Figure 4.3.2.1. Raw EMG traces displaying $M_{\text{MAX}}$ of the RF muscle for a) HST, b) HYT, and c) CONT from a single participant at pre, immediately post training and 2 hrs.
4.3.3. Single pulse MEP

Figure 4.3.3. shows the percentage change in MEP for HST, HYT and CON conditions from baseline to 72 hrs post-training. A 3x7 repeated measures ANOVA showed a significant group x time interaction ($F_{12,132} = 3.213$, $P < 0.001$). Post-hoc analyses revealed MEP was significantly increased immediately post-training for HST ($p = 0.044$), and HYT ($p = 0.005$) when compared to control. No differences were observed immediately post-training between HST and HYT ($p = 0.468$).
Figure 4.3.3. MEP as a percentage of baseline values for HST, HYT and CON. (*) indicates a significant interaction between HST and CON while (#) indicates a significant interaction between HYT and CON. No differences were observed immediately post training between HST and HYT (p = 0.468).
4.3.4. Corticospinal silent period

Figure 4.3.4. shows the percentage change from baseline in CSP for HST, HYT and CON conditions from baseline to 72 hrs post-training. A 3x7 repeated measures ANOVA showed a significant group x time interaction ($F_{12,132} = 2.755, P = 0.002$). Post-hoc analyses revealed CSP was significantly shorter immediately post-training for HST ($p < 0.001$) and HYT ($p < 0.001$), 2 hrs for HST ($p = 0.023$) and HYT ($p = 0.041$), 6 hrs for HYT ($p = 0.013$) and at 24 hrs for HYT ($p = 0.017$) when compared to CON. No differences were observed between HST and HYT immediately post-training ($p = 0.598$) and at all other time points ($p > 0.05$).
Figure 4.3.4. CSP as a percentage of baseline values for HST, HYT and CON. (*) indicates a significant interaction between HST and CON while (#) indicates a significant interaction between HYT and CON. No differences were observed immediately post training between HST and HYT (p = 0.598) and across all time points (p > 0.05).
Table 4.1. Raw data for MVIC, $M_{\text{MAX}}$, MEP/$M_{\text{MAX}}$ and CSP presented as Mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>2 hrs</th>
<th>6</th>
<th>24</th>
<th>48</th>
<th>72</th>
<th>ICC</th>
<th>SEM, SDC95</th>
<th>CV %</th>
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<tr>
<td><strong>MVIC (Nm)</strong></td>
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<tr>
<td>CON</td>
<td>223 ± 24.2</td>
<td>224 ± 13.2</td>
<td>217 ± 22.8</td>
<td>218 ± 29.5</td>
<td>220 ± 19.4</td>
<td>220 ± 16.3</td>
<td>226 ± 21.7</td>
<td>0.91, $r$ = 0.001</td>
<td>5.31, 14.73</td>
<td>7.94</td>
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<tr>
<td>HST</td>
<td>225 ± 63.7</td>
<td>204 ± 60.4*</td>
<td>198 ± 62.0*</td>
<td>217 ± 53.3</td>
<td>223 ± 67.2</td>
<td>232 ± 62.6</td>
<td>222 ± 60.5</td>
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<tr>
<td>HYT</td>
<td>242 ± 79.7</td>
<td>193 ± 70.7*</td>
<td>220 ± 67.5</td>
<td>222 ± 67.8</td>
<td>231 ± 71.6</td>
<td>214 ± 93.9</td>
<td>236 ± 70.2</td>
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<tr>
<td><strong>ICC</strong></td>
<td>0.65, $r$ = 0.011</td>
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<td><strong>SEM, SDC95</strong></td>
<td>30.8, 85.37</td>
<td>22.32</td>
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<td><strong>M_{MAX} (mV)</strong></td>
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<td>CON</td>
<td>4.8 ± 1.8</td>
<td>4.7 ± 1.7</td>
<td>4.8 ± 1.7</td>
<td>4.8 ± 1.9</td>
<td>4.9 ± 2.0</td>
<td>4.7 ± 1.9</td>
<td>4.6 ± 1.5</td>
<td>0.99, $r$ = 0.001</td>
<td>0.13, 0.35</td>
<td>37.65</td>
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<td>HST</td>
<td>4.3 ± 1.8</td>
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<td>4.8 ± 1.8</td>
<td>4.4 ± 0.9</td>
<td>4.3 ± 1.5</td>
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<tr>
<td>HYT</td>
<td>4.6 ± 2.4</td>
<td>3.2 ± 2.0*</td>
<td>3.9 ± 1.7*</td>
<td>4.1 ± 1.7</td>
<td>4.6 ± 1.5</td>
<td>4.0 ± 1.7</td>
<td>4.1 ± 2.0</td>
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<tr>
<td><strong>ICC</strong></td>
<td>0.91, $r$ = 0.001</td>
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<tr>
<td><strong>SEM, SDC95</strong></td>
<td>0.58, 1.61</td>
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<td><strong>CV %</strong></td>
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<td><strong>MEP/$M_{MAX}$</strong></td>
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<tr>
<td>CON</td>
<td>0.19 ± 0.17</td>
<td>0.18 ± 0.14</td>
<td>0.19 ± 0.14</td>
<td>0.14 ± 0.06</td>
<td>0.19 ± 0.16</td>
<td>0.21 ± 0.19</td>
<td>0.25 ± 0.19</td>
<td>0.64, $r$ = 0.001</td>
<td>0.023, 0.065</td>
<td>61.85</td>
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<tr>
<td>HST</td>
<td>0.21 ± 0.12</td>
<td>0.32 ± 0.14</td>
<td>0.27 ± 0.17</td>
<td>0.22 ± 0.12</td>
<td>0.22 ± 0.12</td>
<td>0.27 ± 0.16</td>
<td>0.25 ± 0.17</td>
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<tr>
<td>HYT</td>
<td>0.26 ± 0.17</td>
<td>0.59 ± 0.27*</td>
<td>0.42 ± 0.30*</td>
<td>0.31 ± 0.28</td>
<td>0.31 ± 0.26</td>
<td>0.31 ± 0.29</td>
<td>0.26 ± 0.21</td>
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<tr>
<td><strong>ICC</strong></td>
<td>0.65, $r$ = 0.001</td>
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<tr>
<td><strong>SEM, SDC95</strong></td>
<td>0.07, 0.20</td>
<td>85.94</td>
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<td><strong>CV %</strong></td>
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<td><strong>CSP (ms)</strong></td>
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<tr>
<td>CON</td>
<td>121.5 ± 19.2</td>
<td>122.5 ± 19.5</td>
<td>121.0 ± 18.5</td>
<td>125.0 ± 21.4</td>
<td>126.4 ± 20.7</td>
<td>124.1 ± 20.8</td>
<td>124.4 ± 20.7</td>
<td>0.98, $r$ = 0.001</td>
<td>2.53, 7.02</td>
<td>14.86</td>
</tr>
<tr>
<td>HST</td>
<td>138.6 ± 18.2</td>
<td>121.2 ± 15.6*</td>
<td>129.8 ± 19.3*</td>
<td>128.9 ± 18.8</td>
<td>131.6 ± 24.6</td>
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<td>132.3 ± 19.8</td>
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<tr>
<td>HYT</td>
<td>126.0 ± 17.8</td>
<td>105.3 ± 13.4*</td>
<td>110.7 ± 15.2*</td>
<td>116.3 ± 15.7*</td>
<td>121.1 ± 17.4*</td>
<td>121.3 ± 16.9</td>
<td>122.8 ± 19.8</td>
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<tr>
<td><strong>ICC</strong></td>
<td>0.81, $r$ = 0.001</td>
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<tr>
<td><strong>SEM, SDC95</strong></td>
<td>8.23, 22.89</td>
<td>14.97</td>
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</table>

* indicates a significant difference from baseline for each condition. ICC and Pearson’s $r$ show the reliability of each measure between conditions at baseline (pre column) and of the CON condition over the 72 hr period (far right). SEM, SDC95 and CV % show the absolute variability of repeated measurements.
Figure 4.3.4.1. MEP and CSP of the RF muscle for a) HST, b) HYT, and c) CON from a single participant at pre, post-training and 2 hrs.
4.3.5. Intra-cortical facilitation and inhibition

Figure 4.3.5. shows the percentage change from in a) ICF b) SICI and c) LICI for HST, HYT and CON conditions from baseline to 72 hrs. There were no significant interactions observed between conditions for ICF ($F_{11,132} = 0.907$, $P = 0.478$), SICI ($F_{11,132} = 0.849$, $P = 0.066$) or LICI ($F_{11,143} = 1.225$, $P = 0.288$).
(a) ICF (% of baseline) over time for HYT, HST, and CON groups.

(b) SICI (% of baseline) over time for HYT, HST, and CON groups.

(Baseline)
Figure 4.3.5. A comparison of post-training TMS measures for ICF, LICI and SICI in HST, HYT and CON. No significant group x time interactions were observed for ICF (a), SICI (b) and LICI (c) between conditions.
Table 4.2. Raw data for intra-cortical outcome measures of ICF, SICI (not normalised to the unconditioned MEP) and LICI (as a ratio of the test to the conditioning stimulus presented as Mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>2 hrs</th>
<th>6</th>
<th>24</th>
<th>48</th>
<th>72</th>
<th>ICC</th>
<th>SEM, SD95</th>
<th>CV %</th>
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<tr>
<td>CON</td>
<td>0.13 ± 0.13</td>
<td>0.14 ± 0.11</td>
<td>0.15 ± 0.10</td>
<td>0.20 ± 0.15</td>
<td>0.14 ± 0.09</td>
<td>0.14 ± 0.09</td>
<td>0.14 ± 0.05</td>
<td>0.81, r = 0.001</td>
<td>0.045, 0.02</td>
<td>65.85</td>
</tr>
<tr>
<td>HST</td>
<td>0.17 ± 0.11</td>
<td>0.34 ± 0.28</td>
<td>0.22 ± 0.13</td>
<td>0.20 ± 0.11</td>
<td>0.18 ± 0.11</td>
<td>0.25 ± 0.25</td>
<td>0.18 ± 0.16</td>
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<tr>
<td>HYT</td>
<td>0.19 ± 0.10</td>
<td>0.46 ± 0.15*</td>
<td>0.31 ± 0.07</td>
<td>0.27 ± 0.05</td>
<td>0.25 ± 0.03</td>
<td>0.24 ± 0.03</td>
<td>0.19 ± 0.02</td>
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<td><strong>SICI (mV)</strong></td>
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<tr>
<td>CON</td>
<td>0.07 ± 0.06</td>
<td>0.07 ± 0.08</td>
<td>0.09 ± 0.06</td>
<td>0.09 ± 0.06</td>
<td>0.08 ± 0.08</td>
<td>0.08 ± 0.11</td>
<td>0.08 ± 0.10</td>
<td>0.62, r = 0.001</td>
<td>0.010, 0.027</td>
<td>79.12</td>
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<tr>
<td>HST</td>
<td>0.09 ± 0.06</td>
<td>0.24 ± 0.15*</td>
<td>0.14 ± 0.08</td>
<td>0.14 ± 0.09</td>
<td>0.13 ± 0.09</td>
<td>0.15 ± 0.13</td>
<td>0.13 ± 0.11</td>
<td></td>
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<tr>
<td>HYT</td>
<td>0.09 ± 0.02</td>
<td>0.38 ± 0.12*</td>
<td>0.22 ± 0.04*</td>
<td>0.21 ± 0.04</td>
<td>0.19 ± 0.03</td>
<td>0.17 ± 0.04</td>
<td>0.12 ± 0.02</td>
<td></td>
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<tr>
<td><strong>LICI (Test/Cond Pulse Ratio)</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>CON</td>
<td>90.5 ± 31.4</td>
<td>95.0 ± 27.2</td>
<td>88.7 ± 39.4</td>
<td>90.5 ± 32.2</td>
<td>92.3 ± 31.0</td>
<td>86.7 ± 33.1</td>
<td>90.2 ± 30.7</td>
<td>0.30, r = 0.192</td>
<td>23.08, 66.46</td>
<td>39.55</td>
</tr>
<tr>
<td>HST</td>
<td>84.9 ± 35.3</td>
<td>89.1 ± 27.6</td>
<td>82.7 ± 57.4</td>
<td>87.6 ± 50.9</td>
<td>70.7 ± 51.2</td>
<td>61.8 ± 29.6</td>
<td>58.0 ± 35.7</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>HYT</td>
<td>77.8 ± 30.2</td>
<td>94.1 ± 17.3</td>
<td>92.8 ± 30.3</td>
<td>90.2 ± 18.4</td>
<td>83.9 ± 38.7</td>
<td>84.4 ± 25.7</td>
<td>90.2 ± 33.0</td>
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</tr>
</tbody>
</table>

