The effects of muscle mass, digoxin and high-intensity interval training on arterial and venous [K^+], excitability and fatigue during and after intense exercise

Submitted by

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B.Sc (Hons), M.Sc

2019

A thesis submitted in fulfilment of the requirements for the degree

Doctor of Philosophy

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ABSTRACT

Potassium (K^+) regulation during exercise is vital in preserving muscle membrane excitability, a failure of which has been linked to muscle fatigue. This thesis investigated the regulation of arterial and venous plasma K^+ concentration ($[K^+]$) during and following intense exercise and its importance for exercise performance, muscular force and excitability via three interventional studies, comparing two- versus one-legged cycling (Study 1), acute oral digoxin versus placebo intake (Study 2), and high-intensity intermittent training versus non-training control (Study 3).

Study 1. The effects of different contracting muscle mass were investigated on arterial and venous plasma $[K^+]$, fatigability and muscle torque following exhaustive two- versus one-legged high-intensity intermittent cycling exercise. Eleven recreationally active adults performed two- (2L) and one-legged (1L) trials, which comprised cycling for six, 2 min repetitions at 80% $\dot{V}O_{2peak}$, then at 90% $\dot{V}O_{2peak}$ continued to fatigue. Radial arterial (a) and antecubital venous (v) plasma $[K^+]$ ($[K^+]_a$, $[K^+]_v$, respectively) were measured prior to and during exercise bouts, and for 30 min recovery. The quadriceps maximal isometric voluntary contraction (MVC), as well as potentiated quadriceps twitch force ($Q_{tw,pot}$), doublet and tetani (20 Hz) and vastus medialis (VM) and vastus lateralis (VL) M-wave (amplitude, duration and area) evoked via magnetic stimulation, were measured prior to exercise, 1 min after exercise bouts 1, 3 and 6, and up to 30 min in recovery. Plasma $[K^+]_a$ increased throughout exercise ($P < 0.05$, time main effect), being greater in 2L than 1L ($P < 0.05$, treatment main effect) and with $[K^+]_a$ being greater in 2L than 1L during 90% $\dot{V}O_{2peak}$ after 2 min and at fatigue, reaching 6.03 ± 0.58 vs 5.21 ± 0.52 $mmol.1^{-1}$ at fatigue for 2L and 1L, respectively ($P < 0.05$). Plasma $[K^+]_v$ increased at fatigue for 2L and 1L, reaching 5.98 ± 0.64 and 5.34 ± 0.43 $mmol.1^{-1}$ respectively, but did not differ significantly between trials. The $[K^+]_{a-v}$ difference across the inactive forearm was higher throughout exercise to fatigue ($P < 0.05$, time main effect) and

was greater in 2L than 1L (treatment main effect, $P < 0.05$). Plasma $[Lac^-]_a$ increased throughout exercise, reaching 7.40 ± 1.74 and 5.28 ± 1.12 $mmol.1^{-1}$ at fatigue for 2L and 1L, respectively ($P < 0.05$), with 2L greater than 1L during recovery at 2-30 min ($P < 0.05$). The MVC was decreased after exercise and in recovery ($P < 0.05$, time main effect), falling at fatigue ($P < 0.05$) by 17% for 2L (rest 135 ± 59 vs. fatigue 112 ± 57 Nm) and by 26% for 1L (rest 144 ± 57 vs. fatigue 107 ± 63 Nm). Each of the evoked $Q_{tw,pot}$, doublet and 20 Hz torque declined after fatigue and remained depressed at 30 min recovery ($P < 0.05$, time main effect), with $Q_{tw,pot}$ less in 1L than 2L at 30 min recovery ($P < 0.05$). The twitch M-wave amplitude declined throughout exercise and recovery, whilst duration was extended after fatiguing exercise, in both VM and VL ($P < 0.05$, time main effect), with area also reduced after fatigue only in VM ($P < 0.05$); there were no significant differences between 1L and 2L. In conclusion, exercise with a large contracting muscle mass augmented $[K^+]_a$, suggesting a greater K^+ release from contracting muscles. The greater $[K^+]_{a-v}$ across the forearm in 2L cycling suggests also greater K^+ uptake by inactive muscle, probably via activation of muscle Na^+,K^+-ATPase. Nonetheless, plasma $[K^+]$ was tightly regulated during intense exercise, with only relatively small differences evident between trials, despite substantially differing contracting muscle mass. Despite elevated $[K^+]_a$, 2L was accompanied by lesser percentage declines in MVC compared to 1L exercise; whilst the M-wave characteristics give some evidence of excitability changes with fatigue, but with minimal differences between trials. Thus, the slightly greater $[K^+]_a$ disturbances during cycling to fatigue with 2L than 1L exercise, were not accompanied by greater post-exercise reductions in muscle torque and changes in M-wave characteristics.

Study 2. The effects of acute digoxin intake on K^+ regulation, muscle performance, muscle excitability, and fatigability were investigated in ten recreationally active adults, in a randomised, crossover, double-blind, counterbalanced study design. Ten healthy adults received orally 0.50 mg digoxin or placebo 60 min prior to cycling exercise, which was 1

min at 60% $\dot{V}O_{2peak}$ and at 95% $\dot{V}O_{2peak,}$ then continued at 95% $\dot{V}O_{2peak}$ until fatigue. Radial arterial (a) $[K^+]$ ($[K^+]_a$) was measured pre-exercise, during exercise and for up to 60 min recovery. Quadriceps MVC, as well as muscle torque ($Q_{tw,pot}$, doublet and 20 Hz tetani) and M-wave characteristics (amplitude, duration and area) evoked via magnetic stimulation were measured pre-exercise, 1 min following exercise and for 60 min recovery. Serum digoxin concentration at 60 min post-ingestion was 3.36 ± 0.8 nM (mean ± SD) in digoxin and less than the detectable level of 0.2 nM in placebo. Time to fatigue was 7.8% shorter during digoxin than placebo ($P < 0.05$). Plasma $[K^+]_a$ increased during exercise and decreased early in recovery, being lower than baseline at 3-20 min recovery ($P < 0.05$, time main effect). During digoxin, plasma $[K^+]_a$ was slightly greater than placebo (4.93 ± 0.2 vs. 4.88 ± 0.2, respectively) and the post-exercise $[K^+]_a$ decline was less (both $P < 0.05$, treatment main effect). After exercise, the MVC torque, $Q_{tw,pot}$, doublet and 20 Hz tetani (percentage pre-exercise) each decreased 1 min after fatigue and remained less than baseline at 60 min post-exercise ($P < 0.05$, time main effect) but did not differ between trials. Following exercise to fatigue the M-wave characteristics demonstrated variability between muscles and with time; amplitude was increased post-exercise in VL, duration increased at 60 min recovery in both VL and VM, whilst area increased at 60 min recovery in VM and 10 min post-exercise in VL ($P < 0.05$, treatment main effect). In VL, duration was greater with digoxin than placebo at fatigue ($P < 0.05$). Thus digoxin impaired cycling exercise performance to fatigue, with a slight increase in $[K^+]_a$ but did not affect the fatigue-induced reductions in MVC, evoked torque or M-wave characteristics, other than a prolonged M-wave duration in VL. Hence, although plasma $[K^+]$ was increased and fatigability during cycling lessened with digoxin, it was not possible to conclude that acute digoxin treatment is linked to worsened muscle excitability.

Study 3. The effects of High Intensity Interval Training (HIIT) were investigated on plasma $[K^+]_a$ and $[K^+]_v$, muscle performance and muscle excitability Sixteen healthy adult participants

were randomly allocated to training (HIIT, n = 8) or control (CON, n = 8). Exercise testing comprised a 2 min cycling bout at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, then followed by two 30s maximal sprints, separated by 120 s; these tests were repeated Pre and Post HIIT and CON. Radial arterial (a) and antecubital venous (v) blood samples were measured prior to and during exercise bouts, and in recovery for 60 min. Quadriceps MVC, and the potentiated quadriceps twitch force ($Q_{tw,pot}$), doublet and tetani (20 Hz) and the vastus medialis (VM) and vastus lateralis (VL) M-wave (amplitude, duration area) evoked via magnetic stimulation, were measured prior to exercise, 1 min after 80% $\dot{V}O_{2peak}$, after sprint exercise bouts, and for 60 min recovery. HIIT comprised repeated 30 s sprints during 3 sessions per week for 7 weeks. Plasma $[K^+]_a$ was increased above rest during 60% and 80% $\dot{V}O_{2peak}$ exercise and returned to resting values at 2 min recovery, for both HIIT and CON ($P < 0.05$, time main effect). There was no trial main effect for $[K^+]_a$. For HIIT, there was a significant trial x time interaction, with lower $[K^+]_a$ evident at Post compared to Pre during 80% $\dot{V}O_{2peak}$ and at 1 min recovery after the sprint bouts ($P < 0.05$). Plasma $[K^+]_v$ increased during 60% $\dot{V}O_{2peak,}$ 80% $\dot{V}O_{2peak}$ exercise and the two sprint bouts ($P < 0.05$, time main effect) and was slightly above rest late in recovery ($P < 0.05$, time main effect); there was no trial main effect for $[K^+]_v$. There were significant trial x time interactions with higher $[K^+]_v$ Post than Pre at fatigue for HIIT ($P < 0.05$) and 1 min recovery for CON ($P < 0.05$). The $[K^+]_{a-v}$ difference across the forearm was increased with submaximal and sprint exercise for both HIIT and for CON ($P < 0.05$,time main effect). Plasma $[K^+]_{a-v}$ did not differ between trials. The peak power, total work and fatigue index were unchanged after HIIT. Sprint performance during the four 30 s sprints of the last training session after HIIT was unchanged compared to the first training session. There were decreases for all torque values with fatigue and also changes in M-wave characteristics (amplitude, duration and area). For MVC, there was no trial main effect, although MVC during HIIT was greater than CON after the first sprint bout (88 ± 9 vs. 65 ± 14% pre-exercise MVC, respectively, $P < 0.05$, trial x time

interaction). For each of the quadriceps twitch, doublet and 20 Hz tetani torque or M-wave characteristics, there were no differences between trials. Thus, whilst HIIT improved K^+ regulation with submaximal exercise and after two sprint bouts, this did not result in corresponding improvements in muscle voluntary and evoked contractile performance and muscle excitability.

In conclusion, this thesis investigated the effects of differences in the active muscle mass, acute digoxin treatment and HIIT, on each of K^+ regulation, muscle performance, muscle excitability and fatigue in humans. Plasma $[K^+]_a$ increased during exercise then decreased early in recovery, with elevations in plasma $[K^+]_a$ during 2L compared to 1L cycling, and in digoxin compared to placebo, lower $[K^+]_a$ after HIIT during sub-maximal exercise and 1 min after sprint exercise. Interestingly, the MVC torque decline was less for 2L than 1L and for HIIT Post compared to Pre, whilst no difference was found between digoxin and placebo trials. The time to fatigue showed no significant difference between trials during the active muscle mass study but was 7.8% shorter for digoxin than placebo. Whilst considerable variability was evident in M-wave measures, there is evidence to suggest impaired muscle excitability after exercise. Thus, greater active muscle mass, acute digoxin and HIIT interventions that differentially affected K^+ regulation during and after exercise did not show corresponding changes in muscle voluntary or evoked torque or excitability after exercise.

DECLARATION

I, Trevor Michael Farr, declare that the Doctor of Philosophy thesis entitled, '*The effects of muscle mass, digoxin and high-intensity interval training on arterial and venous [K^+], excitability and fatigue during and after intense exercise',* is no more than 100,000 words in length, exclusive of tables, figures, appendices, references and footnotes. This thesis contains no material that has been submitted previously, in whole or in part, for the award of any other academic degree or diploma. Except where otherwise indicated, this thesis is my own work.

Signature  Date 20/4/2019

ACKNOWLEDGEMENTS

This PhD thesis is the product of an exciting and challenging journey, which would not have been possible without the contributions of many caring and skilful individuals.

Firstly, my PhD thesis is dedicated to my partner Sharyn and my children, Cooper and Rosie as it would not have been possible without their love, support, strength and inspiration. I am eternally grateful and indebted to them for their patience and understanding as they have endured many sacrifices; “it has not been easy but we got there” thank you for the strength you have given me. I also wish to express my sincere thanks to my parents, Arthur and Beverley, who gave me the impetuous to seek out my dreams whilst providing their unconditional love and support. To my sisters, Leanne and Jan, I thank you for your support, encouragement and understanding during difficult times and providing the magnificent accommodation and fun times when we stayed with you during our holidays in Queensland.

On a professional note, I wish to acknowledge Professor Michael McKenna for his expert knowledge, advice, support and encouragement in the preparation of my thesis. I also thank you for your compassion, patience and friendship during this journey. I have learnt many aspects associated with research but none more important than the need to hold one-self to the highest standards, attention to detail, dedication and creating a passion for exploration.

I extend my appreciation to Dr Aaron Petersen for his expert assistance throughout this project.

I extend my sincere gratitude to Dr Francois Billaut for his expert knowledge and support in the muscle stimulation and data collection, including his feedback on Chapter 3. I would also like to acknowledge Mr Brad Gatt for his friendship, support and encouragement, Jessica Meilak, Collene Steward and Samantha Cassar for their friendship and technical support in the laboratory. A special thank you to Ian Fairweather for his technical expertise in developing the computer hardware and software that was critical to the success of incorporating stimulation and M-wave methods. I wish to acknowledge Muath Altarawneh for his assistance and

friendship throughout my PhD which will always be remembered with great fondness and appreciation. It is acknowledged that Tania Atanasovska collaborated with me on the digoxin study and that the K^+ and cycle exercise data were shared. Finally, to those subjects who participated in my research projects I extend my sincere appreciation and gratitude as this project would not have been possible without your assistance. Thank you to the PhD candidates in the IHES office for their contribution to my thesis and for their assistance during trials, including sharing their expert knowledge and guidance. I wish all a memorable and happy journey through life.