* indicates a significant difference from baseline for each condition. ICC and Pearson’s r show the reliability of each measure between conditions at baseline (pre column) and of the CON condition over the 72 hr period (far right). SEM, SD95 and CV % show the absolute variability of repeated measurements.
4.3.6. Superimposed twitch force

4.3.6. shows the percentage change in SIT$_{25}$, SIT$_{50}$ and SIT$_{75}$ for HST, HYT and CON conditions from baseline over 72 hrs. Three-way ANOVA showed a significant group x time interaction for SIT$_{25}$ ($F_{12,84} = 3.440$, $P < 0.001$). Post-hoc analyses revealed SIT$_{25}$ was significantly reduced immediately post-training for HST ($p = 0.046$) and HYT ($p = 0.048$), when compared to CON. No differences were observed immediately post-training between HST and HYT ($p = 0.626$). No significant interactions were observed for SIT$_{50}$ ($F_{12,84} = 1.318$, $P = 0.244$) or SIT$_{75}$ ($F_{12,84} = 1.800$, $P = 0.061$).
Figure 4.3.6. Super imposed twitch force as a percentage of baseline values for HST, HYT and CON. SIT_{25} is shown in figure (a). (*) indicates a significant interaction between HST and CON while (#) indicates a significant interaction between HYT and CON. No differences were observed between HST and HYT (p = 0.626). No significant group x time interactions were observed for SIT_{50} (P = 0.224) (b) or SIT_{75} (P = 0.061) (c)
Figure 4.3.7 Voluntary activation

4.3.7 shows the change in VA for HST, HYT and CON conditions from baseline over 72 hrs. Three-way ANOVA showed no significant group x time interaction for VA (F_{12,60} = 0.498, P = 0.498).
**Figure 4.3.7.** Changes in VA as a percentage of full activation (100%) for HST, HYT and CON. No differences were observed between HST and HYT (p = 0.626). No significant group x time interactions were observed for VA (P = 0.498).
4.4. Discussion

The primary aim of this chapter was to investigate the acute behaviour of neurophysiological and neuromuscular responses between HST and HYT following a single session of either mode of training of the leg extensors. The results showed that the neurophysiological changes in intra-cortical, corticospinal and peripheral nerve excitability response were similar for both training paradigms across the specified stages of the super-compensation cycle (Bompa & Haff 2009). Specifically, the post exercise increase in MEP amplitude and shortened CSP duration, decreased M_MAX, MVIC and SIT_25 were similar between HST and HYT. No changes were observed between conditions for SICI, ICF and LICI. Collectively, the results suggested that the post exercise responses to HST and HYT were not different between training modalities.

The results showed that the magnitude of force impairment resulting from HST and HYT did not differ between training conditions. Due to the different intrinsic training variables, training to repetition maximum close to the point of momentary voluntary muscular failure may be an important factor in this finding. In support of this, Nicholson et al. (2014) showed no change for peak force between HST and HYT squat protocols using equated loads between conditions. Howatson et al. (2016) also reported significant reductions in MVIC of the knee extensors following strength (4 x 5 RM) and power (5 x 5 repetitions at 30% of the strength condition) training, and also with heavy (85% of 1 RM), moderate (75% of heavy condition) and light (50% of heavy condition) back squat exercise to repetition
maximum (Brandon et al. 2015). Conversely, a reduction in MVIC was shown to be greater with HYT loading strategies compared to HST in the leg extensors (Walker et al. 2012). However the large discrepancy in volume between protocols HST (15 x 1 RM) or HYT (5 x 10 RM) may reflect the disparity in this findings by Walker et al. (2012) compared to Nicholson et al. (2014) and the current findings of this study.

A similar response between HST and HYT was observed for $M_{\text{MAX}}$. Impairment of $M_{\text{MAX}}$ is thought to occur from processes at the neuromuscular junction via changes in membrane potentials and reduced efficacy of sodium/potassium pump (Nielsen & Clausen 2000; Kirkendall 1990; Mileva et al. 2012; Tucker et al. 2005; Deschenes et al. 1994; Behm & St-Pierre 1997). Recent evidence showed conflicting responses of the $M_{\text{MAX}}$ following resistance exercise in the upper and lower limbs. Nuzzo et al. (2016a) showed a suppression in $M_{\text{MAX}}$ amplitude from the biceps brachii muscle following 12 sets of 8 maximal ballistic isometric elbow flexion contractions separated by 4 secs rest. Conversely, the authors reported a potentiation effect of $M_{\text{MAX}}$ after 2 and 12 sets of isometric training (Nuzzo et al. 2016b) with no differences reported between groups, suggesting that the differences observed between studies may be due to posture of the resting limb during stimulation (Nuzzo et al. 2016c). The discrepancies were attributed to different arm posture during testing. Interestingly, the findings of chapter four were dissimilar to Behm and St-Pierre (1997) who reported different effects on $M_{\text{MAX}}$ depending on the duration of resistance exercise. Despite the discrepancies in exercise volume from chapter 4 no differences were observed in the impairment of $M_{\text{MAX}}$ between conditions. The results from this chapter suggested that the
Peripheral nerve stimulation response was similar to that observed in *chapter 3*, and the magnitude of reduction was similar between RT protocols despite differences in training volume, intensity and recovery.

An increase in MEP amplitude and decrease in CSP was observed following training, which was not different between HST and HYT but were not comparable to the response to HST in the elbow flexors in *chapter 3*. However, these findings were in line with recent research showing a similar increase in MEP amplitude and cervico-medullary MEP following slow ramp or ballistic isometric exercise of the elbow flexors (Nuzzo et al. 2016a). An increase in MEP amplitude was similarly reported by Ruotsalainen et al. (2014) following HYT protocol of the elbow flexors. Further support from other studies observing changes in electrical muscle activity between a 5, 10 or 20 RM elbow flexion protocol (Behm et al. 2002) suggest that maximal effort close to momentary voluntary muscular failure rather than repetition selection was an important factor in factors such as VA. The current findings suggested that the increase in excitability and decrease in inhibition may be a compensatory mechanism in an attempt to attenuate the concurrent peripheral fatigue observed with a reduction in $M_{\text{MAX}}$ and MVIC. Despite the work by Ruotsalainen et al. (2014), Nuzzo et al. (2016a) and Nuzzo et al. (2016b), this was the first study to show similarity of corticospinal behaviour following HST and HYT protocols reflective of intrinsic session parameters (intensity, repetition and volume) recommended in current RT guidelines (Ratamess et al. 2009).
The measurement of super imposed twitch force response did not reveal any differences between HST and HYT at submaximal and maximal contraction intensities and when used to calculate VA using the method established by Todd et al. (2003). The application of superimposed twitches has previously been used to calculate VA and assess central fatigue during maximal contractions (Taylor & Gandevia 2008; Behm et al. 2002) or at rest (Nuzzo et al. 2016a). The superimposed twitch response had previously been shown to be facilitated at rest immediately following both ballistic and slow-ramp isometric exercise (Nuzzo et al. 2016a) but impaired following HYT (Routsalainen et al. 2014) in the elbow flexors. Furthermore, the twitch force response has provided evidence of suboptimal VA during fatigue at maximal contraction intensities following sustained voluntary contractions (Gandevia 1996) and HYT (Routsalainen et al. 2014). These reports do not coincide with the results from this study for several reasons. Firstly, twitch contractile properties could be specific to the muscle tested (Behm et al. 2002), with a reduction in quadriceps twitch force response during maximal contractions under fatiguing conditions shown with electrical evoked twitches (Behm & St-Pierre 1997). Secondly, the twitch responses could be affected by the fatiguing protocol (Behm et al. 2002; Behm & St-Pierre 1997) and the type of super imposed stimulus used by other studies (Rouatsalianen et al. 2014; Behm & St-Pierre 1997; Nuzzo et al. 2016a) and in the current chapter. The results of chapter 4 showed no differences between training modalities. This has been similarly reported between 5 RM and 10 RM dynamic contractions of the elbow flexors following training (Behm et al. 2002). However the isometric and concentric protocols used by Nuzzo et al. (2016) may not be reflective of typically applied RT protocols. Therefore the current findings of this chapter suggested that the efficacy of neural drive to both low and
high threshold MUs were not differentially modulated by HST and HYT in the leg extensors, however due to no direct measurement of individual motor units these suggestions are only speculative at this stage.

Furthermore we have presented evidence for similar neuromodulation between HST and HYT with intra-cortical facilitation and inhibition. The findings showed that SICI, ICF and LICl were not different between training paradigms or control across time as observed in chapter 3. This indicated that changes in the responsiveness of the corticospinal pathway following one session of acute HST or HYT were likely to be modulated downstream of the M1 (Nuzzo et al. 2016a). These findings were also in line with chapter 3, which showed that HST of the arm was primarily modulated by changes in corticospinal and peripheral excitability in the absence of any intra-cortical changes following training. Recently (Hunter et al. 2016) showed a decrease in ICF and increase in SICI during and 2 mins following a sustained submaximal contraction of the biceps brachii, which suggested that intra-cortical facilitatory and inhibitory networks become less excitable during fatigue. However to date, measures of intra-cortical facilitation and inhibition have seldom been reported with a single session of applied HST or HYT in the leg extensors. The discrepancies observed between the current study and chapter 3 may be representative of the differences in facilitatory and inhibitory control that existed in the musculature of the upper and lower limbs. The upper limbs are more commonly used in the control of fine motor tasks compared to the lower limbs. Therefore, the responses of the corticospinal tract may in part be reflective of the functional differences in the musculature.
In light of the findings, it is acknowledged that several limitations existed in the current experimental design. Firstly, the acute training session design was in line with current RT guidelines (Ratamess et al. 2009), however the interaction of several other variables such as exercise selection (gross versus isolated motor task) and movement velocity could have influenced the neurophysiological outcomes. Secondly, the measures of MEP, MMAX, CSP, SICI, ICF and LICI were taken from the RF muscle and may not correlate with the behaviour or contribution to force generation of the other quadriceps musculature under fatigue. Intense leg extension exercise is known to recruit slow and fast twitch fibre types and activate all portions of the quadriceps group (Staron et al. 2000; Krstrup et al. 2004), therefore the neurophysiological behaviour under fatigue may be differently modulated in fast or slow twitch dominant muscle groups.
4.5. Conclusion

In conclusion, the findings of the current study showed that the profile of neurophysiological responses were similar between HST and HYT. Although MVIC and $M_{\text{MAX}}$ responses were similar to *chapter 3*, the increase in MEP in the leg extensors may be indicative of the differences in neuromodulation between the upper and lower limbs during fatigue or the application of TMS during an active contraction, overriding some of the initial corticospinal inhibition present at rest. These findings provide important and novel information for the understanding of the acute neurophysiological behaviour in response to real world training programs to be applied in strength and conditioning practice. The findings support the idea that training to repetition maximum may be an important factor in activating neural mechanisms. Therefore the neurophysiological mechanism governing the acute responses from both HST and HYT should be considered in the design, application and progression of RT programs in a properly implemented periodised training structure.
CHAPTER FIVE: STUDY THREE

The super-compensation time course of fatigue, recovery and adaptation with heavy-strength- or hypertrophic-training in the leg extensors
5.1. Introduction

The spatiality of RT sessions is a crucial variable for progression, minimising the risk of injury and burnout and to encourage performance improvements. The suggested frequency of RT stimuli for general populations is based largely upon the concepts of fatigue, recovery and adaptation as proposed by the super-compensation model (Bompa & Haff 2009). In light of this theory, recommendations of HST frequencies are 2-3 days per week, at least 72 hrs apart (Ratamess et al. 2009). A similar approach has been adopted for HYT with each muscle group recommended to be trained 2 times per week, and a minimum of 48 hrs between subsequent homologous training (Ratamess et al. 2009). Despite these guidelines, physiological evidence has shown that endocrine and protein synthesis responses may peak within a 24 hr period suggesting a shortened time course of recovery (MacDougall et al. 1995; Phillips 1997; Chesley et al. 1992; Walker et al. 2012). In line with the suggested shortened time course, chapter 3 revealed that neurophysiological recovery following HST returned towards baseline by 1 hr. Furthermore, there is growing evidence to suggest that ultra-high-frequent RT may have functional benefits on performance adaptations and load management in strength and power athletes (Raastaad et al. 2012; Hartman et al. 2007; Storey et al. 2012; Hakkinen & Kallinen 1994).

Despite current recommendations for HST and HYT to optimise neuromuscular performance (Howatson et al. 2016; Ide et al. 2011; Hakkinen 1994; Hakkinen 1993), the characteristics of neurophysiological fatigue, recovery and adaptation
over the super-compensation cycle, in particular the lower limbs, have not been well established. While the results of chapter 3 suggested a shortened time course of recovery in the BB muscle, differences in lower limb musculature, functionality and fibre type (Behm et al. 2002) make application of the findings difficult to compare between the upper and lower limbs. Although there is evidence for the impairment of neuromuscular force generating capacity following fatiguing RT and acute exercise in the lower limbs (Marshall et al. 2015; Walker et al. 2012; Howatson et al. 2016; Nicholson et al. 2014; Brandon et al. 2015; Hakkinen 1994; Hakkinen 1993), the cortical, corticospinal and peripheral nerve responses are not well understood.

Therefore the aim of this chapter was to provide evidence for the time course of neurophysiological fatigue, recovery and adaptation with HST and HYT in the leg extensors. Specifically, neurophysiological responses were measured via TMS to assess corticospinal excitability, intra-cortical inhibition and facilitation and cortical voluntary activation. In addition to the TMS measures, peripheral nerve excitability and maximal force producing capacity of the leg extensors were recorded immediately post training; 10, 20 and 30 mins and at 1, 2, 6, 24, 48, 72 and 96 hrs. Based on the findings from chapter 3, it was hypothesised that the time-course of fatigue and recovery will be shorter than previous suggestions by super-compensation theory (Bompa & Haff 2009).
5.2. Methods

For the purpose this chapter, HST, HYT and CON have been analysed comprehensively over the time course corresponding to the phases of the super-compensation cycle. For methodological detail on participants, experimental protocol, maximal force testing, TMS measurements, SIT forces and $M_{\text{MAX}}$ measurements the reader is directed to section 4.2.

5.2.1. Participants

Refer to section 4.2.1

5.2.2. Experimental protocol

Refer to section 4.2.2.

Measures were recorded at immediately post training, 10, 20, and 30 mins, 1, 2, 6, 24, 48, 72 and 96 hrs and compared to pre training values (see figure 5.1.)
Figure 5.1. Schematic overview of chapter five protocol.
5.2.3. Maximal voluntary isometric contraction of the leg extensors

Refer to section 4.2.3.

5.2.4. Transcranial magnetic stimulation measurements

Refer to section 4.2.4.

5.2.5. Transcranial magnetic stimulation superimposed twitch force

Refer to section 4.2.5.

5.2.6. Maximal M-wave measurements

Refer to section 4.2.6.

5.2.7. Statistical analysis

All data was screened with a Kolmogorov–Smirnov test and was found to be normally distributed prior to further analysis. One way repeated measures (1 x 12) analysis of variance (ANOVA) was used to compare changes in outcome measures (MVC, M_{MAX}, MEP, CSP, SICI, ICF, LIC and SIT force at 25, 50 and 75% of MVIC, and VA) across time points for each condition (HST, HYT and CON). Where statistical significance was detected a post hoc comparison with Bonferroni correction was conducted. Alpha level was set at \( P < 0.05 \), and all results are
displayed as means ± SD. Where significance was not met, but approached the
alpha level (p ≥ 0.05 ≤ 0.07), effect size was calculated using Cohen’s d formula:

- Cohen's $d = \frac{M_1 - M_2}{SD_{pooled}}$

Calculations were grouped into moderate $d = 0.5 < 0.79$ or large $d = \geq 0.80$. Only
interactions with a moderate or large effect were reported in the analysis.
5.3. Results

5.3.1. Maximal voluntary isometric contraction

Figure 5.3.1. shows the percentage change in MVIC for a) HST, b) HYT and c) CON conditions from baseline to 96 hrs post-training. One-way ANOVA showed a main effect of time for HST ($F_{11,143} = 10.108, P < 0.001$) and HYT ($F_{11,99} = 4.502, P = 0.013$). Post-hoc analyses revealed MVIC was significantly reduced for HST immediately post-training by -12.1% ($p = < 0.001$), at 10 mins, -9.0% ($p = 0.017$), 20 mins, -9.7%, ($p = 0.06$), 30 mins, -10.8% ($p = 0.002$), 1 hr, -9.7% ($p = 0.004$) and 2 hrs, -12.1% ($p = 0.003$) when compared to baseline (100%). MVIC gradually returned to pre-training values by 6 hrs. Post-hoc analyses also revealed a significantly lower MVIC for HYT immediately post training by -19.5% ($p < 0.001$), 10 mins, -15.4% ($p = 0.001$), 20 mins, -14.1% ($p = 0.001$) and 30 mins, -9.4% ($p = 0.002$) when compared to baseline (100%). Moderate to large effects were detected at 1 hr, -7.8% ($d = 1.10, 95\%\ CI [0.28, 1.86]$), 2 hrs, -8.4% ($d = 1.26, 95\%\ CI [0.42, 2.03]$) and 6 hrs, -5.2% ($d = 0.82, 95\%\ [0.03, 1.57]$). No main effect of time was detected for CON ($F_{11,121} = 0.731, P = 0.707$).
Figure 5.3.1. MVIC as a percentage of baseline for (a) HST, (b) HYT and (c) CON.

MVIC was decreased compared to baseline immediately post training by -12.1% and -19.5% for HST and HYT respectively. MVIC returned to baseline values by 6 and 24 hrs for HYT and HST respectively. (*) indicates a significant main effect over time while (#) indicates a moderate to large effect size. No significant main effects were observed across time for CON ($P = 0.707$).
5.3.2. Peripheral nerve excitability

Figure 5.3.2. shows the percentage change in $M_{\text{MAX}}$ in a) HST, b) HYT and c) CON conditions from baseline to 96 hrs post-training. One way ANOVA showed a main effect of time for HST ($F_{11,143} = 7.097, P = 0.004$) and ($F_{11,110} = 5.281, P = 0.002$). Post-hoc analyses revealed $M_{\text{MAX}}$ was significantly reduced for HST immediately post-training by -27.5% ($p < 0.001$), 10 mins, -24.9% ($p < 0.001$), 20 mins, -25.8% ($p < 0.001$), 30 mins, -30.2% ($p < 0.001$) and 1 hr, -24.4% ($p < 0.001$) when compared to baseline. Post-hoc analyses also revealed $M_{\text{MAX}}$ was significantly reduced for HYT immediately post training by -28.1% ($p = 0.001$), 10 mins, -23.4% ($p = 0.002$), 20 mins, -13.1% ($p = 0.002$), 30 mins, -24.2% ($p = 0.002$), 1 hr, -20.8% ($p = 0.001$) and 2 hrs, -15.2% ($p = 0.004$) when compared to baseline (100%). No main effect of time was detected for CON ($F_{11,99} = 0.656, P = 0.776$).
Figure 5.3.2. $M_{\text{MAX}}$ as a percentage of baseline values for (a) HST, (b) HYT and (C) CON. $M_{\text{MAX}}$ was decreased compared to baseline immediately post training by -27.5% and -28.1% for HST and HYT respectively. $M_{\text{MAX}}$, returned to within baseline levels by 2 and 6 hrs for HST and HYT, respectively. (*) indicates a significant main effect over time. No significant main effects were observed across time for CON ($P = 0.776$).
5.3.3. Single pulse MEP

Figure 5.3.3. shows the percentage change in normalised MEP amplitude for a) HST, b) HYT and c) CON conditions from baseline to 96 hrs post-training. One way ANOVA showed a main effect of time for HST ($F_{11,143} = 5.701, P = 0.001$) and HYT ($F_{11,110} = 8.734, P < 0.001$). Post-hoc analyses revealed a moderate to large effect of the MEP for HST immediately post training 203.2% ($d = 0.83, 95\% CI [0.03, 1.58]$), and significant increase at 10 mins, 208.2% ($p = 0.004$), 20 mins, 198.6% ($p = 0.005$), 30 mins, 202.3% ($p < 0.001$) and 1 hr, 185.3% ($p = 0.002$) when compared to baseline (100%). A moderate to large effect was detected at 2 hrs, 153.0% ($d = 1.11, 95\% CI [0.29, 1.87]$). Post-hoc analyses also revealed significantly higher MEP for HYT immediately post training 253.8% ($p < 0.001$), 10 mins, 266.7% ($p = 0.002$), 20 mins, (240.0%, $p = 0.001$) and 30 mins, 256.4%, ($p = 0.002$) when compared to baseline (100%). A moderate to large effect was detected for HYT at 1 hr, 214.2% ($d = 1.51, 95\% CI [0.63, 2.30]$) and 2 hrs, 155.9%, ($d = 1.26, 95\% CI [0.42, 2.03]$). No main effect of time was detected for CON ($F_{11,110} = 2.423, P = 0.076$).
Figure 5.3.3. Changes in normalised MEP as a percentage of baseline for (a) HST, (b) HYT and (c) CON. MEP was increased compared to baseline immediately post training by 103.2% and 153.8% for HST and HYT respectively and remained elevated up until 30 mins for HYT and 1 hr for HST, indicating greater corticospinal drive during fatigue. (*) indicates a significant main effect over time while (#) indicates a moderate to large effect size. No significant main effects were observed across time for CON (P = 0.076).
5.3.4. Corticospinal silent period

Figure 5.3.4. shows the percentage change in CSP for a) HST, b) HYT and c) CON conditions from baseline to 96 hrs post-training. One way ANOVA showed a main effect of time for HST \( (F_{10,110} = 4.823, \ P = 0.008) \) and HYT \( (F_{11,110} = 11.30, \ P < 0.001) \). Post-hoc analyses revealed a significantly shorter CSP for HST immediately post training of -18.5% \( (p < 0.001) \), at 10 mins, -16.1% \( (p < 0.001) \), 20 mins, -17.6% \( (p < 0.001) \), 30 mins, -12.8% \( (p < 0.001) \) and 1 hr, -9.4% \( (p < 0.001) \) when compared to baseline. A moderate to large effect was detected at 2 hrs, -6.2% \( (d = 1.14, 95\% \ CI [0.28, 1.93]) \) and 6 hrs, -6.7% \( (d = 1.10, 95\% \ CI [0.24, 1.89]) \). Post-hoc analyses also revealed a significantly shorter CSP for HYT immediately post training of -17.7% \( (p < 0.001) \) and at 10 mins, -19.7% \( (p < 0.001) \), 20 mins, -21.5% \( (p < 0.001) \), 30 mins, -19.5\%, \( (p < 0.001) \), 1 hr, -12.7% \( (p = 0.003) \) and 6 hrs, -6.7% \( (p = 0.004) \) when compared to baseline. A moderate to large effect was detected at 2 hrs, -12.0 \( (d = 1.38, 95\% \ CI [0.52, 2.16]) \) and 24 hrs, -5.8% \( (d = 1.51, 95\% \ CI [0.63, 2.30]) \). No main effect of time was detected for CON \( (F_{11,143} = 0.816, \ P = 0.624) \).
Figure 5.3.4. CSP as a percentage of baseline for (a) HST, (b) HYT and (c) CON. CSP duration was shortened compared to baseline immediately post training by -18.5% and -17.7% for HST and HYT respectively. CSP duration remained shortened up until 6 and 24 hrs for HST and HYT respectively indicating reduced corticospinal inhibition through the recovery phase of the super compensation cycle. (*) indicates a significant main effect over time while (#) indicates a moderate to large effect size. No significant main effects were observed across time for CON ($P = 0.624$).
5.3.5. Paired pulse TMS measures

5.3.5.1. Intra-cortical facilitation

Figure 5.3.5.1. shows the percentage change in ICF for a) HST, b) HYT and c) CON conditions from baseline to 96 hrs post-training. One way ANOVA showed a main effect of time for HYT (F\(_{11,143} = 4.213\), \(P < 0.001\)). Post-hoc analyses revealed a significant increase in ICF for HYT at 6 hrs (128.0\%, \(p = 0.002\)) when compared to baseline (100%). No main effect was detected for HST (F\(_{11,132} = 1.546\), \(P = 0.237\)) or CON (F\(_{11,77} = 0.762\), \(P = 0.676\)).
(a) ICF (% of baseline) over time with HST treatment.