ABBREVIATIONS

Subscript		Units
i	intracellular	
e	extracellular	
I	interstitial	
E_M	Membrane potential	
a	Arterial	
v	Venous	
a-v	Arterio-venous difference	

Electrolytes

K^+	Potassium ion	
mM		
Na^+	Sodium ion	mM
Cl^-	Chloride ion	mM
Ca^{2+}	Calcium ion	mM
Mg^{2+}	Magnesium ion	mM
Lac^-	Lactate ion	mM
[ ]	Concentration	
Δ $[K^+]$	rise in plasma $[K^+]$ from rest	mM
Δ$[K^+]$.work^{-1} ratio	rise in $[K^+]$ relative to work done	nmol.L^{-1}J^{-1}

Acid-Base

pH	Measure of acidity	

Cardiovascular

HR	Heart rate	beats.min^{-1}
rating of perceived exertion	RPE	scale (6-20)
$\dot{V}O_2$	Oxygen consumption	l.min^{-1}
$\dot{V}CO_2$	Carbon dioxide output	l.min^{-1}
$\dot{V}O_{2peak}$	Peak absolute oxygen consumption	l.min^{-1}

Muscle

E_m	resting muscle membrane potential	
P_i	inorganic phosphate ion	
t-tubules	transverse tubules	

Haematology & Fluid Shifts

Hb	Haemoglobin	g.dl^{-1}
Hct	Haematocrit	%
ΔPV	Change in plasma volume	%

ΔBV	Change in blood volume	%

Work & Power

PO	Power output	Watts

Experimental interventions

1L	1 leg cycling
2L	2 leg cycling
CON	Control (placebo)
DIG	Digoxin treatment
HIIT	High Intensity Interval Training Group

Other

CV	Coefficient of variation
ATP	Adenosine triphosphate
CSA	cross-sectional area
wk	weeks

LIST OF PRESENTATIONS

Farr T.M, Petersen A.C, and McKenna M.J. Effects of contracting muscle mass on arterial plasma [K^+] and fatigue during exercise. *Australian Physiological Society, Proceedings 152P, 2013, Geelong, Australia.*

Farr T.M, Petersen A.C, Smith R, and McKenna M.J. Effects of contracting muscle mass on arterial and venous plasma [K^+], muscle excitability and fatigue during high-intensity cycling. *Sports Medicine Australia, Abstract 19 e67-68, 2015, Gold Coast, Australia.*

Farr T.M, Petersen A.C, and McKenna M.J. Effects of contracting muscle mass on arterial plasma [K^+], muscle excitability and fatigue during high-intensity cycling. *Victoria University; Higher Degree by Research Student Conference, 2015, Melbourne, Australia.*

Farr T.M, Petersen A.C, and McKenna M.J. The effects of an acute oral dose of digoxin on plasma K^+ regulation, muscle performance and muscle excitability during and following high-intensity cycling in healthy. *Sports Medicine Australia, Abstract 20S e17, 2016, Melbourne, Australia.*

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CHAPTER 1

Introduction

In skeletal muscle, exercise causes an increase in interstitial potassium concentration ($[K^+]_I$) as a result of K^+ efflux from skeletal muscle (Medbø and Sejersted 1990, Green S, Langberg H et al. 2000, Juel, Pilegaard et al. 2000). A rapid increase in plasma $[K^+]$ then occurs, with the excess K^+ cleared once exercise ceases (Carlsson, Fellenius et al. 1978, Sejersted, Medbo et al. 1984, Raja 2006, Allen, Lamb et al. 2008a). Arterial plasma $[K^+]$ has been shown to increase to a peak of 8 mM during intense cycling exercise (Vøllestad, Hallén et al. 1994). However, during single knee extensor exercise, the mean plasma $[K^+]_a$ increased to only 5.81 mM (Juel 1990). During high-intensity exercise, peripheral fatigue may result from gradual changes in muscle membrane depolarisation and reduced excitability (Sjøgaard, Adams et al. 1985, Juel 2000).

The sodium potassium ATPase (Na^+,K^+-ATPase) is vital in regulating intra- and extra-cellular sodium concentration ($[Na^+]$) and $[K^+]$. The Na^+,K^+-ATPase are mainly located in the sarcolemma and t-tubular system, and are critical in maintaining transmembrane $[Na^+]$ and $[K^+]$ gradients and membrane excitability, impairment of which has been linked with fatigue (Fowles, Green et al. 2002, Fraser, Li et al. 2002, Aagaard, Andersen et al. 2003). In isolated muscles, contractile endurance depends in part on Na^+,K^+-ATPase, where sufficient activation of the Na^+,K^+-ATPase protects muscle excitability, contractility and against fatigue (Clausen 2003a).

Changes in muscle contractile properties and excitability (i.e., sarcolemmal) after exercise can be assessed by changes in muscle force and relaxation, and in the compound muscle action potential characteristics, which have been shown to be perturbed with fatigue (Bigland-Ritchie, Furbush et al. 1986, Garland and McComas 1990, Behm and St-Pierre 1997). Previous studies have investigated the relationships between plasma $[K^+]$, muscle excitability and fatigue during

voluntary exercise in humans (West 1996, Fowles, Green et al. 2002). Following an isometric quadriceps contraction at an intensity at 30% of MVC for 3 min, femoral venous [K^+] increased by 1.9 mmol.L^{-1}, although there was no loss of muscle membrane excitability during the period of increased extracellular [K^+], with the M-waves actually potentiated early in the recovery phase (West 1996). This was consistent with an earlier finding suggesting elevated Na^+,K^+-ATPase activity increased muscle M-waves in exercised muscles (Hicks and McComas 1989). Conversely, a decrease in Na^+,K^+-ATPase activity was shown to be associated with fatigue in numerous studies (McKenna, Bangsbo et al. 2008) and also with indications of a loss of excitability following isometric leg exercise. Fowles, Green et al. (2002), showed post-exercise M-wave amplitude, area (vastus medialis) and K^+-stimulated 3-*O*-methylfluorescein phosphatase (3-*O*-MFPase) activity (a marker of Na^+,K^+-ATPase activity) were decreased by 25-38% whilst maximal voluntary contraction force decreased by 30–55%, and failed to recover by 4 h (Fowles, Green et al. 2002). However, Changes in circulating extracellular [K^+] during intense dynamic exercise and post-exercise reductions in muscle voluntary and evoked torque, and excitability measured by M-waves, have been studied sparsely and are a major focus of this thesis.

During exercise involving large muscle mass, the increase in plasma $[K^+]_a$ is greater than in studies in which small muscle mass exercise has been utilised (Vøllestad, Hallén et al. 1994, Sostaric, Goodman et al. 2005). Consequently, utilising a large active muscle mass is potentially a way of elevating circulating [K^+] and studying the associated exercise effects on muscle function and fatigue, and the relationship of [K^+] with muscle force and M-waves. This is investigated in Study 1 in this thesis.

Digoxin is a specific inhibitor of the Na^+,K^+-ATPase and is extracted from the foxglove plant (Hollman 1996). It is commonly used in the treatment of arterial fibrillation and sometimes also in heart failure. In patients with severe heart failure, digoxin bound to and inhibited ~13%

of Na^+,K^+-ATPase in skeletal muscle and exacerbated muscle K^+ loss during exercise, contributing to early muscle fatigue (Schmidt, Bundgaard et al. 1995). Therefore, Na^+,K^+-ATPase function is likely to be important for skeletal muscle performance also in healthy individuals (Clausen 2003a, McKenna, Bangsbo et al. 2008). However, the effects of digoxin on exercise performance, potassium and post-exercise muscle function in healthy individuals are not well known and are investigated in Study 2.

Fatigue may be reduced and potassium homeostasis enhanced as a result of exercise training. For example, following a high intensity, 7 week cycle sprint training, work output during 30 second sprints increased by 11%, whilst plasma [K^+] was 19% lower and the rise in plasma [K^+] relative to work output was 27% lower (McKenna, Schmidt et al. 1993). Surprisingly, however, no study has directly determined the effects of training on elevated [K^+] during whole body exercise together with the acute changes in peripheral contractile and M-wave properties. This is investigated in Study 3.

Thus, one of the key areas unresolved in this field of investigation is the careful documentation of [K^+] during intense exercise together with muscle contractile properties and excitability. Therefore, this thesis investigated the effects of high-intensity exercise on circulating [K^+], muscle torque, excitability and fatigue. This was examined utilising three interventional studies which investigated the effects of: 1) increased exercising muscle mass, 2) the cardiac glycoside drug digoxin; and 3) high intensity interval training.

CHAPTER 2

Literature Review

This short literature review explores K^+ dynamics during and following high-intensity exercise, including the consequent effects of K^+ on muscle excitability and the decline in exercise performance due to fatigue. The review comprises three sections, which focus on the effects of: I) the contracting skeletal muscle mass; II) the cardiac glycoside digoxin; and III) high-intensity exercise training, on K^+ regulation during and after exercise and implications for muscle excitability, function and fatigue.

Section I: The effects of contracting skeletal muscle mass on K^+ regulation, and implications for muscle excitability, function and fatigue

2.1 Overview of neuromuscular processes

The neuromuscular system enables rapid internal communication that allows voluntary and involuntary muscle movement, coordinating the inherent excitability of nerves and muscle cells (Lieber 1992). Therefore, the neuromuscular system is vital for human movement and maintaining homeostasis. The nervous system can be described as divided into two main categories, central and peripheral (Catala and Kubis 2013). The central nervous system includes the brain and spinal cord, whereas the peripheral nervous system consists of the nerve cells distal to this (Gandevia 2001). The peripheral nervous system can be further subdivided into two sections, the sensory division and the motor division (Catala and Kubis 2013) and is comprised of motor neurons in the spinal cord, sensory neurons in the dorsal root ganglion, and skeletal muscle fibres (Lieber 1992, Gandevia 2001, Catala and Kubis 2013). The sensory division is responsible for transmission of neural impulses from sensory organs (receptors) to the central nervous system. These sensory nerve fibres, afferent fibres, conduct information

towards the central nervous system (Gandevia 1998). The motor portion of the peripheral nervous system can be further divided into the somatic division, which innervates skeletal muscle, and autonomic motor division which innervates involuntary effector organs such as smooth muscle. The motor nerve fibres that conduct impulses away from the central nervous system are the efferent fibres (Carson and Buick 2019). The muscle spindles and Golgi tendon organs are sensory organs in skeletal muscle that detect changes in the muscle fibre length and tension (Gandevia 2001). The information is conveyed by electrical impulses propagating along sensory fibres of dorsal root ganglion neurons, which, in turn, innervate motor neurons in the spinal cord (Gandevia 2001).

Motor neurons in the spinal cord receive synaptic inputs from the brain to perform voluntary movements (Del Vecchio, Germer et al. 2019). Electrical impulses triggered from the motor neuron propagate along the motor axon and result in the release of the neurotransmitter acetylcholine from the motor nerve terminal at the neuromuscular junction (Hellsten, Krustrup et al. 2009, Nishimune and Shigemoto 2018). Acetylcholine binds to acetylcholine receptors results in the opening of sodium channels, thereby depolarising the muscle membrane potential (Hille 2001). The membrane depolarisation triggers the release of calcium ions from internal stores in the sarcoplasmic reticulum that leads to a cascade of events resulting in muscle contraction (MacIntosh 2012).

2.2 Excitation-contraction coupling in skeletal muscle

Skeletal muscle contractions are activated when action potential (AP) are generated and propagated along the outer cell membrane, known as the sarcolemma (Figure 2.1). An AP consists of an initial depolarisation phase, from a resting membrane potential (E_m) of around -80 mV to 0 mV, then an overshoot phase where E_m increases to +30 mV, followed by a repolarisation phase, where E_m returns to its resting value. The depolarisation and overshoot

phases are influenced by Na^+ influx via voltage-sensitive Na^+ channels (N_{av}), whilst the repolarisation phase involves K^+ efflux via voltage-sensitive K^+ channels (Sejersted and Sjøgaard 2000, Hille 2001, Clausen 2003a). Thus, an AP is produced by a rapid and large influx of Na^+ via the Na^+ channels, immediately followed by an efflux of K^+. The capability to sustain repeated AP is dependent on the capacity to counter these Na^+/K^+ fluxes associated with each AP. Active transport of Na^+/K^+ is mediated by the membrane-bound Na^+,K^+-ATPase, that uses the energy from ATP hydrolysis to transport 3 Na^+ ions out of the cell and 2 K^+ ions into the cell. Insufficient Na^+,K^+-ATPase activity during muscle contractions is likely to result in a decrement in Na^+ and K^+ gradients, causing an impairment of membrane excitability (Green 2004, McKenna, Bangsbo et al. 2008). In skeletal muscle, Na^+ and K^+ exchange across the membrane of sarcolemma and t-tubules via numerous transport systems and ion channels, with passive movements of Na^+ and K^+ are counterbalanced by the Na^+, K^+-ATPase (Figure 2.1). The voltage-sensitive Na^+ channels and four different K^+ channels mediate the passive fluxes of these ions (Hille 2001).

Skeletal muscle cells are surrounded by a membrane called the sarcolemma, that is protected by a glycocalyx layer (Clausen 2003a). Invaginations of the sarcolemma extend into the cell to form an internal network of membrane tubules known as transverse tubules (t-tubules) (Sejersted and Sjøgaard 2000, Clausen 2003a) (Figure 2.1). The t-tubule lumina are open to the extracellular space, allowing ions and metabolites to reach transport systems in the walls of t-tubules of the muscle cell (Clausen 2003a). T-tubules are unique, tortuous intramuscular membranous network that makes up a large extracellular space, of up to ~10–15% of the total muscle volume (Sejersted and Sjøgaard 2000). The transverse tubular system (t-system) therefore provides a large membrane surface for various compounds to exchange between the cytoplasm and the extracellular space and enables the propagation of AP from the sarcolemma throughout the t-tubules enabling mechanical contact with the terminal cisternae of the

sarcoplasmic reticulum (SR) within the cell (Huxley and Taylor 1958, Costantin 1970). This provokes the rapid and coordinated release of Ca^{2+} from the SR to the muscle fibrils within the cell (Allen, Lamb et al. 2008a).