(b) ICF (% of baseline) over time with HYT treatment.

*(Hypothetical data points marked with an asterisk).
Figure 5.3.5.1. ICF as a percentage of baseline values for (a) HST, (b) HYT and (c) CON. ICF was significantly increased for HYT at 6 hrs (28.0%). No significant main effects were observed across time for HST ($P = 0.237$) or CON ($0.676$). (*) indicates a significant main effect over time.
5.3.5.2. Short interval cortical inhibition

Figure 5.3.5.2. shows the percentage change in SICI for a) HST, b) HYT and c) CON conditions from baseline to 96 hrs post-training. One way ANOVA showed a main effect of time for HYT ($F_{11,143} = 4.540$, $P < 0.001$). Post-hoc analyses revealed a reduction in SICI for HYT immediately post training 177.3% ($p < 0.001$), 10 mins, 162.9% ($p = 0.001$), 20 mins, 172.3% ($p = 0.002$), 30 mins, 156.2% ($d = 1.26$, 95% CI [0.41, 2.03]), 1hr, 147.0% ($d = 0.83$, 95% CI [0.03, 1.57]), 2 hrs, 140.1% ($d = 0.83$, 95% CI [0.03, 1.57]), 6 hrs, 170.5% ($p = 0.002$), 24 hrs, (160.9%, $d = 1.17$, 95% CI [0.33, 1.93]), 48 hrs, (157.6%, $d = 0.82$, 95% CI [0.02, 1.56]), 72 hrs, 121.2% ($d = 2.64$, 95% CI [1.57, 3.57]) and 96 hrs, 131.6% ($d = 1.52$, 95% CI [0.64, 2.31]) when compared to baseline (100%). No main effect was detected for HST ($F_{11,132} = 1.546$, $P = 0.237$ or CON ($F_{11,99} = 1.423$, $P = 0.246$).
Figure 5.3.5.2. Changes in SICI as a percentage of baseline values for (a) HST, (b) HYT and (c) CON. SICI was significantly reduced for HYT throughout the 96 hrs period. HYT appears to reduce the amount of SICI within the M1. (*) Indicates a significant main effect over time while (#) indicates a moderate to large effect size. No significant main effects were observed across time for HST ($P = 0.237$) or CON ($P = 0.246$).
5.3.5.3. Long interval cortical inhibition

Figure 5.3.5.3. shows the percentage change in LICI for a) HST, b) HYT and c) CON across all time points. One way ANOVA showed a main effect of time for HST ($F_{11,143} = 2.012, P = 0.031$). Post-hoc analysis revealed an increase in LICI as shown by a greater reduction from baseline (100%) for HST at 24 hrs, -18.8% ($d = 0.56, 95\% \text{ CI } [-0.21, 1.30]$), 48 hrs, -20.5% ($d = 0.66, 95\% \text{ CI } [-0.12, 1.40]$), 72 hrs, -20.5% ($d = 1.01, 95\% \text{ CI } [0.19, 1.76]$) and 96 hrs, -26.8% ($d = 0.97, 95\% \text{ CI } [0.16, 1.73]$). No main effect of time was detected for HYT ($F_{11,143} = 0.908, P = 0.534$) or CON ($F_{11,77} = 0.874, P = 0.569$).
Figure 5.3.5.3. Changes in LICI as a percentage of baseline values for (a) HST, (b) HYT and (c) CON. Greater LICI was present for HST at 24-96 hrs. (#) Indicates a moderate to large effect over time. No significant main effects were observed across time for HYT ($P = 0.534$) or CON ($P = 0.569$).
5.3.6. Super imposed twitch force

5.3.6.1. SIT25

Figure 5.3.6.1. shows the percentage change in SIT25 for a) HST, b) HYT and c) CON across all time points. One way ANOVA showed a main effect of time for HST ($F_{11.132} = 8.022$, $P < 0.001$). Post-hoc analysis revealed a decrease in SIT25 for HST immediately post training of -17.9% ($p < 0.001$), at 10 mins, (-28.4%, $p < 0.001$), 20 mins (-11.9%, $p = 0.002$), 30 mins, -13.3% ($p = 0.004$) when compared to baseline (100%). Moderate to large effects were detected at 1 hr, -10.8% ($d = 0.64$, 95% CI [0.15, 1.40]). One way ANOVA also showed a main effect of time for HYT ($F_{11.132} = 9.336$, $P < 0.001$). Post-hoc analysis revealed a moderate to large decrease in SIT25 for HYT immediately post, -21.5% ($d = 1.06$, 95% CI [0.22, 1.83]) at 10 mins, -19.1% ($d = 1.16$, 95% CI [0.32, 1.94]), 20 mins, -16.1% ($d = 1.52$, 95% CI [0.62, 2.32]) and at 2 hrs, -10.5% ($d = 0.80$, 95% CI [0.00, 1.56]) when compared to baseline. Significant decreases compared to baseline were observed at 30 mins, -16.2% ($p < 0.001$) and 1 hr, -15.0% ($p = 0.001$). No main effect of time was detected for CON ($F_{11.110} = 0.972$, $P = 0.477$).
Figure 5.3.6.1. Changes in SIT$_{25}$ as a percentage of baseline for (a) HST, (b) HYT and (c) CON. SIT$_{25}$ was impaired post training and gradually returned to baseline values by 6 hrs for both HST and HYT, indicating potential low threshold fatigue. (*) Indicates a significant main effect over time while (#) indicates a moderate to large effect size. No significant main effects were observed across time for CON ($P = 0.477$).
Figure 5.3.6.2. shows the percentage change in SIT$_{50}$ for a) HST, b) HYT and c) CON. One way ANOVA showed a main effect of time for HST (F$_{11,132} = 5.119$, $P < 0.001$). Post-hoc analysis revealed a decrease in SIT$_{50}$ for HST immediately post training of -4.0 ($d = 0.92$, 95% CI [0.09, 1.70]), at 10 mins, -6.4% ($d = 0.68$, 95% CI [0.13, 1.45]), 20 mins, -4.2% ($d = 0.91$, 95% CI [0.08, 1.69]), 30 mins, -5.6% ($d = 0.97$, 95% CI [0.13, 1.75]), 1 hr, -4.9% ($p = 0.002$) and 2 hrs post training, -4.75 ($d = 0.82$, 0.01, 1.59) when compared to baseline (100%). One way ANOVA showed a main effect for time for HYT (F$_{11,132} = 3.694$, $P < 0.001$). Post-hoc analysis revealed moderate to large effects of SIT$_{50}$ for HYT immediately post-training -5.3% ($d = 0.68$, 95% CI [0.13, 1.45]), 10 mins, -6.5% ($d = 0.63$, 95% CI [0.17,1.40]), 20 mins, -6.7% ($d = 0.72$, 95% CI [0.10, 1.49]), 30 mins, 2.4% ($d = 0.52$, 95% CI [0.28, 1.28]) and 2 hrs, -1.7% ($d - 0.54$, 95% CI [0.25, 1.31]) when compared to baseline. No main effect of time was detected for CON (F$_{11,110} = 0.717$, $P = 0.720$).
Figure 5.3.6.2. Changes in SIT$_{50}$ as a percentage of baseline values for (a) HST (b) HYT and (c) CON. SIT$_{50}$ was impaired post training and gradually returned to baseline values by 6 hrs for both HST and HYT, indicating potential low threshold fatigue. (*) Indicates a significant main effect over time while (#) indicates a moderate to large effect size. No significant main effects were observed across time for CON ($P = 0.720$).
5.3.6.3. SIT_{75}

Figure 5.3.6.3. shows the percentage change in SIT_{75} for a) HST, b) HYT and c) CON. No main effect of time was detected for HST (F_{11,132} = 2.661, P = 0.056), HYT (F_{11,121} = 1.987, P = 0.143) or CON (F_{11,110} = 0.816, P = 0.624).
(a) 

![Graph (a)](image1)

(Baseline)

![Graph (b)](image2)

(Baseline)

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225

90

95

100

105

90

105

100

95

90

Pre Post 10 min 20 30 1 hr 2 6 24 48 72 96

Time

HST

Pre Post 10 min 20 30 1 hr 2 6 24 48 72 96

Time

HYT
Figure 5.3.6.3. Changes in SIT$_{75}$ as a percentage of baseline values for (a) HST (b)HYT and (c) CON. No significant main effects were observed across time for HST ($P = 0.048$), HYT ($P = 0.143$) or CON ($P = 0.720$).
5.3.7. Voluntary activation

Figure 5.3.7. shows the change in VA for a) HST, b) HYT and c) CON. No main effect of time was detected for HST (F_{11,143} = 1.366, P = 0.195), HYT (F_{11,121} = 1.987, P = 0.143) or CON (F_{11,110} = 1.118, P = 0.354).
Figure 5.3.7. Changes in VA as a percentage of full activation (100%) for (a) HST (b) HYT and (c) CON. No significant main effects were observed across time for HST ($P = 0.195$), HYT ($P = 0.143$) or CON ($P = 0.354$).
5.4. Discussion

The primary aim of this chapter was to map the super-compensation time course of central and peripheral adaptations and maximal force output, up to 96 hrs post-training following HST or HYT in the leg extensors. The results indicate an immediate decrease in MVIC and $M_{\text{MAX}}$ with a concurrent increase in corticospinal drive for HST and HYT, respectively. Following HST, MVIC was impaired up until 2 hrs, with a reduction in $M_{\text{MAX}}$ and CSP up to 1 and 6 hrs, respectively, and a concomitant increase in MEP amplitude up until 2 hrs. Similarly, for HYT, MVIC was impaired up until 2 hrs, with reductions in $M_{\text{MAX}}$ and CSP observed up until 2 and 24 hrs respectively. MEP amplitude was also significantly increased up to 2 hrs post-training. A reduction in the SIT force was observed during submaximal but not maximal contractions for both training conditions. Following HYT, changes in ICF were observed at 6 hrs and SICI up until 24 hrs. Following HST an increase in LICI was observed between 24-96 hrs. Collectively, the results suggested that changes in CSE, $M_{\text{MAX}}$ and MVIC following a single session of either HST or HYT followed a shorter time course than suggested previously by super-compensation theory with alterations in SICI, ICF and LICI occurring at different time points over the cycle.