Muscle excitability is essential for muscle contractions, it is a property of a cell which responds to stimulation by ionic concentrations, conduction, ion transporter activities, temperature and the circulatory system (Pedersen, de Paoli et al. 2005, McKenna, Bangsbo et al. 2008). Muscle excitability is reliant on propagation of repetitive AP along the sarcolemma and t-tubules, activating voltage-sensitive Ca^{2+} channels in the t-tubules, known as dihydropyridine receptors, which interacts with the ryanodine receptors in the SR, stimulating Ca^{2+} release from the SR (Melzer, Herrmann-Frank et al. 1995). In response to an AP, cytosolic [Ca^{2+}] increases enabling the binding of myosin to actin, generating force and/or shortening of sarcomeres (Homsher and Kean 1980). The Ca^{2+} ions diffuse through the cell binding to troponin and calmodulin, to allow cross-bridge cycling (MacIntosh 2012). The myosin ATPase utilises ATP, releasing energy to produce force and shortening. As Ca^{2+} is removed from the cytoplasm by SR Ca^{2+}-ATPase, tropomyosin returns to its blocked position and relaxation occurs (MacIntosh 2012).

Three ATPase proteins are critical in EC coupling, Na^{+},K^{+}-ATPase, myosin ATPase and Ca^{2+} ATPase, and each therefore contribute to increased ATP use during muscle contractions (Figure 2.1). These ATPases contribute ~10, ~60 and ~30% of total ATP use during muscle contractions, respectively (Homsher 1987).

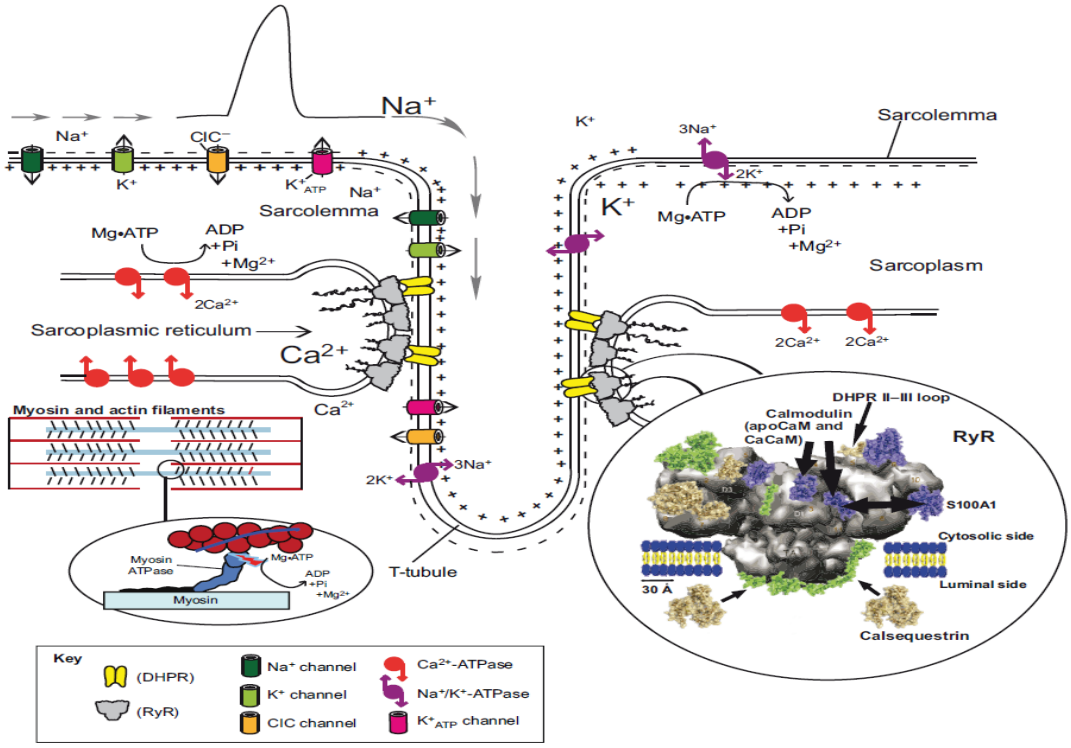

Figure 2.1 Schematic representation of the major components of a muscle cell's excitation-contraction coupling and ATP usage. The processes using ATP are illustrated with the proteins involved in excitation–contraction coupling. ATP is used by the Na^+,K^+-ATPase at the surface and t-tubules, by myosin ATPase within the cell and by Ca^{2+} ATPase in the membranes of the sarcoplasmic reticulum. (From MacIntosh 2012).

2.3 Skeletal Muscle Na^+,K^+-ATPase

The Na^+,K^+-ATPase enzyme is a trans-membranous protein that exists in all cells, and in skeletal muscle, is located primarily in the sarcolemma and transverse tubules (Clausen 2003a). Other studies have explored the location of Na^+,K^+-ATPase isoforms in muscle, using biochemical membrane fraction procedures and found to be principally in the surface membrane, intracellular membrane and plasma membrane, but also in the cytoplasm, mitochodria and sarcoplasmic reticulum (Hundal, Marette et al. 1992, Hundal, Marette et al.

1993, Lavoie, Roy et al. 1996, Tsakiridis, Wong et al. 1996). The Na^+,K^+-ATPase is an electrogenic pump, transporting three Na^+ and two K^+ ions against their electrochemical gradients (Skou 1965). This transport requires energy, which comes from adenosine triphosphate (ATP) (Hoffman 1980). The Na^+,K^+-ATPase is made up of α and β subunits, which are expressed in isoforms (Blanco and Mercer 1998); three of the four α (α_1, α_2, α_3) and all three β subunits (β_1, β_2, β_3) are expressed in skeletal muscle (Murphy, Snow et al. 2004, Murphy, Macdonald et al. 2006).

In order to regulate Na^+/K^+ fluxes across cell membranes, the Na^+,K^+-ATPase in muscle is rapidly activated during exercise (Blanco and Mercer 1998, Clausen 2008a, Clausen, Nielsen et al. 2011) and this elevated activity continues in the post-exercise recovery period (Juel, Nielsen et al. 2000). In addition to the high extracellular [K^+], several exercise-induced changes in muscle, such as increased $[Na^+]_i$, intracellular lactic acid accumulation, high beta-adrenergic activity, increased muscle temperature and released calcitonin from nerve endings, all contribute to the stimulation of Na^+,K^+-ATPase (Clausen, Nielsen et al. 2011). Exercise may also induce translocation of Na^+,K^+-ATPase from cytoplasm to sarcolemma (Galuska, Kotova et al. 2009). During whole body exercise, such as cycling, β-adrenergic receptors are activated by increased adrenaline and noradrenaline, which each directly stimulate skeletal muscle Na^+,K^+-ATPase activity (Clausen 1986, Cheng, Kuo et al. 2013). However, high-dose catecholamines increased serum [K^+], which may suggest that activation of α–adrenoceptor may inhibit the Na^+,K^+-ATPase (Cheng, Kuo et al. 2013).

2.3.1 Na^+,K^+-ATPase function during exercise

Both the activity and abundance of Na^+,K^+-ATPase are tightly regulated (Clausen and Nielsen 1998). Acute regulation over seconds to minutes modulates the pump activity, whereas chronic regulation modulates the abundance of pump protein. The activity of Na^+,K^+-ATPase pump is

stimulated by increased intracellular [Na^+] and to a much lesser extent also by increased extracellular [K^+] (Clausen 2003a, Cheng, Kuo et al. 2013).

High [K^+] in T-tubules depolarises the membrane, which leads to inactivation of voltage-gated Na^+ channels and may contribute to muscle fatigue (Clausen 2003a, Cheng, Kuo et al. 2013). To prevent excessive rises in extracellular [K^+], skeletal muscle Na^+,K^+-ATPase is activated during muscle contraction and for initial periods of recovery. Exercise-induced changes in muscle, including intracellular sodium and lactic acid accumulation, increased muscle temperature, calcitonin gene-related peptide released from nerve endings, as well as high beta-adrenergic activity, all contribute to the stimulation of Na^+,K^+-ATPase activity (Clausen, Nielsen et al. 2011). Furthermore, chronic skeletal muscle activity causes an upregulation of the abundance of Na^+,K^+-ATPase. Exercise training leads to an increase in the content of Na^+,K^+-ATPase in muscle, measured by [^{3}H]ouabain binding site content (Clausen 2003a). This up-regulation of Na^+,K^+-ATPase improves the clearance of plasma K^+ during exercise, a mechanism for reducing fatigue (McKenna, Schmidt et al. 1993). Also increased uptake of K^+ by Na^+,K^+-ATPase in the T-tubules of skeletal muscle in conditioned individuals may reduce the rise of serum [K^+] during exercise (Kjeldsen, Norgaard et al. 1990). Exercise training leads to an increase in the content of Na^+,K^+-ATPase in muscle, measured by [^{3}H]ouabain bind ingsite content. It has been shown that K^+ deficiency in human skeletal muscles reduces the content of Na^+,K^+-ATPase as well as grip strength and fatigue (Clausen 1998, Clausen 2003a). Therefore, increased Na^+,K^+-ATPase transport capacity, either acutely via increased activity, or chronically via enhanced content will increase extracellular K^+ clearance, reduce the exercise-induced increases in extracellular [K^+] clearance and thereby enhance muscular performance (Clausen 2013a).

2.3.2 In vitro Na^+,K^+-ATPase function assessed using blockade with ouabain

Assessing the physiological and clinical significance of the Na^+,K^+-ATPase typically involves measuring the transmembrane Na^+ and K^+ fluxes in intact muscles or in cultured muscle cells. A simple approach involves incubating intact muscles isolated from small animals in temperature-controlled and oxygenated buffers with electrolyte and glucose concentration comparable to that normally present in blood plasma (Clausen 2013b). The '[^{3}H]ouabain and other labelled cardiac glycosides bind stoichiometrically to the extra- cellular surface of the α subunit of the Na^+,K^+-ATPase (one drug molecule per Na^+,K^+-ATPase molecule) (Clausen 2013a). Therefore, incubation of tissues, cells, or plasma membranes with [^{3}H]ouabain enables the quantification of the content in molar units by liquid scintillation counting of extracts of the tissue, cells, or membranes (Clausen and Hansen 1977, Hansen and Clausen 1988).

As K^+ interferes with the binding of cardiac glycosides, [^{3}H]ouabain binding to intact rat, mouse, or guinea pig muscles are performed using K^+-free buffer (Clausen and Hansen 1974). The [^{3}H]Ouabain binding is saturable and reversible without showing [^{3}H]ouabain penetration into the intracellular space in intact muscles. In isolated soleus muscle from 4-week-old rats, [^{3}H]ouabain binding was 720 pmol/g wet wt, corresponding to 3,350 molecules of Na^+,K^+-ATPase per μ^2 of sarcolemma (not including t-tubules). When injected intraperitoneally, [^{3}H]ouabain binds rapidly to the outer surface of the muscle cells, showing saturation and the same content of [^{3}H]ouabain-binding sites per gram tissue wet weight as measured in intact muscles incubated with [^{3}H]ouabain in vitro (Clausen and Hansen 1982, Murphy, Nielsen et al. 2008). The [^{3}H]ouabain binding in vivo is faster than in vitro, reaching saturation in 20 min, partly due to the higher temperature and better access to the muscle cells via the capillaries. When bound to the outer surface of intact muscles, [^{3}H]ouabain is rapidly displaced by the additional excess of unlabelled ouabain during a subsequent wash performed both after binding

in vitro and in vivo, indicating that the [^{3}H]ouabain is not internalised into the cytoplasm (Clausen and Hansen 1974, Clausen, Hansen et al. 1982).

2.4 Na^+ and K^+ concentrations and membrane potential

Fluid compartments of the body and their respective volumes and ion concentrations are indicated in Figure 2.2. In skeletal muscle, interstitial $[Na^+]$ ($[Na^+]_I$), at rest, is approximately 132-143 mM (McKenna, Bangsbo et al. 2008), whilst intracellular $[Na^+]$ ($[Na^+]_i$) is around 6-13 mM at rest (Sjøgaard 1983, Sjøgaard, Adams et al. 1985, Juel 1986). At rest, plasma $[K^+]$ is kept within narrow limits ranging from around 3.5 to 5.3 mM (Sterns, Cox et al. 1981, Worth 1985).

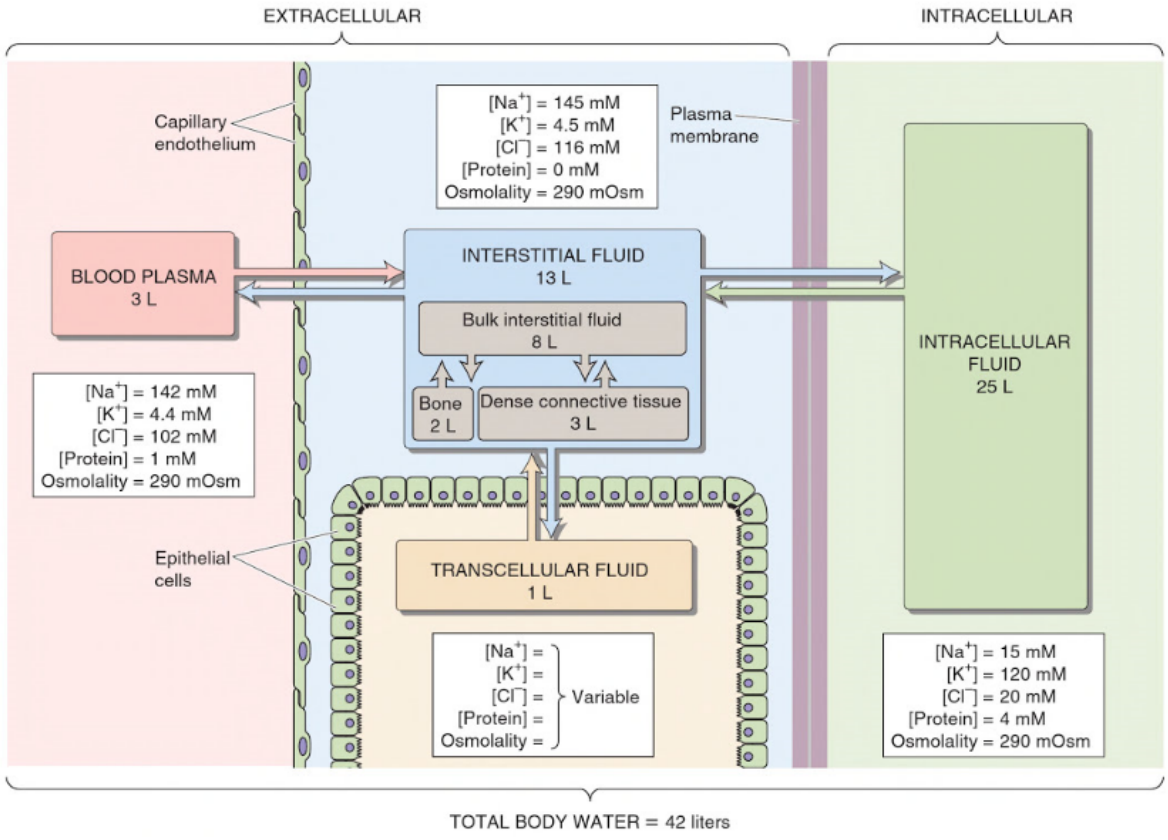

Figure 2.2 Fluid compartments of a typical 70 Kg adult male. Total body water is separated into four compartments. Intracellular fluid, indicated in green; interstitial fluid, indicated in blue; blood plasma, indicated in red; and transcellular water such as synovial fluid, indicated in tan (Adapted from Boron and Boulpaep 2017).

The electrochemical charge along the transmembrane is influenced by the resting muscle membrane potential (E_m) and Cl^-, Na^+ and K^+ ions, with the major influence being K^+ (Cunningham et al., 1971). The E_m is estimated from the trans-sarcolemmal differences in electrochemical potential and permeability of each of these charged ions; during resting conditions, E_m is approximately –90 mV in skeletal muscle (Cunningham, Carter et al. 1971). An action potential (AP) is generated when the sarcolemma Na^+ channels open, triggering a rapid influx of Na^+ and depolarisation of the membrane (Ruff 1996). The E_m may increase to approximately -50 mV within 2-3 ms, which causes further Na^+ channels to open, the ensuing E_m peaks between +20 to +35 mV (Balog 1994). The membrane potential returns to its resting level after the peak voltage is achieved via the rapid inactivation of the Na^+ channels, and opening of the K^+ channels generating the AP (Sejersted and Sjøgaard 2000), Furthermore, depending on membrane potential and $[Ca^{2+}]_i$, the large conductance Ca^{2+}-dependent K^+ channel (BK channel) opens (Blatz and Magleby, 1987 and McManus and Magleby, 1988), whilst the small conductance (SK) Ca^{2+}-dependent K^+ channel is voltage-insensitive (Blatz and Magleby, 1986, Blatz and Magleby, 1987, Leinders and Vijverberg, 1992 and Köhler et al., 1996). During the repolarising phase of the action potential, BK channels are activated and deactivate close to the resting potential; as long as $[Ca^{2+}]_i$ is sufficiently elevated, SK channels stay open which leads to a rise in K^+ permeability and K^+ efflux (Balog 1994). The maintenance of chemical gradients for Na^+ and K^+ leads to the propagation of the AP.

2.5 Interstitial and plasma [K^+] with exercise

During exercise, contracting skeletal muscle cells release potassium initially into the interstitial space within the muscle, with K^+ then diffusing into the capillaries, and then mixed into the venous circulation. Thus, repeated AP and skeletal muscle contraction result in the release of a considerable amount of K^+ into the extracellular space. Excessive accumulation of K^+ in the

muscle extracellular space may lead to depolarisation of the sarcolemma and t-tubules, which leads to inactivation of voltage-gated Na^+ channels and contributes to muscle fatigue (Sjøgaard, Adams et al. 1985, Clausen 2015). The increased $[K^+]_I$ depresses excitability, possibly caused by a slow inactivation of Na^+ channels initiated by depolarisation (Ruff, Simoncini et al. 1988). Thus muscle excitability can be adversely affected by elevated $[K^+]_I$ (Sejersted and Sjøgaard 2000). Whilst resting plasma $[K^+]$ is typically between 3.5 to 5 mM during high-intensity exercise, microdialysis studies have shown $[K^+]_I$ of 10–14 mM (Green S, Langberg H et al. 2000, Juel, Pilegaard et al. 2000, Nordsborg, Mohr et al. 2003, Clausen, Overgaard et al. 2004, Mohr, Nordsborg et al. 2004, Street, Nielsen et al. 2005).

In skeletal muscle, at 37°C, maximal force was unaffected by increasing extracellular $[K^+]$ ($[K^+]_e$), until $[K^+]_e$ increased to 10 mM or more, when it was then decreased (Cairns, Leader et al. 2011). In contrast, twitch and tetanic forces were potentiated when $[K^+]_e$ increased to 12 mM (Holmberg and Waldeck 1980), however twitch force was depressed when the $[K^+]_e$ exceeded 12 mM (Yensen, Matar et al. 2002). Although a mechanism for the elevated $[K^+]_e$ - induced potentiation is not understood, it may influence muscle performance at the beginning of exercise. The force decline is due to a K^+ induced depolarisation of the membrane, as Na^+ channels are inactivated, leading to a decreased AP overshoot (Yensen, Matar et al. 2002). It has been suggested that the Ca^{2+} released by the SR declines once the AP overshoot is <5 mV, and when the overshoot is between 5 and 30 mV twitch force is unaffected (Yensen, Matar et al. 2002, Cairns, Buller et al. 2003). The concentration at which K^+ potentiates or depresses force is influenced by various factors. The notion fatigue is partially related to a decrease in membrane excitability has implications for identifying factors limiting muscle force/power and cellular Ca^{2+} homeostasis and energy metabolism (McKenna, Bangsbo et al. 2008). There are at least three membrane components which are sensitive to either ATP or Ca^{2+}; chloride channel protein (CIC-1), Ca^{2+}-sensitive K^+ channel and the ATP-sensitive K^+ (K_{ATP}) channel

(Kristensen, Hansen et al. 2006). The Ca^{2+}-sensitive K^+ channel allows greater K^+ efflux which lowers AP amplitude (Gong, Legault et al. 2003), whilst increased CI^- channel activity also lowers AP amplitude as CI^- influx increases (McKenna, Bangsbo et al. 2008). Thus, voltage-gated CIC-1 is important for controlling skeletal muscle excitability, any reduction in a muscle cells excitability during metabolic stress may protect muscle cells from metabolic exhaustion and is suggested to be a major influence in fatigue (Bennetts, Rychkov et al. 2005). It has been suggested that CIC-1 opens during muscle contractions with lactic acidosis allowing increased CI^- conductance and that this actually stabilises the membrane when it would otherwise be depolarised with high K^+ (Pedersen, Nielsen et al. 2004, Pedersen, de Paoli et al. 2005).

An AP amplitude can be influenced by ion channel activity, as the amplitude of the AP is dependent on the resting E_m and the exchange of ions during the AP through voltage-gated Na^+ and K^+ channels (Cunningham, Carter et al. 1971). The large, rapid increases in the plasma $[K^+]$ during exercise are due to the K^+ loss from contracting muscle exceeding the rate of K^+ reuptake, by active and inactive muscle, as well as other tissues. During high-intensity exercise, plasma $[K^+]$ has been shown to increase from around 4 mM at pre-exercise, to as high as 8.34 mM during 1 min of exhausting treadmill running (Medbo and Sejersted 1990). It was calculated that if all K^+ released by muscle completely entered the systemic circulation, the venous K^+ concentration after 5 minute of cycling exercise would reach a level 7-fold higher than the pre-exercise level (Clausen 2003a). However, since the highest plasma $[K^+]$ reported during strenuous exercise is around 8 mM, this indicates that most of the exercise-induced K^+ release is retained within the extracellular space of muscle, especially in the interstitium of muscle, including in the t-tubules, and/or removed by other tissues (Lindinger 1995a). The K^+ extracellular and intracellular concentrations in skeletal muscle influence muscle cell function (Lindinger and Sjøgaard 1991). Therefore, the major passive fluxes of Na^+ and K^+ are largely balanced by the increased Na^+,K^+-ATPase activity of exercising and non-exercising muscle

including other tissues (Sejersted and Sjøgaard 2000). However, impairment of Na^+,K^+-ATPase activity during repeated muscle contractions may exacerbate disturbances in transmembrane Na^+ and K^+ gradients, causing a reduction/loss of membrane excitability (McKenna, Bangsbo et al. 2008). Increases in plasma [K^+] with exercise are influenced by independent factors such as the magnitude of the active contracting muscle mass and the exercise intensity, and occurs regardless of exercise type (Medbo and Sejersted 1990, Sejersted and Sjøgaard 2000).

2.6 Effects of contracting muscle mass on K^+ regulation

There are no studies that have comprehensively investigated [K^+] during exercise using different active muscle mass, that utilised the same muscle movement modality, in the same individuals. During two-legged cycling exercise, the rise in plasma arterial [K^+] ($[K^+]_a$) at fatigue described earlier (Vøllestad, Hallén et al. 1994) was ~9-fold greater when compared to during finger flexion exercise in the same individuals (Sostaric, Goodman et al. 2005). This strongly suggests that the magnitude of the contracting muscle mass effects plasma [K^+] dynamics during exercise. Others have also suggested such an effect, but based on comparisons of rise in [K^+] in different studies that used different exercise modalities (Hallén, Gullestad et al. 1994). Therefore the role of the size of the active muscle mass on plasma $[K^+]_a$ during and after intense exercise was investigated in Study 1.

During electrical stimulation of muscle preparations *in vitro,* elevated extracellular [K^+] was associated with reductions in the muscle M-wave amplitude and area, corresponding to reductions in muscle force (Overgaard, Nielsen et al. 1999, Pedersen, Clausen et al. 2003). Whilst the rises in muscle interstitial and plasma [K^+] during exercise are well characterised, the effects of a different contracting muscle mass on circulating [K^+], and the relationship with

muscle force and M-wave during and after high-intensity cycling to fatigue have not been investigated.

Previous investigations have compared muscle mass effects on muscle function. Small muscle mass, such as one-legged knee extensor exercise, induced larger decreases in quadriceps MVC and potentiated twitch ($Q_{tw,pot}$) force evoked by magnetic femoral nerve stimulation, compared to large muscle mass, comprising two legged cycling; further these declines were proportionate to exercise time (Abbiss, Karagounis et al. 2011, Rossman, Venturelli et al. 2012, Rossman, Garten et al. 2014). Greater declines were also reported for single compared to two-legged knee extensor exercise for each of the vastus lateralis integrated electromyogram, and the MVC quadriceps and twitch force fatigue, respectively (Rossman, Garten et al. 2014). Therefore, these findings demonstrate that exercise involving a large muscle mass induced less of a decline in MVC, twitches and M-wave characteristics in healthy individuals. This would be anticipated to also occur with greater increases in $[K^+]_I$ and plasma $[K^+]$, suggesting a possible disconnect with these measures of K^+ disturbances and fatigue. Rossman et al., (2012) concluded that with the different muscle afferent feedback during small muscle mass exercise, the CNS tolerates a greater magnitude of peripheral fatigue and a greater intramuscular metabolic disruption (Rossman, Venturelli et al. 2012). A recent study investigated the roles of Ca^{2+} handling by SR and central fatigue during MVCs (7 s contraction, 3 s rest) repeated for 3 min and compared quadriceps and adductor pollicis muscles, using electrical tetanic stimulation superimposed on MVC (Cairns, Inman et al. 2017). The peak MVC decline with fatigue was similar for both muscles, with even greater declines in tetanic and twitch forces; during exercise the plasma venous $[K^+]$ increased by 1.4 mM. It was concluded that skeletal muscles performing repeated MVC to fatigue primarily involves peripheral fatigue with impaired SR Ca^{2+} handling, whilst an earlier decrease of force in quadriceps may indicate central fatigue (Cairns, Inman et al. 2017).

Therefore, it was important to investigate the effects of different contracting muscle mass on $[K^+]$ dynamics, muscle excitability, force and fatigue. Study 1 therefore investigated whether elevated arterial and antecubital venous plasma $[K^+]$ during bouts of exhaustive two- versus one-legged high-intensity intermittent cycling was associated with different reductions in muscle excitability, muscle force and earlier onset of fatigue.

2.7 Fatigue, mechanisms of muscle fatigue and assessing fatigue

2.7.1 Overview of fatigue

Muscle fatigue is defined as a "transient and recoverable decline in muscle force and/or power with repeated or continuous muscle contractions" (McKenna, Bangsbo et al. 2008). Muscle fatigue is a multifactorial phenomenon; whilst this has been studied extensively, substantial debate and controversies still exist (Cairns and Lindinger 2008, McKenna, Bangsbo et al. 2008, Allen, Lamb et al. 2008a, Bishop 2012).

Skeletal muscles are innervated via a complicated set of neural pathways commencing within the cortex, exciting the motor neurons in the spinal cord and finishing in the motor nerve at the neuromuscular junction (Allen, Lamb et al. 2008a). Fatigue may potentially occur at any point along this pathway and within the muscle itself and as a consequence has been described as being categorised into either central or peripheral fatigue (Millet, Muthalib et al. 2012). Most research indicates fatigue occurring predominantly via peripheral factors distal to the neuromuscular junction and to central factors which control the discharge rate of motoneurons (Figure 2.3). Central fatigue may result within the neural pathways, proximal to the neuromuscular junction which is divided into spinal and supraspinal, whilst peripheral fatigue develops within the muscle, predominately involving disturbances to muscle excitation-contraction coupling or energetics (Kent-Braun 1999, Gandevia 2001, McKenna 2003).