The main finding from this study showed that MVIC returned to within baseline levels by 6 hrs for both training conditions. This time frame suggested a shorter time course of neuromuscular fatigue and recovery compared to the super-compensation model (Bompa & Haff 2009) and other studies measuring
neuromuscular force impairment following RT (Howatson et al. 2016; Ide et al. 2011). The recovery period was also shorter than suggested in current RT guidelines (48 hrs for HYT and 72 hrs for HST) to prevent overtraining (Ratamess 2009; Halson & Jeukendrup 2004; Meeusen et al. 2013; Smith 2003). In support of the current findings, previous studies have shown that neuromuscular mechanisms, such as improvements in strength and power performance can be facilitated as early as 4-6 hrs after an initial training bout (Cook et al. 2014; Ekstrand et al. 2013; Latella et al. 2016). This was further supported by the findings from chapter 3 showing a shorter time to recovery for maximal force production using a similarly HST (5 x 3 RM) protocol in the upper limb. Although the recovery in both the upper and lower limbs was shorter than suggested in super-compensation theory the discrepancies in the time course between chapter 3 and this chapter may be reflective of the difference in recruitment between muscle groups of the upper and lower limbs or muscle fibre type (Bortoluci et al. 2014; Staron et al. 2000; Krstrup et al. 2004). The biceps brachii has been shown to have a mixed fibre type (Bortoluci et al. 2014), whilst the leg extensors recruit slow and fast twitch fibre types activating all portions of the muscle during intense knee extensor exercise (Staron et al. 2000; Krstrup et al. 2004), which may explain the longer time course of recovery.

Similarly, the changes in M\text{MAX} following HST and HYT followed a shortened time-course of fatigue and recovery. A significant suppression of M\text{MAX} was observed for HST and HYT immediately post exercise before returning to within baseline levels by 2 and 6 hrs respectively. This response was similar to that of chapter 3 and other recent studies. Nuzzo et al. (2016a) showed a reduction in
M_{MAX} after isometric training of the elbow flexors, however other studies using repeated maximal shortening or lengthening contractions in the upper (Loscher and Nordlund 2002; Nuzzo et al. 2016b) and lower limbs (Hicks et al. 2004) have reported disparate findings, and was likely due to the posture of the tested limb or potentiation effects of shorter duration exercise (Nuzzo et al. 2016c; Behm et al. 1997; Rodriguez-Falces et al. 2015). Reductions in peripheral nerve excitability, as discussed in chapters 3 and 4 are thought to be related to changes within and downstream of the neuromuscular junction (Kirkendall 1990; Mileva et al. 2012; Tucker et al. 2005; Deschenes et al. 1994). As shown with MVIC, the time course of fatigue and recovery of M_{MAX} was shorter than the neural fatigue time-course proposed by Bompa and Haff (2009). These findings offered further support for the capability of the neuromuscular system and peripheral nerve structures to undertake more frequent RT sessions than the current recommendations (Ratamess et al. 2009). The shortened time to recovery of MVIC and M_{MAX} provided, in part, evidence for the capability of the body to undertake higher RT frequencies (McKenzie 1981; Serra et al. 2015) and the rationale for ultra-high-frequent RT in athletic populations (Raastaad et al. 2012; Hartman et al. 2007; Storey et al. 2012; Hakkinen & Kallinen 1994).

Contrary to MVIC and M_{MAX}, single pulse TMS responses showed an increase in MEP amplitude indicating an increase in corticospinal drive. The increase in MEP amplitude was maintained up to 2 hrs post exercise for both HST and HYT with a concurrent reduction in CSP duration lasting 6 and 24 hrs for HST and HYT respectively. This net increase in corticospinal drive has also been reported following RT interventions in the upper and lower limbs (Kidgell and Pearce 2010;
Latella et al. 2012; Perez and Cohen 2008) and may indicate a central compensatory process in the presence of neuromuscular fatigue (Marshall et al. 2015). However, the changes in post exercise corticospinal excitability seemed dependent the muscle in which MEPs were recorded from and type of motor task, with some studies reporting an increase in MEP amplitude from the plantar flexors (Griffin & Cafarelli 2007), while others have demonstrated a decrease in the arms (Jensen et al. 2005, Carroll et al. 2009). Additionally, the current findings of a shortened CSP have recently been shown in exhaustive cycling efforts (O’Leary et al. 2016), which suggested that the level of effort required for an exercise task subsequently may have reduced cortical inhibition. Further, these findings were not in agreement with the notion of a reduced central output as proposed by super-compensation theory (Bompa & Haff 2009). In contrast to these studies, evidence has shown that ballistic and slow ramp isometric resistance type exercise can acutely increase the efficacy of corticospinal projections (Nuzzo et al. 2016). Similarly, an increase in the size of the MEP has been reported during and after hypertrophic fatiguing exercise of the elbow flexors (Ruotsalainen et al. 2014) and provide some rationale for a greater corticospinal drive observed in the leg extensors from this chapter. The discrepancies in the literature may be due to the testing methodology such as the musculature, contraction type and active versus resting testing conditions used. The current findings suggested a concurrent increase in excitatory output of the CNS in the presence of neuromuscular and peripheral fatigue (Enoka et al. 2011; Marshall et al. 2015). An increase in CSE may be required to maintain the discharge of fatiguing motor neurons (Heroux et al. 2015) whilst a reduction in the CSP is reflective of changes in GABA_b mediated inhibition that facilitated an increase in corticospinal drive to the muscle. This increase in CSE may be in an attempt to
compensate for suboptimal excitability and neuromuscular performance at the peripheral level. Due to the changes in GABA\textsubscript{b} mediated inhibition this increased responsiveness is likely to occur above the peripheral level and outside of the M1.

An interesting finding from this chapter was the change in measures of intra-cortical inhibition and facilitation following HST and HYT. Measures of SICI was reduced (less inhibition) up until 24 hrs post-training following HYT. A reduction in GABA\textsubscript{A} mediated intra-cortical inhibition have previously been observed with short term strength RT interventions of the upper limbs (Hendy et al. 2013; Hendy et al. 2014; Leung et al. 2015), however, has been shown to increase by as much 24% acutely after an exhaustive bout of aerobic exercise (O’Leary et al. 2015). Recently, Hunter et al. (2016) showed a reduction in efficacy of ICF networks (-22.1%) during and increased SICI (8.1%) following a sustained submaximal contraction of the BB muscle. The differences in comparison to the current findings may be reflective of the different nature of motor neuron pool existing in the leg musculature, or the influence of a sustained versus intermittent contractions on neural networks. The novelty of this finding is that HYT training may also have the ability to impact intra-cortical mechanisms providing an important scope for RT interventions. Conversely, HST showed greater LICI from 24-96 hrs following HST. While the reasons for the delayed modulation of LICI are uncertain at this stage, it is speculated that the changes in GABA\textsubscript{B} mediated cortical inhibition may only be affected following highly intense forms of exercise (Benwell et al. 2007) and represent later stages of exercise-induced neuroplasticity.
Another interesting observation in the findings suggested that SIT forces were reduced at submaximal but not maximal voluntary contraction levels following HST and HYT. Further, the twitch response returned to within baseline levels between 2 and 6 hrs for HST and HYT respectively and was within a similar time frame to measures of MVIC, M\text{MAX} and MEP responses. The reduction in SIT response with a decrease in contraction intensities was used to calculate VA via the method established by Todd et al. (2003). Interestingly a decrease in SIT response for intensity (≤ 50% MVIC) was reduced following training. Although it could be speculated that neuromuscular fatigue could affect low threshold motor unit innervation after HST and HYT, the main finding was that VA was not impaired by this reduction. Despite the reductions in SIT response at submaximal voluntary contraction intensities when analysed separately over time, twitch force responses during high and maximal (≥ 75% MVIC) contractions were preserved. The evidence suggested that during maximal efforts, central activation is maintained in an attempt to maintain force output in spite of the presence of peripheral fatigue. Taken together, the observation that 1) post exercise corticospinal excitability was increased, 2) cortical inhibition was reduced and 3) VA at maximal contraction intensities was sustained, indicated that the origin of fatigue following 1 session of HST and HYT were likely to be peripheral in nature rather than of central origin.

In light of the findings, it is acknowledged that several limitations exist in interpreting the results. Firstly, the locus of the increase in CSE was attributed to origins above the peripheral but below the cortical level. However without the use of CMEPs and spinal stimulation this suggestion may require further investigation. Changes in the MEP and CMEP have recently been shown in response to RT
Secondly, previous reports of a reduced MEP amplitude following RT (Gruet et al. 2014) and HST in particular as shown in *chapter 3* were conducted while the muscle was at rest, whilst MEPs from the leg extensors were measured under light voluntary isometric contraction. Active conditions are thought to display a greater response due to the removal of initial inhibitory mechanisms during contraction (O’Leary et al. 2015; Darling et al. 2006; Weber 2002). However, an active condition was deemed to be more representative of the behaviour of the corticospinal tract with exercise and allowed for the additional measurement of the CSP.
5.5. Conclusion

Collectively, the findings from the present chapter provided evidence for a shortened super-compensations time course of neurophysiological fatigue and recovery from HST and HYT in the leg extensors. The findings suggested that an increase in CSE occurs during fatigue and recovery to compensate for decreases in peripheral nerve excitability and MVIC. Secondly, neural inhibition present with submaximal contractions during fatigue is abolished during maximal efforts. The overall shortened neurophysiological recovery period of the super-compensation cycle provides some support for the rationale behind higher frequency training interventions used in applied settings to optimise gains in neuromuscular performance.
CHAPTER SIX: GENERAL DISCUSSION
The primary aim of this thesis was to investigate the time course of the acute neurophysiological responses to RT so as to understand the neural basis of the super-compensation cycle. The experimental studies undertaken for this thesis have produced several key and novel findings that contribute to strength and conditioning literature, and are applicable to exercise prescription and programming. In chapter 3, the concept of super-compensation in the elbow flexors was investigated following a single session of HST. Measures of force and neural excitability were reduced in the initial stages following HST; MEP, M\text{MAX} and MVIC, with a gradual return towards baseline levels within 1 hr and, chronologically, a super-compensation effect was observed for M\text{MAX} at 6 hrs and MVIC between 6 and 48 hrs. No changes were observed for intra-cortical measures of inhibition and facilitation. In chapter 4, the differences in the central and peripheral behaviour of the neurophysiological responses from HST and HYT were measured in the leg extensors. The analysis was conducted at time points specific to the stages of fatigue (post-training - 2 hrs), recovery (6-48 hrs) and adaptation (72 hrs) as suggested by the super-compensation theory (Bompa and Haff 2009).

The results from chapter 4 showed a decrease in MVIC, CSP, M\text{MAX}, and SIT\text{25} while MEP was increased for HST and HYT during fatigue compared to CON. No differences were observed between HST and HYT across all time points. In chapter 5, a secondary analysis of the data was conducted to comprehensively track the neurophysiological super-compensation response to HST and HYT of the leg extensors over time. Significant reductions were observed for MVIC, M\text{MAX} of up to 2 hrs post training with a gradual return toward baseline by 6 hrs. Reductions in CSP were evident until 6 and 24 hrs for HST and HYT respectively. Conversely,
an increase in MEP amplitude was observed for HST and HYT up until 2 hrs post
training which returned toward baseline by 6 hrs. An increase in LICI (more
inhibition) was observed from 48-96 hrs for HST, and an increase in ICF and
reduction in SICI (less inhibition) was observed for HYT at 6 and 24 hrs
respectively. A reduction in SIT_{25} was observed up until 1 and 2 hrs for HST and
HYT, respectively and 2 hrs for SIT_{30} in both training conditions. No significant
differences were detected for SIT_{75} or SIT_{100}.