A substantial amount of attention has focussed on potential fatigue mechanisms that include slowing of motor neuron firing rates (Gandevia 1992, Taylor and Gandevia 2001). It has been suggested that fatigue is linked to changes in the motor pathway, including the muscle fibre, motoneuron and motor cortex and that transcranial magnetic stimulation (TMS) over the human motor cortex demonstrates change in both motor evoked potentials (MEPs) and the silent period during and after fatiguing voluntary contractions in healthy subjects (Taylor and Gandevia 2001). The relationship of these changes to loss of force or fatigue is still unclear.

However, during a sustained maximal contraction TMS evoked extra force from the muscle and therefore demonstrates the development of suboptimal output from the motor cortex, that is, fatigue at a supraspinal level. In some fatigue symptomatic subjects, the response to TMS after exercise is altered, however the change in MEP behaviour has not yet associated to a particular symptom or pathology (Taylor and Gandevia 2001).

Factors which may also be potential mechanisms contributing to fatigue include, greater muscle group III & IV afferent feedback (Bigland-Ritchie, Furbush et al. 1986). The discharge of muscle groups III and IV afferents increase according to the temperature, chemical and the mechanical environment of their free nerve endings (Kaufman, Longhurst et al. 1983, Hayward, Wesselmann et al. 1991). They have minimal or no background discharge, thus small changes in their discharge will produce large increases in ensemble input to the central nervous system (Gandevia 1998). Following fatiguing contractions most group III mechanosensitive afferents have increased discharge rates and increased sensitivity to stretch and palpation but a reduced responsiveness to additional contractions (Hayward, Wesselmann et al. 1991).

Hyperthermia-mediated fatigue (González-Alonso 2007) and reduced systemic O_2 availability (Siebenmann and Rasmussen 2016) have also been reported to contribute to fatigue. During exercise in hot humid conditions dehydration causes hyperthermia and the synergistic effects reduce cardiac output and blood flow to muscle and the brain (González-Alonso 2007). The decrease in blood flow beyond the regulatory adjustment to concurrent increases in blood O_2 content leads to declines in O_2 delivery, suppresses muscle aerobic energy turnover and greater reliance of the exercising muscles on anaerobic metabolism during the onset of fatigue (González-Alonso 2007).

Metabolic factors suggested to contribute to peripheral fatigue may include impaired ATP supply (Layec, Trinity et al. 2015), linked with creatine phosphate (PCr) degradation during intense exercise (McCartney, Spriet et al. 1986, Bogdanis, Nevill et al. 1995) and muscle glycogen depletion during sustained exercise (Bergstrom, Hermansen et al. 1967, Hermansen, Hultman et al. 1967). These metabolic changes are likely to impede the function of the myosin-ATPase, Na^+,K^+-ATPase and the Ca^{2+}-ATPase enzymes (Fitts 1994, Allen, Lannergren et al. 1995, Allen and Westerblad 2001, Westerblad, Allen et al. 2002, Allen, Lamb et al. 2008b), with the potential to reduce muscular force, impair excitability and Ca^{2+} re-uptake and therefore likely to have a role in muscle fatigue. The extracellular and intracellular [K^+] in skeletal muscle affect muscle cell excitability and function with K^+ disturbances purported to contribute toward fatigue (Clausen 2015).

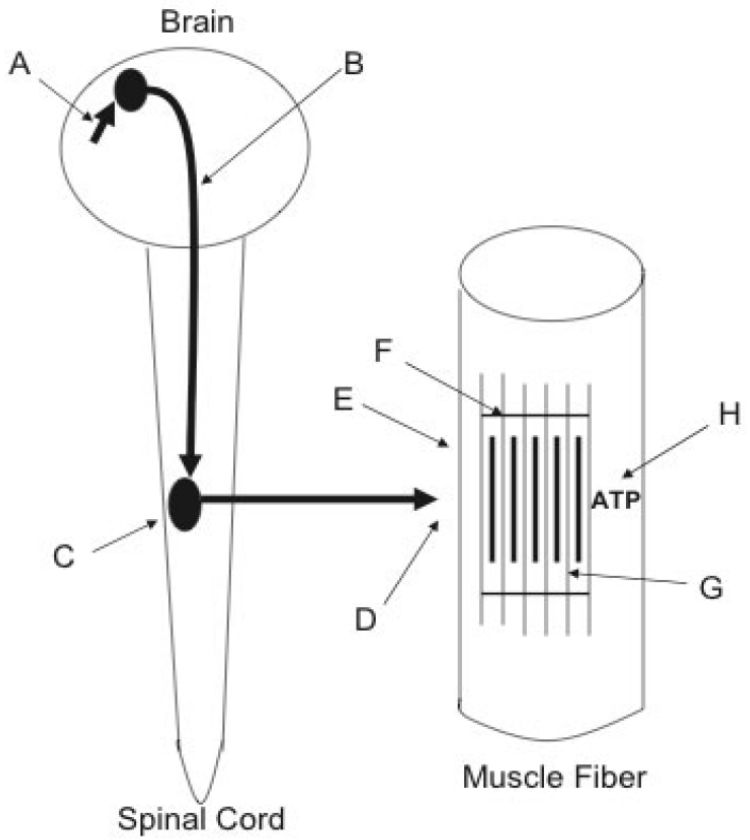

Figure 2.3: Potential muscle fatigue locations. A: excitation to motor cortex; B: excitation to lower motoneuron; C: excitability of lower motoneuron; D: neuromuscular transmission; E: sarcolemma excitation; F: excitation-contraction coupling; G: contractile mechanism; H: metabolic energy supply. (From Bigland-Ritchie, 1981).

Muscle contractions depend on AP triggering adequate release of Ca^{2+} from the SR (Allen, Lamb et al. 2008b). It is generally accepted that impaired SR Ca^{2+} release is a well-established mechanism in isolated muscles and contributes to the decline in force, which is a feature of muscle fatigue (Allen, Lamb et al. 2008a). The Ca^{2+} release channels play a vital role during exercise by sensing any depletion of cellular ATP and respond by reducing Ca^{2+} release. This decreases the rate of ATP usage as it reduces cross-bridge cycling and SR Ca^{2+} uptake, two processes causing ATP hydrolysis, resulting in muscle fatigue. However, the benefit is that it would minimise complete exhaustion of all cellular ATP and cellular damage (Allen, Lamb et al. 2008b).

2.7.2 Mechanisms of muscle fatigue during high-intensity exercise.

Intense intermittent exercise influence the main pathways for adenosine triphosphate (ATP) resynthesis, creatine phosphate (CP) breakdown and muscle glycogen degradation to lactic acid (McCartney, Spriet et al. 1986, Spriet, Lindinger et al. 1989, Green 1997). Metabolic responses to exercise are dependent on exercise intensity and duration and have implications for the contribution to the fatigue processes at the muscle level

(Allen, Lamb et al. 2008a, Morris, Dawes et al. 2012). The ATP utilisation within the muscle cell fuels the mechanisms involved in excitation and contraction, such as sarcolemmal Na^+/K^+ exchange, restoration of cytosolic [Ca^{2+}] via sarcoplasmic reticulum Ca^{2+}ATPase activity and actomyosin cross-bridge cycling (Green 1997). During intense exercise, ATP concentrations are largely maintained via the transfer of high-energy phosphates, glycolysis and to a lesser extent oxidative phosphorylation. During intense-exercise, ATP production rates are not able to match ATP utilisation rates, thus reductions in ATP turnover (Bogdanis, Nevill et al. 1996; this leads to accumulation of various metabolic by-products, such as lactate and hydrogen ions, inorganic phosphate, AMP, ADP and IMP (Green 1997). Various metabolic by-products have

been found to disrupt the balance between Na^+/K^+, Ca^{2+} cycling and actomyosin cross-bridge cycling (Allen 1995, Green 1997) and contribute to the decline in power and work performed during exercise (McCartney, Spriet et al. 1986, Spriet, Lindinger et al. 1989). Any disruption to the exchange of Na^+/K^+ may impair membrane excitability and thus prevent normal SR Ca^{2+} release and consequent contractile function. Therefore, major passive Na^+/K^+ fluxes are compensated by increased Na^+, K^+-ATPase activity (Sejersted and Sjøgaard 2000), as high increases of $[K^+]_I$ depolarises the sarcolemma and is likely to decrease excitability excitability (Sjøgaard 1990, Lindinger 1991, McKenna 1992, Cairns, Hing et al. 1997), and contribute to the development of muscle fatigue (Allen 1995).

Furthermore, intense exercise induces shifts (fluxes that alter ion contents), water movements, physicochemical reactions, and metabolic processes lead to ion concentration changes in compartments proximal to the sarcolemma (Cairns and Lindinger 2008). Therefore, the potential roles of changes of Na^+, Cl^-, lactate concentrations and pH need to be considered in the fatigue processes. It has been observed that intense exercise or electrical stimulation causes multiple ionic changes (K^+, Na^+, Ca^{2+}, Cl^-, H^+, $lactate^-$) in intracellular and extracellular compartments (Lindinger and Heigenhauser 1988, Lindinger and Heigenhauser 1991). This includes a loss of muscle K^+ and gain of muscle Na^+, Cl^-, Ca^{2+} and water, whilst H^+ is elevated both in muscle and interstitial fluid/plasma. The significance of these ion shifts depends on the fatigue model employed, the exercise or stimulation regime, preparation type, and muscle environmental conditions (Cairns, Knicker et al. 2005).

The Na^+ gradient ($[Na^+]_I/[Na^+]_i$), often falls during intense exercise (Cairns and Lindinger 2008), whilst increased $[Na^+]_i$ attenuates fatigue by stimulating Na^+,K^+-ATPase activity (Clausen 2003a, Lindinger, Hawke et al. 2005). However, lowering extracellular $[Na^+]$ ($[Na^+]_o$)

avoids the potential benefit of raised $[Na^+]_i$ to stimulate the Na^+,K^+-ATPase (Clausen 2003a, Lindinger, Hawke et al. 2005). Hence, in most forms of exercise any decline of the trans-sarcolemmal Na^+ gradient is likely to induce minimise fatigue.

In general, it is accepted that reduced SR Ca^{2+} release occurs in fatigued muscles, making a substantial and measurable contribution to the decline in force. Several major mechanisms have been postulated which are capable of reducing SR Ca^{2+} release, although there is little agreement on which is most important in the development of fatigue (Allen, Lamb et al. 2008a). These include reduction in amplitude of the AP, reduced effectiveness of SR Ca^{2+} channel opening or a rise in cytosolic Mg^{2+} concentrations during fatigue (Allen, Lamb et al. 2008b).

Intense dynamic exercise, such as undertaken in HIIT, leads to severe acidosis potentially inhibiting myosin cross bridge force and increasing fatigue (Cady, Jones et al. 1989). Whole-body studies show that induced-acidosis is linked with fatigue, and that induced alkalosis may be ergogenic for events lasting 1–10 minutes, suggesting lactic acid may impair exercise performance by attenuating the role of fatigue (Cairns and Lindinger 2006). Whilst intracellular acidosis is thought to contribute to skeletal muscle fatigue, it is suggested that intracellular acidosis also conserves muscle excitability as muscles depolarize, during muscle contractions (Nielsen, de Paoli et al. 2001). It has been suggested that the preservation of muscle excitability is mediated by impaired chloride permeability, which allows action potentials to propagate along the t-system in skeletal muscle fibers, regardless of muscle depolarisation (Pedersen, Nielsen et al. 2004). Therefore, chloride ion channels reduce CI^- permeability, with intracellular acidosis, are linked in muscle excitability, muscle function and emphasise that intracellular acidosis of muscle has a counteracting effect on muscle fatigue (Pedersen, Nielsen et al. 2004).

2.7.3 Assessing fatigue via evoked muscle contraction

Both magnetic and electrical stimulation of muscle have been used to assess muscle fatigue (Amann and Dempsey 2008, Verges, Maffiuletti et al. 2009, Millet, Martin et al. 2011). During maximal or submaximal intermittent voluntary contractions, both central and peripheral fatigue develops (Taylor, Allen et al. 2000, Amann, Romer et al. 2006, Decorte, Lafaix et al. 2010). Previously, (Polkey, Kyroussis et al. 1996) quadriceps neuromuscular function assessments have been performed whilst lying in a supine position with 180^0 hip extension, and with the knee flexed at 90°, whilst a stimulating coil head was positioned high in the femoral triangle just lateral to the femoral artery, with the best placement for maximal torque and concomitant vastus lateralis (VL) and vastus medialis (VM) M-wave determined via minor placement adjustments to obtain the largest response; this position was marked on the skin using an indelible marker for the remainder of the experiment (Verges, Maffiuletti et al. 2009). M-wave signals were recorded from the *vastus lateralis* (VL) and *vastus medialis* (VM) muscles of the right thigh using bipolar electrodes (Blanc and Dimanico 2010). The surface electrodes were placed in a bipolar configuration over the middle of the muscle belly, with reference electrodes placed on an eclectically neutral site, the anterior iliac spine; the interelectrode distance was 2 cm (Amann and Dempsey 2008). To assess neuromuscular function the action potential, potentiated quadriceps twitch torque ($Q_{tw,pot}$) and M-wave were measured prior to exercise, at 1 min after completion of each exercise bout until fatigue and during recovery (Amann and Dempsey 2008).