Collectively, the findings of the thesis provided evidence for several key concepts
regarding the neurophysiological basis of super-compensation from RT. Firstly, it
was concluded that after a single session of HST of the elbow flexors the time
course of neurophysiological fatigue and recovery was 18-40 hrs shorter than
proposed by previous super-compensation theory (Bompa & Haff 2009). A
shortened period of fatigue and recovery was also observed with HST and HYT in
the leg extensors. It was concluded that the time course of neurophysiological
fatigue and recovery from HST and HYT in the leg extensors was also shorter than
previous suggestions by super-compensation theory. The second major finding was
that the magnitude of the acute neurophysiological responses were similar between
HST and HYT paradigms. All neurophysiological measures of intra-cortical,
corticospinal and peripheral nerve excitability, SIT forces and MVIC were similar
for HST and HYT during the stages of fatigue (0-2 hrs), recovery (6-48 hrs) and
adaptation (72 hrs). Further, the neurophysiological measures suggested that
fatigue from HST in the elbow flexors and both HST and HYT in the leg extensors
occurred primarily downstream of the M1. The findings also suggested that fatigue
is due to peripheral rather than central mechanisms. Evidence for these suggestions
can be found in chapter 3 with a decrease in MVIC, $M_{MAX}$ and MEP amplitude during fatigue but no subsequent change in intra-cortical measures. In support of these findings, HST and HYT of the leg extensors revealed similar reductions in MVIC, $M_{MAX}$ with a concomitant increase in net CSE; increased MEP amplitude, decreased CSP duration, providing further evidence of fatigue occurring at a peripheral rather than central level. Lastly, assessment of super imposed twitch force responses during submaximal and maximal contractions revealed different neuro-modulation of the motor neuron pool with fatigue. The capacity of neural drive was impaired during submaximal but not maximal contraction intensities for HST and HYT respectively. These key themes will be discussed in more detail in the following sections of the discussion.
6.1. The time course of fatigue, recovery and adaptation

The findings from all three chapters provide strong evidence for a shortened time course of neurophysiological super-compensation with HST and HYT. In chapter 3, a single HST session of the elbow flexors showed acute post training reductions in force by 19.5% immediately post training which remained impaired by 5.7% up until 30 mins with a return toward baseline by 1 hr. This was followed by an increase in peripheral nerve excitability above baseline by 27.9% at 6 hrs and MVIC at by 5.6, 8.5 and 10.0% at 6, 24 and 48 hrs respectively. The observed post exercise central and peripheral neural responses were comparable to that of the current super-compensation model (Bompa & Haff 2009), however it revealed a dissimilar time course of neurophysiological fatigue and recovery. The results indicated that the recovery period was 18-40 hrs shorter than suggested by the super-compensation theory. Further, the increase in MVIC between 6-48 hrs indicated that strength improvements could be observed after a single training stimuli. These improvements may be related to skill acquisition (Hinder et al. 2013) and improved neural efficiency in the absence of any structural changes. Support of these suggestions comes from studies investigating motor skill performance following an acute task (Hinder et al. 2013; Lee et al. 2010). Hinder et al. (2013) found significant motor improvements in the trained and untrained hand following maximal finger abduction training. Further evidence is provided by Lee et al. (2010) who associated strong descending neural drive and mechanism within the ipsilateral cortex with the retention of performance on a ballistic finger abduction task. Although the neuro-modulation between these motor tasks and gross RT exercise may be different and the primary focus of the studies by Hinder et al.
(2013) and Lee et al. (2010) was on the cross over effect of learning, they provide at least some rationale for the contribution of neural mechanism governing acute increases in performance. The results from chapter 5, also revealed a shortened time course of fatigue and recovery following HST and HYT of the leg extensors. MVIC showed post exercise fatigue lasting up to 2 hrs and returned to within baseline levels by 6 hrs. These findings provided evidence in support of a shortened time course of fatigue and recovery with RT with several possible mechanisms to explain these findings. Firstly, the shortened recovery period provided further support for the work of Cook et al. (2014) and Ekstrand et al. (2013) using short inter-session recovery periods to facilitate performance. These findings may be due to a neuromuscular ‘priming’ effect that initial HST has on subsequent 4-6 hrs post-training on same day performance (Cook et al. 2014; Ekstrand et al. 2013). Further the natural circadian rhythm has been shown to influence strength (Teo et al. 2011a; Teo et al. 2011b; Reilly et al. 2006; Nicolas et al. 2005). Reilly et al. (2006) showed that dynamic leg extension strength was 4-10% greater when conducted later in the day between 5 and 7 pm. Maximal torque values of the knee extensors was also shown to be 7.7% greater when conducted at 6 pm rather than 6 am (Nicolas et al. 2005). The reports may provide some rationale for the strength increases observed at the 6 hr time point in chapter 3. However, the findings of Cook et al. (2014) and Ekstrand et al. (2013) are dissimilar to other studies investigating acute neuromuscular responses to resistance exercise (Howatson et al. 2016; Ide et al. 2011). 1RM strength was impaired for 24-48 hrs following strength and power training (Howatson et al. 2016) and fast or slow velocity RT in the lower limbs (Ide et al. 2011). These differences may be explained by the intra-session training variables such as exercise selection and total session volume (Platonov 2001) which
may account for the differences observed between our findings and that of Howatson et al. (2016) and Ide et al. (2011). Further, the relatively simplistic nature of the MVIC may at least in part contribute to the shortened time course of recovery over highly complex, multi segmental dynamic motor tasks observed in other research (Howatson et al. 2016; Ide et al. 2011). However, due to the limited evidence with applied RT protocols we can only speculate at this stage as to the exact mechanisms behind the shortened neurophysiological time course.

In support for a shorter time course of neuromuscular fatigue and recovery, chapter 3 showed MEP suppression immediately post training followed by a recovery back to within baseline levels by 1 hr post exercise. These findings are in agreement with other studies showing a decreased MEP amplitude returning rapidly to baseline in the initial stages following fatiguing motor tasks (Brasil-Neto et al. 1994; Brasil-Neto 1992; Gruet et al. 2014; Teo et al. 2012, Teo et al. 2013). Gruet et al. (2014) showed a rapid recovery of CSE within 2 mins in the quadriceps whilst Teo et al. (2012) showed a return to baseline of cortico-motor depression 10 mins after a dynamic maximal finger flexion-extension task. Conversely, chapter 5 showed increased corticospinal excitability (immediately post - 2 hrs) and decreased inhibition (immediately post - 6 hrs) for HST, and (immediately post - 24 hrs) for HYT respectively. An increased responsiveness of the corticospinal tract has also been reported in other similar research. Nuzzo et al. (2016) showed an increase in CSE up to 30 mins following slow ramp and ballistic isometric training of the elbow flexors. Thickbroom et al. (2008) also found an increase in MEP amplitude after an exercise inducing fatigue foot tapping task and concluded that central processes are likely to play a significant role in maintaining task performance. The increase in
MEP observed in chapter 5 compared to chapter 3 may be due to TMS stimulation being performed during light voluntary isometric contraction rather than at rest. At rest, CSE is low and increases rapidly as contraction intensity increases (Temesi et al. 2014) likely due to a facilitation of responses at the spinal level, and a subsequent release of cortical inhibition contributing to the increase in CSE during high intensity contractions (Ugawa et al. 1995). Impaired peripheral nerve excitability in all training conditions was consistent with the time course of CSE changes. The findings of reduced $M_{\text{MAX}}$ following exercise has previously been shown in several studies (Sacco et al. 1997; Fuglevand et al. 1993; Nuzzo et al. 2016a). A depression in M-wave response of between 12-23% has been reported following a sustained isometric contraction of the index finger (Fuglevand et al. 1993) and by as much as 35% has been shown in the lateral gastrocnemius with fatigue (Sacco et al. 1997). The corticospinal and peripheral outcome measures collectively showed that fatigue and recovery was 18-40 hrs shorter than previously suggested by super-compensation theory.

The findings of this thesis suggests an altered time course of neurophysiological fatigue, recovery and adaptation compared to the current super-compensation theory (refer to appendix g). The overarching findings suggested that maximal force-producing capacity, corticospinal excitability, cortical inhibition and peripheral nerve excitability recovered within 1 and 6-24 hrs following HST in the elbow flexors and from HST or HYT in the leg extensors, respectively. While the current results demonstrated the post exercise dynamics of acute neurophysiological responses to typically applied type RT, careful interpretation must be given based upon the array of applied HST and HYT methods used in
strength and conditioning practice. Further consideration must also be given regarding the methodologies used in the assessment of neuromuscular function and performance in previous research (Howatson et al. 2016; Ide et al. 2011; Walker et al. 2012).
6.2. Similarity of neurophysiological responses with strength and hypertrophy training

It is known that HST (≥ 80% of 1RM) facilitates adaptations within the CNS and neuromuscular system (Latella et al. 2012; Hendy & Kidgell 2013; Kidgell & Pearce 2010; Carroll et al. 2011; Selvanayagam et al. 2011) however, less is understood regarding neurophysiological mechanisms with HYT. In chapter 4, central and peripheral excitability were compared between HST, HYT and CON conditions in the leg extensors. The results showed similar changes between HST and HYT compared to CON for all neurophysiological responses assessed. The current findings are novel, and to our knowledge, no other studies have directly compared the neurophysiological responses following a real-world applied HST or HYT protocol using recommended RT guidelines (Ratamess et al. 2009). One study by Routsalainen et al. (2014) investigated CSE during and in the acute stages post dynamic HYT of the elbow flexors and showed that MEP amplitude initially increased followed by and increase CSP duration. The findings of the thesis provide evidence that both HST and HYT caused a post-training ‘net increase’ in CSE (Latella et al. 2012) due to increased MEP amplitude and decreased CSP duration. A possible reason for these findings may be due to an increased responsiveness within the corticospinal tract, which suggests an increased efficacy of synapses between the corticospinal tract and motor neurons or increased motor-neuron excitability (Nuzzo et al. 2016a). Similar to the findings of Nuzzo et al. (2016a) assessing different isometric tasks, this effect was apparent with both HST and HYT protocols. The findings suggested that the increase in CSE observed across training modalities is a global response to fatiguing RT.
Furthermore, the findings of chapter 4 showed that there were no differences in the level of neuromuscular impairment between HST and HYT. Similar findings have been reported by Nicholson et al. (2014) comparing a (4 x 6 at 85% 1RM) or (4 x 10 at 70% 1RM) back squat protocol. Conversely Walker et al. (2012) showed a greater reduction in neuromuscular output (maximal isometric leg extension force) following 5 x 10 RM at 80% 1RM compared to 15x 1 RM at 100% 1 RM leg presses. The findings of the thesis and Nicholson et al. (2014) used protocols in which the repetition volume of the HST condition was between 41-60% of the HST condition compared to 30% by Walker et al. (2012). Given the current findings of the thesis, it is suggested that the difference in exercise volume between HST and HYT protocols may not be responsible for this effect above a certain percentage volume similarity between protocols. Rather, exercising at or near maximal repetition loading close to momentary muscular failure is likely to contribute to the impaired neuromuscular contractility observed post training (Behm et al. 2002). Similarly, the M\text{MAX} response did not significantly differ between HST and HYT. As previously discussed, changes in peripheral nerve excitability may be due to impairment of neuromuscular propagation, muscle fibre action potentials, changes within muscle contractile apparatus and reduced efficacy of the sodium/potassium pump (Nielsen & Clausen 2000; Kirkendall 1990; Mileva et al., 2012; Tucker et al. 2005; Deschenes et al. 1994; Bigland-Ritchie et al. 1986; Sandercock et al. 1985; Eererk & Kernell 1991). Therefore it is likely that these mechanisms rather than an accumulation of H+, adenosine di-phosphate and lactate expected to occur with higher training volumes (Behm et al. 2002; Cady et al. 1989; Favero et al. 1997) are the primary cause of M\text{MAX} impairment following HYT and HST.
In light of the results, and the novelty of the findings, that being the similarity of neurophysiological behaviour in response to HST and HYT, represents an important finding for understanding and implementation of RT practice. HYT is likely to impact neural mechanisms in much the same way that was conceptualised about HST. These early responses may reflect the neural adaptations reported in RT interventions (Latella et al. 2012; Hendy et al. 2014; Kidgell & Pearce 2010; Carroll et al. 2011; Selvanayagam et al. 2011) and so, the importance of responses in HYT protocols should be considered. These findings hold significant implications for our understanding of the impact of HYT on intra-cortical, corticospinal and peripheral neural outcomes in conjunction with evidence already available on strength training.
6.3. The nature of central vs peripheral fatigue with intermittent resistance training

The nature of fatigue and human performance has been a widely discussed topic (Noakes 2010; Noakes 2011; Enoka et al. 2012; Enoka et al. 2011; Enoka & Duchateau 2016; Gandevia et al. 2001; Gandevia et al. 2008; Froyd et al. 2016) with contributing central and peripheral mechanisms thought to occur following exercise. Further, fatigue has recently been portrayed as a combination of subjective and objective measures (Enoka & Duchateau 2016). For the purpose of this thesis, the discussion will focus on the objective nature of neurophysiological mechanisms which provide evidence for the locality of fatigue within the motor system following applied RT. In chapter 3, HST of the elbow flexors showed a decrease in the MEP, $M_{\text{MAX}}$ and MVIC with no accompanying intra-cortical changes. It was concluded from these observations that fatigue occurs primarily downstream of the M1. Similar reductions in CSE have been shown with and repetitive motor tasks (Zannette et al. 1995; Teo et al. 2012; Teo et al. 2013; Brasi-Neto 1994; Brasil-Neto 1993) with fatigue. However in a study by Gruet et al. (2014) the MEP amplitude was not shown to change with isometric tasks in the leg extensors and may reflect different motor task specific neuro-modulation of CSE.

In subsequent chapters, TMS testing conducted during a low-level voluntary isometric contraction and the introduction of super imposed twitch force assessment provided further evidence for underlying mechanisms of neurophysiological fatigue. Fatigue resulting in the reduction of MVIC and $M_{\text{MAX}}$
following HST and HYT which returned to within baseline levels by 6 hrs post-training appears to be 1) primarily peripheral in nature, and 2) specific to low threshold MUs. Contrary to the reductions in MVIC and $M_{\text{MAX}}$ a net increase in corticospinal drive was observed via an increased MEP amplitude and decreased CSP duration. These findings were in line with other recent neurophysiological investigations (Nuzzo et al. 2016a; Nuzzo et al. 2016b; Routsalainen et al. 2014; Hoffman et al. 2009) of an increased MEP amplitude during and acutely following resistance exercise. The increased responsiveness was likely due to the greater excitation of the corticospinal system during contraction or a central compensatory mechanism to generate the required motor output in lieu of the reduced force-producing capability of the muscle (Hoffman et al. 2009; del-Olmo et al. 2011; Marshall et al. 2015). The observed increase in MEP amplitude was supported in other studies (Nuzzo et al. 2016a; Routsalainen et al. 2014) who showed an acute increase in CSE following voluntary isometric muscular contractions and HYT of the elbow flexors. However, the findings of a shortened CSP have not been reported by other acute studies measuring corticospinal responses with resistance exercise (Routsalainen et al. 2014; Gruet et al. 2014). The mechanisms behind the observed reduction in CSP at this stage are unclear but were similar to neural adaptations shown by Latella et al. (2012), and those observed during skill acquisition and motor task performance (Tinazzi et al. 2003; Pearce et al. 2009) that may reflect a release of cortical inhibition (Christie & Kamen 2014) following RT of the lower limb. However as CSP was not measured in the elbow flexors we can only speculate at this stage that the same response would be observed following upper limb HST. Further, changes in intra-cortical facilitation and inhibition did not occur during the initial 2 hr period whereby CSE was increased, providing further evidence that
change in neuro-modulation with fatigue occur downstream of the M1. Coupled with the increased CSE and decreased $M_{\text{MAX}}$ and MVIC, the results provide strong evidence that these changes were associated with fatigue at the peripheral level, such as impairment of neuromuscular propagation, muscle fibre action potentials and changes within muscle contractile apparatus (Bigland-Ritchie et al. 1986; Sandercock et al. 1985; Eerbeck & Kernell 1991). Importantly, the observed net increase in CSE from chapter 4 and 5 do not support suggestions of central impairment occurring as proposed by super-compensation theory (Bompa & Haff 2009) and therefore fatigue should be viewed as a construct of the interaction of multiple physiological systems and at different levels in response to exercise (Noakes 2010; Noakes 2011).

In chapter 5 the SIT force was reduced at SIT$_{25}$ and SIT$_{50}$ for HST and HYT, but not impaired at SIT$_{75}$ or SIT$_{100}$ for either training condition. These findings are similar to Bigland-Ritchie (1986) who showed a decline of the twitch force during associated target forces of 30 and 50% MVC of the quadriceps group with fatigue and no associated change in VA or twitch force responses during maximal efforts. Reports of a reduced twitch force at submaximal contraction intensities have also been reported following endurance cycling exercise (Jubeau et al. 2014; O’Leary et al. 2015). The findings suggest that fatigue causes an impairment in neural drive of smaller, low threshold motor units rather than large, high-threshold MU’s (McNeil et al. 2011). Therefore, rather than quantifying these changes as a holistic approach to central fatigue (Taylor & Gandevia 2008) they are likely to be localised within the motor neuron pool. Low threshold MU are recruited during the initial stages of contraction and during times of low force requirements relative to
maximal contractions according to the size principle of MU recruitment (Henneman 1965). Thus an impairment of the efficacy of neural drive may reflect the contribution levels required by low threshold MUs during HST and HYT when training to repetition maximum. Interestingly the efficacy of the twitch force during maximal contraction efforts was not affected. Large, higher-threshold MUs are recruited secondly and during times of large changes in force (Henneman 1965). Bigland-Ritchie (1986) provided evidence that during fatigue of the quadriceps musculature produced by intermittent medium-intensity exercise the CNS remains capable of fully activating the associated muscle fibres. Nuzzo et al. (2016a) reported an increase in the super imposed twitch response after resistance isometric or concentric exercise in the elbow flexors. The authors concluded that acute strength training led to an increased efficacy of corticospinal-motorneuronal synapses or increased motor neuron excitability. This finding was contrary to reports of impaired VA following sustained maximal contractions after exercise (Taylor & Gandevia 2008; Gandevia et al. 1996; Gruet et al. 2014). Taylor and Gandevia (2008) suggested that during sustained maximal contractions motor neurons become less responsive to synaptic input. The results of chapter 5 are somewhat novel, with the measurement of the twitch force response at various contraction intensities following RT, which showed that fatigue causes an inhibitory effect within low threshold MUs or a decreased responsiveness of the corticospinal tract during submaximal contractions. Conversely, this inhibition appeared to be over ridden during maximal efforts either through maintaining the integrity within high threshold MUs or a release of inhibition along the corticospinal pathway in an attempt to maintain performance output.
Collectively, the findings support the idea that fatigue from applied HST or HYT occurs downstream of the M1. These mechanisms are suggested to be peripheral in nature with a concurrent reduction in efficacy of neural drive to low threshold MUs. The nature of training to a maximal RM may reflect the nature of higher intensity exercise efforts inducing greater peripheral fatigue (O’Leary et al. 2016) due to intramuscular metabolites impairing contractile function (Allen et al. 2008). These results suggest that central fatigue as proposed by super-compensation theory (Bompa & Haff 2009) requires re-consideration within applied RT settings and may only occur with longer exercise durations (Froyd et al. 2016).
6.4. Evidence for the prescription of resistance training variables

Collectively, the findings of this thesis suggest an altered time course of fatigue and recovery following HST and HYT. Based on the neurophysiological evidence provided by chapter 3 and 5, it may be that HST and HYT can be scheduled sooner than the 48-72 hrs currently recommended (Ratamess et al. 2009). This was evident by a shortened time course of neurophysiological and neuromuscular measures returning to baseline by 1 and 6-24 hrs in the upper and lower limbs respectively. To provide further rationale for these findings, studies investigating rates of protein synthesis (MacDougall et al. 1995; Phillips 1997; Chelsey et al. 1992), substrate depletion and acute hormonal responses to exercise (Walker et al. 2011) support the idea that post exercise physiological responses peak within a 24 hr period. From an applied exercise programming perspective, there is evidence to suggest that increased athletic performance may be elicited by short rest intervals between subsequent sessions. In particular, Cook et al. (2014) and Ekstrand et al. (2013) have shown that the benefits of strength training in the morning on subsequent strength, power or athletic performance 4-6 hrs later on the same day. Furthermore, applied training studies in elite strength athletes has demonstrated the benefits of high frequency training (6 days per wk) on powerlifting performance with an increase in strength double to that of the 3 d per wk group over 12 wks (Raastad et al. 2012). The distribution of training load may create more optimal conditions to produce effective training stimuli for the nervous system (Hakkinen & Kallinen 1994) and minimise the risk of overtraining in as demonstrated in Olympic weightlifters (Hartman et al. 2007). Although multiple factors can contribute to recovery and subsequent session performance the presented neurophysiological
findings of the thesis combined with physiological research strengthen the evidence supporting high frequency training.

The current recommendations suggested that HST and HYT practice should be treated as separate entities, with each training modality targeted for adaptation specific to either strength gains or increases in muscle mass. However, the findings of chapter 4 show similar neurophysiological responses between HST and HYT. The findings indicate that at training intensities of 60-75% of 1 RM within the hypertrophy range (Ratamess et al. 2009; Bompa & Haff 2009; Haff & Triplett 2016) can also have a significant effect on neural mechanisms. An important factor in this finding may be the nature of training to repetition maximum, whereby the associated fatigue responses as discussed earlier is a sufficient stimulus for changes in neuro-modulation.

Secondly, the short time course of fatigue and recovery from HST and HYT does not support previous applied literature (Bompa & Haff 2009; Baechle & Earle 2008; Ratamess et al. 2009). Currently, most guidelines recommend at least 48 and 72 hrs between subsequent sessions of HST and HYT respectively. These suggestions are largely based upon assumptions that neural fatigue occurs with HST and that this fatigue combined with performance reductions requires 2-3 days rest before the next training stimulus (Bompa & Haff 2009). However, the results from chapter 4 indicate that the neurophysiological time course cannot be differentiated between for each training modality, with the likely contributing factor being the training to repetition maximum.
Lastly, the transient changes in neuro-modulation are similar to those observed with the neural adaptations observed following RT interventions. Training intervention studies between of 2-8 wks (Hendy et al. 2014; Kidgell et al. 2010; Griffen & Caferelli 2007; Latella et al. 2012) have shown increases in corticospinal excitability and reduced intra-cortical and corticospinal inhibition, of which were observed following a single HST or HYT session. As suggested by Nuzzo et al. (2016a) these acute neural responses may provide the basis for longer term neural adaptations to occur with repeated training stimuli. Further, the underlying neural responses may hold important implications for the understanding of the importance of the nervous system in HYT adaptations, particularly in the acute and early stages of training. Consideration should be also be given by strength and conditioning professionals to the similarity of the shortened neurophysiological time course of fatigue and recovery between HST and HYT paradigms when planning the spatiality between subsequent RT sessions in applied athletic practice. Given other research on the rates of protein synthesis and endocrine responses (Phillips et al. 2002; Kim et al. 2005; MacDougall et al. 1995; Phillips 1997; Chesley et al. 1992; Walker et al. 2011), and applied studies on training frequency (Rastaad et al. 2012; Hartman et al. 2007), it may be feasible to consider the implementation of more frequent RT sessions to optimise neural and performance adaptations.
6.5. Limitations

Given that the approach of this thesis was to investigate the neurophysiological basis of super-compensation theory, several limitations must be acknowledged. Firstly, the scope of the findings was only translatable to the neurophysiological responses to HST and HYT, and does not provide support for other exercise modalities such as aerobic training as depicted by the current super-compensation model. Therefore, individual traits of each exercise modality would contribute to a “redevelopment” of the model and provide a holistic picture of different exercise responses. Furthermore, the findings present a shortened super-compensation time course with HST and HYT using variables recommended in current RT guidelines. However within session factors such as a greater volume (Narici et al. 2013) through the implementation of multiple exercises aimed at facilitating continual strength and hypertrophy ‘adaptations’ over time may effect the neurophysiological responses observed.