Decorte, Lafaix et al., (2012) investigated the development of central and peripheral fatigue by magnetic stimulation of the femoral nerve during an intense intermittent cycling exercise, at 80% of maximal power output, in exercise bouts of 6 min with 4 min rest between bouts, to measure fatigue of the quadriceps via MVC and single (1 Hz), paired (10 and 100 Hz) potentiated and interpolated magnetic stimulations of the femoral nerve and M-wave

characteristics (amplitude, duration and area). They found that knee extensor MVC and quadriceps twitch (Q_{tw}) decreased, mostly during the first half of cycling time, and at fatigue (Decorte, Lafaix et al. 2012). Peripheral magnetic stimulation of the femoral nerve has shown MVC to decline by 22%, peripheral magnetic stimulation alone to decrease by 17% and central activation ratio to decrease by 12% after exercise indicating fatigue via a loss of central drive. These results demonstrate significant central fatigue during cycling (Kremenic, Glace et al. 2009).

Morris, Dawes et al., (2012) investigated muscle contractile characteristics following intense exercise, which comprised cycling at maximal effort for 30 s, followed by 30 s rest, repeated every minute for 30 min, versus submaximal-intensity exercise bouts, cycling for 30 min at 50% of peak power. They found significant reductions in muscle function, MVC, torque development, relaxation, fatigue index and torque frequency following intense intermittent exercise compared to submaximal exercise, even though subjects completed the same amount of work (total kJ) per session on a cycle ergometer (Morris, Dawes et al. 2012). Morris, Dawes et al., (2010) also examined the relationship between muscle contractile characteristics via electrical stimulation and intense exercise performance, and found muscle fatigue resistance and changes in the rate of torque development was significantly related to intense exercise performance during a 30 s sprint cycle test (Morris, Dawes et al. 2010). Verges, Maffiuletti et al (2009) compared electrical and magnetic nerve stimulations and found similar quadriceps force and vastus lateralis M-wave characteristics of single and paired stimulations, following 30 min downhill running to exhaustion (Verges, Maffiuletti et al. 2009). The EMG signals for quadriceps muscles, during stimulation and cycling at 80% of maximal power, have shown the contractile responses evoked by magnetic femoral nerve stimulation commonly decreased largely during the first 6 min of exercise, while a decrease in maximum voluntary activation was present at exhaustion (Decorte, Lafaix et al. 2012). The quadriceps M-wave characteristics

during exercise were correlated to the Q_{tw} decline for the knee extensors, suggesting development of peripheral fatigue early during intense cycling was counterbalanced by increased motor drive, whilst central fatigue was likely to be connected with task failure (Decorte, Lafaix et al. 2012).

As muscle fatigue has been linked to plasma [K^+] increases during intense exercise via a decrease in muscle excitability, the effects of HIIT on K^+ dynamics, and fatigue via muscle excitability and muscle performance were investigated in Study 3.

Section II: The effects of digoxin on K^+ regulation muscle excitability, function and fatigue

2.8 Effects of digoxin on K^+ regulation in healthy humans

2.8.1 Digoxin overview

Cardiac glycosides, cardiotonic steroids, include bufalin, ouabain and digoxin; these are potent inhibitors of the Na^+,K^+-ATPase (Laursen, Gregersen et al. 2015) and are used to treat various heart conditions (Rose and Valdes 1994), such as heart failure, atrial and ventricular fibrillation (Schmidt, Bundgaard et al. 1995, Sticherling, Oral et al. 2000, Hallberg, Lindbäck et al. 2007). Digoxin can be administered orally and is the most widely used cardiac glycoside clinically, whereas ouabain is the most widely used experimentally (Bruce, Lind et al. 1968, Cumberbatch, Zareian et al. 1981, Rose and Valdes 1994) Digoxin has been used in the treatment of congestive heart failure (CHF) since 1785 when William Withering described the use of the foxglove plant (*Digitalis purpurea;* Figure 2.4) (Hollman 1996, Hauptman and Kelly 1999).

Figure 2.4: Foxglove plant (Digitalis purpurea) (Adapted from Whitfield 1985).

Clinically, digoxin is typically administered using a dose range of between 0.25 – 0.5 mg and in healthy humans, this dose is without adverse effects (Joreteg and Jogestrand 1983, Joreteg and Jogestrand 1984, Rossi 2006, Schmitt, Kaeser et al. 2010, Teng and Butler 2013, Alves, Alves et al. 2014). Adverse effects are reportedly rare when plasma digoxin concentration is <0.8 mg/I (Rossi 2006). However, participants with low $[K^+]$ (i.e. hypokalemia, <3.5 mM) may potentially be at risk. Although digoxin has been widely used in treating heart failure (Rose and Valdes 1994), the major concern is high dose digoxin, as manifestations of digitalis intoxication are various and nonspecific (Belz, Breithaupt-Grögler et al. 2001). The clinical symptoms of digitalis toxicity include fatigue, muscular weakness, visual disorders including blurriness and changes in colour perception, nausea, loss of appetite, dizziness, vomiting and an array of psychological disturbances (Dick, Curwin et al. 1991).

A major function of cardiac glycosides is to exert a positive inotropic and electrophysiological effect on the left ventricular myocardium (Schmidt, Bundgaard et al. 1995, Hauptman and Kelly 1999). However, rapid changes in plasma potassium levels during and after exercise have been linked with rhythm disturbances (Gettes 1992, Myerburg, Kessler et al. 1992). Digoxin inhibition of the Na^+,K^+-ATPase cause a rise in cellular $[Na^+]_i$ which then increases Na^+/Ca^{2+} exchange activity, increasing cytosolic $[Ca^{2+}]$ and consequent SR Ca^{2+} loading, with a corresponding increase in SR Ca^{2+} release with each action potential (Levi, Boyett et al. 1994, Clausen and Nielsen 1998).

Although digoxin increases cardiac contractility for heart failure symptoms, only ~3% binds to cardiac muscle, with around 50% of digoxin binding to skeletal muscle (Steiness 1978, Smith, Antman et al. 1984, Schmidt, Bundgaard et al. 1995) and with the remainder distributed in plasma, other tissues, and/or excreted by the kidneys (Doherty, Perkins et al. 1967, Steiness 1978). A digoxin dose of 2-4 $\mu g.kg^{-1}.d^{-1}$ in congestive heart failure (CHF) patients, resulted in digoxin binding to 9% of skeletal muscle Na^+,K^+-ATPase (Schmidt, Holm-Nielsen et al. 1993,

Schmidt, Bundgaard et al. 1995), although in another study this binding was reported to be as high as 35% (Green, Duscha et al. 2001). Acute exercise increases digoxin binding to muscle due to increased Na^+ K^+ ATPase activity, causing the serum digoxin concentration to decrease in healthy humans (Joreteg and Jogestrand 1983). Digoxin concentration in the quadriceps muscle increased during exercise, whereas serum and erythrocyte digoxin concentrations decreased; therefore indicating digoxin uptake in skeletal muscle effects digoxin concentrations in other tissues during exercise (Joreteg and Jogestrand 1984).

2.8.2 Digoxin effects on K^+ regulation and skeletal muscle performance

During exercise, digoxin induced a greater rise in plasma [K^+], which varied from 1.1 mM to 2.5 mM in atrial fibrillation patients (Nørgaard, Bøtker et al. 1991). Furthermore, in heart failure patients there is a lower skeletal muscle Na^+,K^+-ATPase content compared to those not suffering a heart condition (Nørgaard, Bjerregaard et al. 1990). An oral digitalisation loading dose of 0.50 mg (0.25 and 0.25 mg separated by 6 h) in 10 CHF patients, augmented femoral venous plasma [K^+] during exercise by 0.2 mM, whilst arterial plasma [K^+] increased by 0.1 mM, when cycling at workloads of 69 and 93 W and by 0.2 mM at 120 W (Schmidt, Bundgaard et al. 1995). Following digitisation, venous plasma [K^+] increases were more pronounced compared to the control group during exercise and early recovery, which corresponded with inhibition of skeletal muscle Na^+,K^+-ATPase (Schmidt, Bundgaard et al. 1995). However, all participants received medications comprising, acetylsalicylic acid, oral nitrates, selective β_1-adrenoceptor antagonists, diuretics and potassium supplementation, or angiotensin converting enzyme inhibitors for their individual myopathy. Therefore, it would be difficult to establish that any changes were due to the effects of digoxin and/or the pharmaceutical interventions. Following digitisation, an extremely high digoxin occupancy of 35% in skeletal muscle Na^+,K^+-ATPase of CHF patients was associated with a decreased $\dot{V}O_{2peak}$ of 24% (Green,

Duscha et al. 2001). It was suggested that a positive correlation between $\dot{V}O_{2peak}$ and Na^+,K^+-ATPase suggests inhibition of Na^+,K^+-ATPase in skeletal muscle plays a role in explaining exercise intolerance in CHF patients. However, in healthy individuals, intravenous infusion of digoxin (0.01 $mg.kg^{-1}$) did not affect venous plasma $[K^+]$ or plasma lactate compared to placebo, during dynamic handgrip exercise at 30% of the MVC for 3 min (Janssen, Lheureux et al. 2009). Digoxin administration of 0.50 $mg.d^{-1}$ for 2 weeks did not affect $\dot{V}O_{2peak}$ or muscle strength in well trained cyclists (Sundqvist, Berglund et al. 1983). It is unknown whether the well trained cyclists had a high muscle Na^+,K^+-ATPase content that might have counterbalanced the digoxin effect. Sostaric (2012) also reported no change in plasma $[K^+]$, muscle Na^+,K^+-ATPase or exercise performance following oral digoxin intake for 14 days at 0.25 $mg.d^{-1}$ (Sostaric 2012). However, after the removal of digoxin from muscle, a 7% digoxin occupancy of Na^+,K^+-ATPase was found, suggesting a likely up-regulation in Na^+,K^+-ATPase content (Sostaric 2012).

While the rate and magnitude of K^+ lost from active muscle during exercise is attenuated by increased skeletal muscle Na^+,K^+-ATPase activity, impaired Na^+,K^+-ATPase function may also contribute to muscle fatigue. Therefore, study 2 investigated the acute oral effects of digoxin on muscle Na^+,K^+-ATPase, $[K^+]$ regulation, muscle performance and fatigue during and following high-intensity cycling.

Section III: The effects of high-intensity exercise training on K^+ regulation, muscle excitability function and fatigue.

2.9 The effects of exercise training on K^+ regulation

It has been reported that extensive K^+ changes with exercise are likely to double extracellular [K^+] (Medbo and Sejersted 1990, Medbo and Sejersted 1994, Bishop 2012), which are likely to lead to fatigue due to a loss of muscle excitability and action potentials (Sejersted and Sjøgaard 2000). Accompanying muscle contractions is a swelling of the cell (Sjøgaard 1983, Sejersted, Vollestad et al. 1986), which contributes to the decrease of exercise-induced intracellular [Na^+]. One adaptation from increased physical activity is an upregulation of the Na^+,K^+-ATPase in skeletal muscle, which may partially explain why exercise training improves exercise endurance. Overall, increased uptake of K^+ by skeletal muscle Na^+,K^+-ATPase in conditioned individuals is thought to reduce the rise in serum [K^+] during exercise (Knochel, Blachley et al. 1985, Kjeldsen, Norgaard et al. 1990). Previous studies have shown High Intensity Interval Training (HIIT) to be effective in improving intense exercise performance, muscle ion regulation, reduced cellular K^+ loss, improved K^+ regulation and increased muscle Na^+, K^+-ATPase content (McKenna, Schmidt et al. 1993, McKenna, Heigenhauser et al. 1997, Nybo, Sundstrup et al. 2010). Sprint training, comprising high-intensity interval cycling, also improved sprint exercise performance, with an increase in the cumulative work output and reduced fatigue; this was associated with lower arterial and venous plasma [K^+] and [Na^+], and higher arterial plasma [Lac^-] and [H^+] (McKenna, Heigenhauser et al. 1997). There was a marked reduction in the $\Delta[K^+]$/work ratio during intermittent exercise following high-intensity training (McKenna, Schmidt et al. 1993). Interestingly the increase of power was constant after sprint training, at ~13%, in previous high-intensity interval training studies (Nevill, Boobis et al. 1989, McKenna, Schmidt et al. 1993). Reductions in plasma K^+

after sprint training were also found and with similar or attenuated muscle metabolic disturbances when compared to before sprint training (Harmer, McKenna et al. 2000). Neilson, Mohr et al., (2004) investigated the effect of HIIT on muscle interstitial K^+ kinetics, measured via microdialysis, as well as in femoral arterial and venous blood. They found that interstitial [K^+] was less during exercise for the trained than the control leg, but was similar at fatigue. During exercise' femoral venous [K^+] was less in the trained than the control leg (Nielsen, Mohr et al. 2004). Thus, HIIT reduces interstitial K^+ accumulation in skeletal muscle during exercise, possibly via a greater re-uptake of K^+ resulting from increased Na^+, K^+-ATPase content. The lower [K^+] in the muscle interstitium in the trained leg was also associated with a delayed onset of fatigue during intense exercise, suggesting increased interstitial [K^+] pays an important role in the onset of fatigue (Nielsen, Mohr et al. 2004).

2.9.1 Effects of different types of training on ionic regulation

Physiological adaptations to acute and chronic exercise are influenced by specific characteristics of a training programme (MacInnis and Gibala 2017). High-intensity interval training (HIIT) is described as 'near maximal' efforts performed at an intensity of $\geq$ 80% of maximal heart rate (Wyckelsma, Perry et al. 2019). In contrast, sprint interval training (SIT) is characterised by exercise training intensities equal to or greater than $\dot{V}O_{2peak}$. The term moderate intensity continuous training (MICT) may be defined as exercise training performed continuously at lower intensities than HIIT. Characteristics of the training programme influence the size of the skeletal muscle, cardiovascular and adaptations to exercise (MacInnis and Gibala 2017).