Secondly, the sample population represented healthy young recreationally trained adults that was conceived to be the most realistic demographic for comparison to super-compensation theory. It is likely that different population groups such as children or elderly, untrained or highly trained would show a different time course of super-compensation. Conversely the application of an unaccustomed training stimuli may yield a greater adaptive response for novice training individuals than highly trained groups or the exercise stimuli may induce DOMS leading to a slower time course of recovery. The time course and magnitude of the response may also
be slowed with age due to slower rates of protein synthesis and recovery from exercise. Furthermore, population was sampled as convenience sampling relying on participants within and who had easy access to the university which fitted the selection criteria. Although the sample size was similar to other studies investigating strength and neural responses from RT (Nuzzo et al. 2016a; Howatson et al. 2016) an increased sample size would have provided better power for the study and possibly yielded stronger results.

Contrary to the extrinsic limitations mentioned, several intrinsic methodological factors must also be acknowledged when interpreting the findings. RT requires many systems of the body to interact simultaneously. While we are confident that TMS and peripheral electrical stimulation provided a valid and robust method of assessing intra-cortical, corticospinal and peripheral nerve excitability it is important to that note that changes in glycogen stores, metabolite build-up (Johnston et al. 2016), endocrine responses (Walker et al. 2011) and muscle damage (Nosaka et al. 2003) are all affected by RT and can contribute to exercise performance. Hence, these systems may also play some part in post exercise neuromuscular output, fatigue and recovery. However, these physiological processes were outside the aims of the thesis.
6.6. Future directions

In light of the findings of this thesis, the comprehensive investigation of the super-compensation cycle from HST and HYT has provided new evidence for the acute neurophysiological responses and provided several recommendations regarding the application of RT in applied settings. The studies collectively suggest a shortened neurophysiological super-compensation cycle in response to RT and a similarity between the neurophysiological responses of HST and HYT. Due to the novelty of these findings and the predicted impact on applied practice several suggestions will be put forward regarding future research in this area.

Firstly the need for a multifaceted approach to understand the demographical characteristics of super-compensation is required. While the super-compensation theory offers a generalised idea of post exercise responses, it does not however take into consideration demographical characteristics such as training experience and age. Given that age-related declines in physical and cognitive function are well established (Runge et al. 2004; Gauthier et al. 2006; Rice and Barone 2000), the importance of appropriate exercise prescription, especially RT is required to combat these processes. The known benefits of RT in minimising age related decline in physical fitness and its ability to combat chronic diseases (Moritani & Akamatsu 2015; Ruiz-Montero & Castillo-Rodriguez 2016) warrants further investigation into acute RT response to optimise exercise programs. In a
performance setting, differences in recovery times and responses to different loading strategies for adolescent and young athletes may impact upon RT prescription that follows planning based upon the super-compensation cycle. Similarly, the concept may provide similar benefits when exploring differences between a novice and experienced athlete regarding session requirements for adaptation and spatiality between subsequent training stimuli.

Secondly, future research could aim to determine the plausibility of high frequency training on neurophysiological mechanisms. The concept of short recovery intervals between training session has showed positive outcomes as previously discussed on performance in acute conditions (Cook et al. 2014; Ekstrand et al. 2013) and longer term interventions (Rastaad et al. 2012; Storey et al. 2012) over traditional prescription methods. Given the current findings of a shorter neurophysiological time course of fatigue and recovery, an investigation into the effect of high frequency training regimes on neurophysiological outcome measures used in this thesis would provide further rationale for both these studies, and the efficacy of applied high frequency RT programs.

Lastly, the thesis investigated two typical RT protocols; HST and HYT based upon recommended guidelines. Although the intrinsic exercise parameters fall within the guidelines, an almost infinite number of training variables can, and are often manipulated in an attempt to optimise training responses (Behm et al. 2002; Marshall et al. 2011; Walker et al. 2012; Howatson et al. 2016). Given that the manipulation of training variables used in previous research; high vs low volume
(Behm et al. 2002), loading intensity (Walker et al. 2012), single vs multiple training set (Galvao & Taaffe 2004), rest period duration, movement velocity/contraction tempo, exercise selection (Howatson et al. 2016) and the concurrent use of different training modalities (i.e. Strength and endurance), (Cadore et al. 2012), can induce specific responses and adaptations, systematic investigation into manipulation of each within training variable is warranted. Further research in this area will provide strength and conditioning coaches and athletes detailed understanding of the impact RT-based program design on optimising acute neurophysiological responses.
6.7. Conclusion

Collectively, the findings from this thesis suggest that the time course of neurophysiological super-compensation following RT in the upper and lower limbs was shorter than previously suggested. Secondly, the fatigue response appeared to be modulated primarily outside of the M1 with reduced efficacy of neural drive within low threshold MUs. Importantly, no differences in neurophysiological responses were observed between HST and HYT. These findings indicate that 1) the upregulation in CSE is an attempt to attenuate the occurrence of sub-spinal and peripheral fatigue from RT, 2) low threshold MUs are fatigued during RT and 3) the prescription of subsequent HST and HYT sessions may be scheduled sooner than previously thought with no difference in the spatiality of each modality. These findings may be particularly useful in the application RT programming and applied practice for athletic and performance settings.
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Appendices

Appendix (a) TMS safety screening questionnaire

Appendix (b) Participant health screening questionnaire

Appendix (c) Participant information questionnaire

Appendix (d) Edinburgh handedness questionnaire

Appendix (e) Waterloo Footedness questionnaire- revised

Appendix (f) Statement of ethical approval

Appendix (g) Proposed revised model of super-compensation following RT
a)

Transcranial Magnetic Stimulation” (TMS) Adult Safety Screen

Name:
Date:
Age:

Please answer the following:

Have you ever:

Had an adverse reaction to TMS? ☐Yes ☐No
Had a seizure? ☐Yes ☐No
Had an electroencephalogram (EEG)? ☐Yes ☐No
Had a stroke? ☐Yes ☐No
Had a serious head injury (include neurosurgery)? ☐Yes ☐No
Had any other brain-related condition? ☐Yes ☐No
Had any illness that caused brain injury? ☐Yes ☐No

Do you have any metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork? ☐Yes ☐No
Do you have any implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines? ☐Yes ☐No
Do you suffer from frequent or severe headaches? ☐Yes ☐No
Are you taking any medications? ☐Yes ☐No
HEALTH SCREENING QUESTIONNAIRE

Responses to this semi-structured questionnaire will be kept strictly confidential.

The responses from this questionnaire will provide the investigators with appropriate information regarding your health history in relation to this project.

PARTICIPANT ID NO.: .........................  AGE: ...... (yrs)  GENDER: ........
BODY MASS: ............ (kg)  HEIGHT: ............ (cm)

Are you currently undertaking any form of regular exercise?  YES  NO

If yes, briefly describe the type and amount (i.e. frequency, duration) of exercise you perform.

Have you ever suffered any musculoskeletal injury?  YES  NO  UNKNOWN
If YES, please elaborate:

Have you ever suffered any concussion injury?  YES  NO  UNKNOWN
If YES, please elaborate:

Are you currently on any medication?  YES  NO
If YES, please describe:

Have you ever suffered any psychiatric illness?  YES  NO  UNKNOWN
If YES, please outline:

Is there any other reason which you know of that would prevent you from undertaking the proposed tests?  YES  NO
If YES, please elaborate:

I believe the information I have provided to be true and correct.

SIGNED: ..................................................  DATE: ..........................
c)

SUBJECT INFORMATION

Subject Details

Subject Name:

Address: __________________________________________________________

Ph: ___________________________ Sex: ___________________________

DOB: ___________________________ Occupation: ___________________________

Ethnic Background: ___________________________

Background information

Do you suffer from any known neurological disorders?

_____________________________________________________________________

Are you currently taking any medication which influences nerve conduction or blood clotting? If so, what?

_____________________________________________________________________

Do you regularly drink beverages containing caffeine? If so, how many cups per day?

_____________________________________________________________________

Which hand do you use for most daily activities when using only one?

_____________________________________________________________________

Are you involved in regular physical activity requiring the use of your hands/arms? If so, what is the activity/activities, the intensity and time commitment?

Activity:

Intensity: __________________________________________________________

Hours per week: _____________________________________________________

Months per year: _____________________________________________________
**Edinburgh Handedness Inventory**

Your Initials: __________

Please indicate with a check (✓) your preference in using your left or right hand in the following tasks.

Where the preference is so strong you would never use the other hand, unless absolutely forced to, put two checks (✓✓).

If you are indifferent, put one check in each column (✓ | ✓).

Some of the activities require both hands. In these cases, the part of the task or object for which hand preference is wanted is indicated in parentheses.

<table>
<thead>
<tr>
<th>Task / Object</th>
<th>Left Hand</th>
<th>Right Hand</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Writing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Drawing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Throwing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Scissors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Toothbrush</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Knife (without fork)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Spoon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Broom (upper hand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Striking a Match (match)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Opening a Box (lid)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total checks: LH = RH =

Cumulative Total: CT = LH + RH =

Difference: D = RH – LH =

Result: R = (D / CT) × 100 =

Interpretation:
- (Left Handed: R < -40)
- (Ambidextrous: -40 ≤ R ≤ +40)
- (Right Handed: R > +40)

---

Instructions: Answer each of the following questions as best you can. If you always use one foot to perform the described activity, circle Ra or Lu (for right always or left always). If you usually use one foot circle Ru or Lu, as appropriate. If you use both feet equally often, circle Eq.

Please do not simply circle one answer for all questions, but imagine yourself performing each activity in turn, and then mark the appropriate answer. If necessary, stop and pantomime the activity.

1. Which foot would you use to kick a stationary ball at a target straight in front of you? La Lu Eq Ru Ra
2. If you had to stand on one foot, which foot would it be? La Lu Eq Ru Ra
3. Which foot would you use to smooth sand at the beach? La Lu Eq Ru Ra
4. If you had to step up onto a chair, which foot would you place on the chair first? La Lu Eq Ru Ra
5. Which foot would you use to stomp on a fast-moving bug? La Lu Eq Ru Ra
6. If you were to balance on one foot on a railway track, which foot would you use? La Lu Eq Ru Ra
7. If you wanted to pick up a marble with your toes, which foot would you use? La Lu Eq Ru Ra
8. If you had to hop on one foot, which foot would you use? La Lu Eq Ru Ra
9. Which foot would you use to help push a shovel into the ground? La Lu Eq Ru Ra
10. During relaxed standing, people initially put most of their weight on one foot, leaving the other leg slightly bent. Which foot do you put most of your weight on first? La Lu Eq Ru Ra
11. Is there any reason (i.e. injury) why you have changed your foot preference for any of the above activities? YES NO (circle one)
12. Have you ever been given special training or encouragement to use a particular foot for certain activities? YES NO (circle one)
13. If you have answered YES for either question 11 or 12, please explain:
Memorandum

To: Dr Wei-Peng Teo
    School of Psychology

B

From: Deakin University Human Research Ethics Committee (DUHREC)

cc: Mr Christopher Latella

Date: 21 July, 2015

Subject: 2013-198

Measuring the time-course corticospinal responses following one strength training session

Please quote this project number in all future communications.

The modification to this project, submitted on 9/07/2015 has been approved by the committee executive on 21/07/2015.

Approval has been given for Mr Christopher Latella, under the supervision of Dr Wei-Peng Teo, School of Psychology, to continue this project as modified to 20/11/2017.

The approval given by the Deakin University Human Research Ethics Committee is given only for the project and for the period as stated in the approval. It is your responsibility to contact the Human Research Ethics Unit immediately should any of the following occur:

- Serious or unexpected adverse effects on the participants
- Any proposed changes in the protocol, including extensions of time.
- Any events which might affect the continuing ethical acceptability of the project.
- The project is discontinued before the expected date of completion.
- Modifications are requested by other HRECs.

In addition you will be required to report on the progress of your project at least once every year and at the conclusion of the project. Failure to report as required will result in suspension of your approval to proceed with the project.

DUHREC may need to audit this project as part of the requirements for monitoring set out in the National Statement on Ethical Conduct in Human Research (2007).

Human Research Ethics Unit
research-ethics@deakin.edu.au
Telephone: 03 9251 7123