High-intensity exercise and SIT invoke marked changes in fluid volumes, metabolites and ion concentrations in skeletal muscle, which may reduce muscular performance (McKenna 1992, McKenna, Heigenhauser et al. 1997). During high-intensity exercise, K^+ and lactate (Lac^-) ions

exit skeletal muscle, as water, Na^+ and Cl^- ions shift from plasma into muscle cell (Lindinger and Heigenhauser 1991, Lindinger, Heigenhauser et al. 1992). During exercise, muscle intracellular and interstitial volumes increase due to fluid shift which leads to a reduction in muscle intracellular and interstitial ion and metabolite concentrations, including plasma ions and metabolites concentration (Sjøgaard and Saltin 1982, Medbo and Sejersted 1985, Lindinger and Heigenhauser 1991). A rapid K^+ efflux may cause muscle membrane depolarisation and impair muscle excitability (Sjøgaard, Adams et al. 1985, Kowalchuk, Heigenhauser et al. 1988), augmenting [Lac^-] in muscle and in blood play a major role in the ensuing intracellular and systemic acidosis (Hermansen and Osnes 1972, Medbo and Sejersted 1985). High-intensity muscle activity leads to cellular Na^+ influx which possibly causes a rise in intracellular [Na^+], and probably attenuates fatigue via Na^+,K^+-ATPase activation, consequently restricting cellular K^+ loss and intracellular acidosis (Medbo and Sejersted 1985, Sjøgaard, Adams et al. 1985, Juel 1986, Clausen and Nielsen 1994). Any increase in intracellular water will exacerbate the contribution of reduced intracellular [K^+] to fatigue, and attenuate the contribution of elevated intracellular [Lac^-]. Changes in plasma ion concentrations during intense exercise have been linked to increases in plasma [H^+] (Jones, McCartney et al. 1985, Kowalchuk, Heigenhauser et al. 1988, Lindinger and Heigenhauser 1991). These ionic and metabolic changes are greater with high-intensity exercise and the onset of fatigue (McCartney, Heigenhauser et al. 1983, Jones, McCartney et al. 1985, Medbo and Sejersted 1990, Vøllestad, Hallén et al. 1994), suggesting there is a relationship between the intramuscular ionic and acid-base disturbances and fatigue. Therefore, it is possible that training at high-intensity stimulates adaptations to regulatory mechanisms controlling ionic homeostasis. The training-induced changes may potentially decrease the rate of fatigue development during exercise (McKenna, Heigenhauser et al. 1997).

Previous studies have shown that following six to seven sessions of HIIT mitochondrial content, measured with CS or COX activity, increased by ~25–35% (Talanian, Galloway et al. 2007, MacInnis, Zacharewicz et al. 2017) or SIT (Burgomaster, Heigenhauser et al. 2006, Gibala, Little et al. 2006). Further, mitochondrial content plateaued after ~5 days of training when exercise intensity and duration were maintained constant (Egan and Zierath 2013) however, mitochondrial content continued to rise for at least several weeks when the intensity was increased progressively (Henriksson and Reitman 1977). Sprint interval training studies have found adaptive ionic regulatory mechanisms, which correlate with improved high-intensity exercise performance. Muscle H^+ regulation is also enhanced following sprint-training, by increased muscle buffering capacity (Sharp, Costill et al. 1986). During whole-body SIT, K^+ regulation is improved, with an increased skeletal muscle Na^+,K^+-ATPase content and an attenuated rise in plasma [K^+] relative to exercise intensity (McKenna, Schmidt et al. 1993).

Therefore, HIIT may improve K^+ homeostasis during intense-exercise, which might be important in delaying the onset of fatigue during high-intensity exercise. This was investigated in Study 3, which examined the effects of HIIT on arterial and venous K^+ regulation, muscle excitability, muscle performance and fatigue.

2.10 Aims and hypotheses

2.10.1 Study 1. Effects of contracting muscle mass on arterial and venous [K^+] and fatigue during intense intermittent cycling

Aims:

To determine the effects of the active muscle mass, by contrasting bouts of exhaustive two- versus one-legged high-intensity intermittent cycling, on [K^+] regulation, measured in arterial and antecubital venous plasma, and fatigability, as measured by time to fatigue during exercise and post-exercise muscle excitability and muscle torque generating capacity.

Hypotheses:

It was hypothesised that: (i) arterial plasma [K^+] would be greater during two- than one-legged intense cycling, and (ii) that this would be disassociated with each of an earlier fatigue-induced cessation of exercise, a greater decrease in muscle voluntary and evoked force and in excitability, demonstrated by lesser declines in M-wave (amplitude and area).

2.10.2 Study 2. The effects of an acute oral dose of digoxin on plasma K^+ regulation, muscle performance and muscle excitability during and following high-intensity cycling in healthy adults

Aims:

To investigate the effects of acute oral digoxin (0.50 mg) intervention on arterial K^+ regulation, fatigue, muscle excitability and muscle force generating capacity, during exercise and recovery in healthy adults.

Hypotheses:

It was hypothesised that acute oral digoxin intake would: (i) increase arterial plasma [K^+] during and following high-intensity exercise, comprised of cycling continuously for 1 minute at a work rate corresponding to 60% $\dot{V}O_{2peak}$, 1 minute at 95% $\dot{V}O_{2peak}$ and until volitional

fatigue at 95% $\dot{V}O_{2peak}$, and recovery; (ii) reduce time to fatigue (i.e. earlier fatigue) during high-intensity cycling; (iii) exacerbate the reduction in quadriceps voluntary, evoked torque and changes in M-wave characteristics after fatiguing exercise.

2.10.3 Study 3. Effects of sprint training on arterial and venous [K^+], muscle excitability and fatigue during and following high-intensity interval cycling

Aims:

To investigate the effects of high-intensity interval training on arterial and antecubital venous plasma [K^+], muscle excitability measured via magnetic stimulation, M-wave and force generating capacity and muscle fatigue during and following high-intensity exercise.

Hypotheses:

It was hypothesised that: (i) arterial and venous plasma [K^+] during exercise would be greater following HIIT compared to CON; (ii) the reduction in quadriceps voluntary and evoked torque and changes in M-wave characteristics would be less after fatiguing exercise following HIIT compared to CON.

CHAPTER 3

Effects of contracting muscle mass on arterial and venous [K^+] and fatigue during intense intermittent cycling

3.1 INTRODUCTION

Muscle fatigue can be defined as a transient but recoverable decline in muscle force/power with repeated or continuous muscle contractions (McKenna, Bangsbo et al. 2008). Although the exact mechanisms of fatigue and their relative importance remains contentious (Allen, Lamb et al. 2008a), one proposed mechanism relates to disturbances to transmembrane potassium (K^+) gradients, inducing inexcitability, defined as a reduction in excitability or response to excitatory synaptic input from activated motoneurons (Allen, Lamb et al. 2008a). During muscle contractions, K^+ shifts from the intracellular to extracellular spaces are extensive and during intense exercise, interstitial K^+ concentration ($[K^+]_I$) rises by more than two-fold, increasing to ~14 mM in human muscle (Green S, Langberg H et al. 2000, Juel, Pilegaard et al. 2000, Mohr, Nordsborg et al. 2004). The exercise-induced increase in $[K^+]_I$ is dependent on exercise intensity and duration during submaximal and high intensity exercise (Green, Roy et al. 2000, Juel, Pilegaard et al. 2000). These K^+ shifts may induce membrane depolarisation, Na^+ channel inactivation and loss of excitability, changes possibly contributing to muscle fatigue (Cairns, Hing et al. 1997, McKenna, Bangsbo et al. 2008, Clausen 2008a). Thus, rapid and precise regulation of K^+ shifts during exercise is crucial for minimising fatigue and maintaining repeated muscle contractile activity (Lindinger, McKelvie et al. 1995).

During exercise arterial plasma K^+ concentrations ($[K^+]_a$) increased with cycling intensity, reaching peak values of 5.7, 6.0 and 8.0 mM at 60, 85 and 110 % $\dot{V}O_{2max}$, respectively (Vøllestad, Hallén et al. 1994). Furthermore, the rise in $[K^+]$ during intense exercise is

considerable, with arterial plasma [K^+] increasing by ~3 mM to reach ~7 mM (Sejersted and Sjøgaard 2000); this rise was ~3-fold greater than during finger flexion exercise with a rise of ~1 mM (Sostaric, Goodman et al. 2005). Consequently, the magnitude of the active muscle mass is likely to affect plasma K^+ dynamics during exercise, with an expected greater K^+ release from contracting muscle. It is likely that the relative amount of inactive muscle also affects [K^+] due to differences in K^+ extraction (Lindinger 1995). However, no studies have comprehensively investigated [K^+] during exercise using different active muscle mass that utilises the same muscle movement, in the same individuals, and this was therefore investigated here.

The size of the active muscle mass affects the magnitude of quadriceps muscle fatigue following exhaustive exercise. Single-legged knee extensor exercise induced greater decreases in quadriceps maximal voluntary contraction (MVC) and muscle twitch force evoked by femoral nerve stimulation, compared to two-legged cycling; these declines were proportionate to exercise time (Abbiss, Karagounis et al. 2011, Rossman, Venturelli et al. 2012, Rossman, Garten et al. 2014). Greater declines were found after single- than two-legged knee extensor exercise for each of the vastus lateralis integrated electromyogram, and the MVC quadriceps and twitch force, respectively (Rossman, Garten et al. 2014). This greater fatigability was found when circulating [K^+] might be anticipated to be lesser. However, the effects of contracting muscle mass on circulating [K^+], and the relationship of [K^+] with muscle force and muscle compound action potential (M-wave) during and after high-intensity cycling to fatigue have not been investigated.

It is important to assess changes in muscle membrane excitability, since during electrical stimulation of muscle preparations *in vitro*, elevated extracellular [K^+] was associated with a reduction of the M-wave amplitude or area that was parallel to the reduction in force (Overgaard, Nielsen et al. 1999, Pedersen, Clausen et al. 2003). This study therefore

investigated the role of the magnitude of active muscle mass on arterial and antecubital venous plasma [K^+], time to fatigue, muscle excitability and muscle force generating capacity following bouts of exhaustive two- versus one-legged high-intensity intermittent cycling. The effects on other plasma electrolytes, acid-base was also investigated. It was hypothesised firstly that arterial plasma [K^+] would be greater during two- than one-legged intense cycling and secondly that this would be disassociated with each of an earlier fatigue-induced cessation of exercise, a greater decrease in muscle voluntary and evoked force and in excitability, demonstrated by lesser declines in M-wave (amplitude and area).

3.2 METHODS

3.2.1 Participants

Ten healthy recreationally active volunteers, comprising nine males and one female (age 25.0 ± 2.4 years; mass 75.3 ± 2.1 kg; height, 177 ± 1.1 cm, mean ± SD) gave written informed consent prior to participation in this study, which was approved by the Victoria University Human Research Ethics Committee and conformed to the Declaration of Helsinki.

3.2.2 Experimental Design

Participants visited the laboratory on five separate occasions. Participants were initially familiarised with the muscle strength testing and peripheral magnetic stimulation, then following 30 min of rest, performed a two-legged (2L) incremental cycle exercise test. All cycling tests were conducted on an electromagnetically braked cycle ergometer (Lode, Groningen, Netherlands), pedalling at a cadence of ~60 $rev.min^{-1}$. Forty-eight hours after the initial visit, participants were again familiarised with muscle strength testing and peripheral magnetic stimulation; then following 30 min rest, a single-legged (1L) incremental cycle exercise test was conducted. During the third visit, participants completed a third familiarisation of the muscle strength testing and magnetic stimulation and underwent the 2L and 1L cycling exercise protocols that were used in subsequent testing. The 2L and 1L cycling trials were conducted on 2 further separate occasions, separated by a minimum of 7 days, (Figure 3.1). During these 2L and 1L trials, measures were made at rest, during and following exercise for arterial and venous plasma electrolytes and acid base status, voluntary and magnetically evoked knee extensor muscle force, M-wave characteristics of the vastus lateralis and vastus medialis muscles, heart rate (HR) and rating of perceived exertion (RPE). Participants were asked to refrain from vigorous exercise, and from consuming alcohol and caffeine for 24 h before all tests.

3.2.3 Exercise Tests

3.2.3.1 Cardiorespiratory and perceived exertion measures

Heart rate was monitored during the incremental test using a Polar T31 heart rate monitor (Polar Electro, Finland). During and after the cycling exercise trials heart rate and rhythm were monitored continuously by 12-lead ECG (Model X-Scribe Stress Test System, Mortara Instrument Inc., Milwaukee, WI, USA).

Respiratory data was obtained continuously throughout exercise. During the 2L and 1L incremental tests and cycling exercise trials participants breathed through a Hans-Rudolph three-way non-rebreathing valve, with the expired air passed through flexible low-resistance plastic tubing into a mixing chamber. Mixed expired oxygen (O_2) and carbon dioxide (CO_2) fractions were continuously analysed by rapidly responding O_2 and CO_2 analysers (Ametek S-3A/II and Ametek CD-3A, Pittsburgh, USA). Expired volumes were obtained from a flow transducer (KL Engineering K520, Sunnyvale, California, USA). Pulmonary oxygen consumption ($\dot{V}O_2$), CO_2 output, ($\dot{V}CO_2$) ventilation ($\dot{V}_E$), and respiratory exchange ratio (RER) were calculated every 15 s on a PC (Turbo fit, California, USA). Gas analysers were calibrated and verified with precision gases of known gas concentrations (BOC, Australia), a volume calibration and verification was performed before every test using a 3 Litre Hans Rudolph syringe.

A rating of perceived exertion (RPE) was measured using a 6-20 scale (Borg 1982) during the final 10 s of each exercise minute during both incremental test and cycling exercise trials.

3.2.3.2 Two and One legged cycle incremental tests

Participants performed a 2L and a 1L incremental test, separated by a minimum of 7 days, on a cycle ergometer, that commenced with two min at 100 W for males, and at 60 W for females, followed by increments of 25 W every 2 min continued until volitional exhaustion, defined as

an inability to maintain pedal cadence above 60 rev.min^{-1}. During the 1L cycling test, a counterweight system was fitted to the contralateral pedal of the cycle ergometer to assist with the upward phase of the pedalling action (Thomas 2009). The peak oxygen consumption ($\dot{V}O_{2peak}$) was determined using the final four 15 s measures, and then the work-rate corresponding to 80 and 90% of $\dot{V}O_{2peak}$ was calculated and prescribed for the 2L and 1L cycling trials.

The intense intermittent cycling protocol was employed because such exercise is accompanied by a dramatic rise in plasma [K^+] with each exercise bout and by marked muscular fatigue, evidenced by progressively declining work output (Hermansen, Orheim et al. 1984).

3.2.3.3 Intense intermittent Two-legged cycle exercise

The 2L cycle exercise comprised six, 2 min exercise bouts (EB) at a work-rate corresponding to 80% $\dot{V}O_{2\ peak\text{-}2L}$, with 2 min recovery after each bout. Participants then performed a final cycling bout at an intensity of 90% $\dot{V}O_{2\ peak\text{-}2L}$, at ~60 rev.min^{-1}, continued until volitional exhaustion, defined as an inability to maintain pedal cadence above 60 rev.min^{-1}. Participants remained seated at all times during the cycle exercise.

3.2.3.4 Intense intermittent One-legged cycle exercise

The 1L cycle exercise was conducted using the dominant leg and comprised six, 2 min EB at a work-rate corresponding to 80% $\dot{V}O_{2peak\text{-}1L}$, with 2 min recovery after each bout. Participants then performed a final cycling bout at 90% $\dot{V}O_{2\ peak\text{-}1L,}$ at ~60 rpm, to volitional exhaustion, defined as an inability to maintain pedal cadence above 60 rpm. During the 1L cycling test, a counterweight was fitted to the contralateral pedal on the cycle ergometer. Participants remained seated at all times during the cycle exercise.

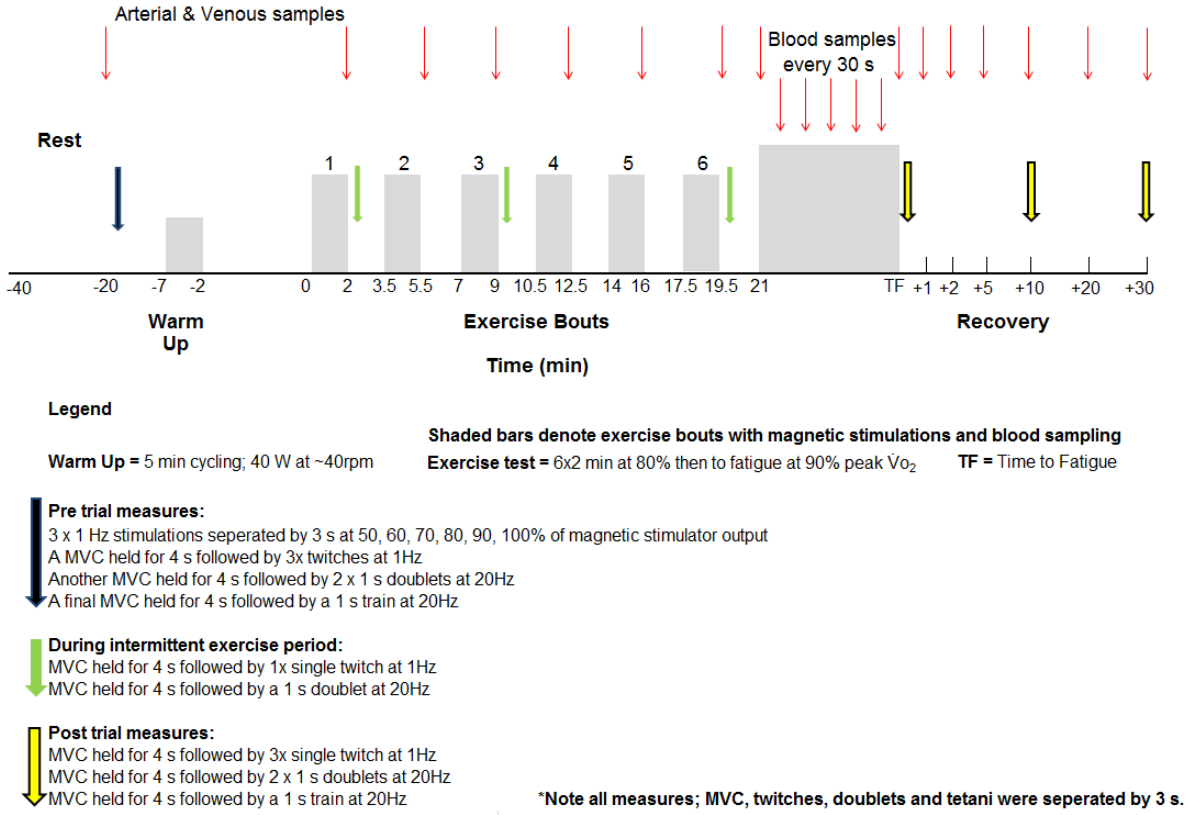

Figure 3.1 A schematic illustrating the cycling testing protocol utilising both large (two-legged) and small (one-legged) muscle mass.

3.2.4 Blood sampling and analysis

A 20G catheter was inserted retrograde into the deep antecubital vein and a 22G catheter inserted anterograde into the radial artery of the left arm, then covered with an adhesive sterile patch (Tegaderm) and attached to a sterile extension tubing set (ITL Arterial Kit), which was affixed to the forearm and upper arm of the participant, under local anaesthesia (1% xylocaine). Arterial and venous lines were kept patent by a slow, sterile, isotonic saline (0.9% NaCl) infusion bag under pressure. Participants rested supine for 20 min before resting blood samples

were obtained prior to the commencement of each trial. Following a series of baseline magnetic stimulations, the participant was seated on the cycle ergometer for 2 min before exercise commenced. Arterial (A) and antecubital venous (V) blood samples were taken simultaneously at rest, during the final 30 s of each exercise bout; every 30 s during the time to fatigue bout and immediately at the time of fatigue, and in recovery at 1, 2, 5, 10, 20 and 30-min post-exercise. Arterial and antecubital venous blood samples were taken, as femoral venous cannulation or interstitial K^+ measurements have not been established in this laboratory, to measure arterio-venous $[K^+]_{a-v}$ differences.

Approximately 3 mL of blood was drawn in a heparin coated blood gas syringe (Siemens, Rapidlyte) for analyses of plasma gas tension, pH balance and electrolyte concentrations, as well as whole blood haematocrit (Hct) and haemoglobin ([Hb]), glucose and lactate concentrations. Duplicate analyses were conducted for the rest sample with single analysis for the exercise and recovery samples. Arterial plasma electrolyte concentrations ($[K^+]$, $[Na^+]$, $[Cl^-]$), gas tensions and pH were analysed using an automated blood gas analyser (Rapid Point 405 Siemens Medical Solutions and Diagnostics, Tarrytown, New York, USA).

Haematocrit (Hct) and haemoglobin ([Hb]) concentration were analysed in duplicate by an automated analyser (Sysmex K800 TOA Medical Electronics, Kobe, Japan), and blood glucose and lactate concentrations for single analysis using an automated analyser (YSI 2300 Stat Plus Analyser, YSI Inc., Yellow Springs, OH, USA). To account for any small intra-individual differences between 2L and 1L trials, the rise from rest in plasma $[K^+]_a$ ($\Delta[K^+]_a$) and $[K^+]_v$ ($\Delta[K^+]_v$) and the $\Delta[K^+]_a.work^{-1}$ ratio were calculated for all EB, including EB to fatigue.

3.2.5 Calculations for blood volume

The change in blood volume (ΔBV), expressed as a percentage from rest, was calculated during and after cycling exercise; from [Hb] using the equation:

$\% \Delta BV = (Hb_1/Hb_2 - 1) \times 100$, (Harrison 1985).

3.2.6 Quadriceps neuromuscular function

The quadriceps neuromuscular function was quantified by the maximal voluntary contraction (MVC) and magnetic stimulation of the femoral nerve (Polkey, Kyroussis et al. 1996, Kufel, Pineda et al. 2002, Amann and Dempsey 2008). The quadriceps neuromuscular function assessments were performed whilst lying in a supine position with 180° hip extension, and with the knee flexed at 90°, using a purpose-built leg mould which was securely attached to a laboratory plinth. The voluntary and evoked muscle torque (Nm) were measured using a calibrated strain gauge (XTran S1W, Australia) that was securely attached to a bench with a non-stretch strap secured to the strain gauge and attached to the participants right leg, ~5 cm above the tip of the lateral malleoli. The potentiated quadriceps twitch torque ($Q_{tw,pot}$) and M-wave were measured prior to exercise, at 1 min after completion of each of EB1, EB3 and EB6, following the final EB to fatigue, and at 10 and 30 min recovery, in both 2L and 1L trials. The 1 min delay post-exercise was necessary to transfer the participants from the cycle ergometer to the adjacent neuromuscular function assessment apparatus and ensure a standardised measurement position time for both trials.

3.2.6.1 Maximal voluntary contraction

Initially three warm up repetitions were performed prior to three 4 s maximal efforts, with each repetition separated by ~15 s. Participants were verbally encouraged to perform a maximal

effort during each repetition, with the largest peak torque achieved from the three repetitions used for analysis.

3.2.6.2 Peripheral magnetic stimulation

Femoral nerve stimulation was performed with a 70-mm figure-of-eight coil powered by one linked magnetic stimulator (Magstim Rapid 200, The Magstim Company, Whitland, Wales). The linking circuitry (Bistim Module, Magstim) was capable of precisely controlling the inter-stimulus interval between 1 and 999 ms to an accuracy of within 0.05 ms. The stimulator was used for single, paired and tetani stimulations, with all stimuli performed at maximum stimulator output (Polkey, Kyroussis et al. 1996). The quadriceps muscles were stimulated with pulses of 200 ms – 1 s duration and 120 V. $Q_{tw,pot}$ pulses were of 200 ms and 120 V, doublet pulses were of (2 pulses 5 ms apart) and 120 V and pulses for 20 Hz tetani were of 1 s and 120 V.

Participants lay supine, as previously described (section 3.2.6), with the stimulating coil head positioned high in the femoral triangle just lateral to the femoral artery, with the best placement for maximal torque and concomitant vastus lateralis (VL) and vastus medialis (VM) M-wave determined via minor placement adjustments to obtain the largest response; this position was marked on the skin using an indelible marker for the remainder of the experiment (Verges, Maffiuletti et al. 2009). To ensure maximal twitches were achieved with the magnetic stimulator (i.e., plateau in twitch torque), a ramp test was performed at the beginning of each session. The ramp protocol (Figure 3.2) consisted of three un-potentiated twitches (Q_{tw}) every ~3 s at 50, 60, 70, 80, 90 and 100% of stimulator output (Smith and Billaut 2010).

Interday and intraday reliability was calculated for the ramp test during each of the stimulator intensities (50%–100%) for torque (Appendix F, Figure A 1.0). A plateau during the ramp

protocol confirmed maximal stimulation when the rise between the 80-100% stimulation intensities did not significantly differ ($P > 0.05$).

3.2.6.3 Magnetically evoked torque

The $Q_{tw,pot}$, doublet and 20 Hz tetani (1 s) torque were measured prior to exercise, 1 min after each of EB1, EB3 and EB6 and the final EB to fatigue, and at 10 and 30 min recovery, in both the 2L and 1L trials.

3.2.6.4 Muscle contractile responses

Representative contractile responses during an MVC and elicited by magnetic femoral nerve stimulation at rest (solid line) and at fatigue (dotted line) in one participant are shown in Figure 3.2.

MVC recruits all motor units and is voluntary activated which involves maximal SR Ca^{2+} release. Evoked measures, single, doublet and 20 Hz are submaximal contractions and are thought to reflect more likely contractile activity during submaximal contractions, thus intracellular [Ca^{2+}] would be at subsaturating levels (Booth, McKenna et al. 1997). Whilst the single twitch is essential for clear M-wave measures.

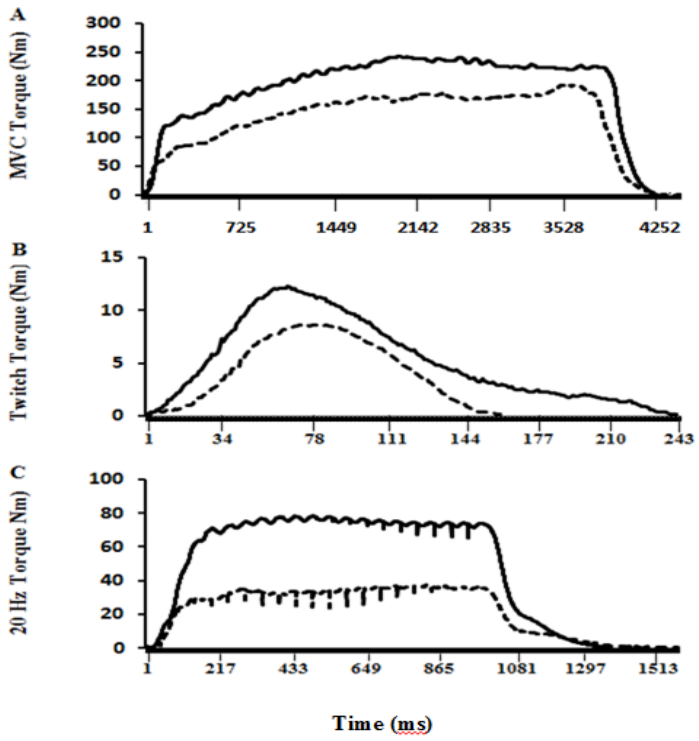

Figure 3.2 Representative muscle contractions in one participant during *A*: maximal voluntary contractions (MVC) and evoked by magnetic stimulation for *B*: maximal twitch contractions, *C*: tetanic contraction evoked at 20 Hz. In each case, torque (Nm) is shown under pre-exercise conditions (solid line) and at 1 min following the EB to fatigue (dotted line), after cycling at 90% $\dot{V}O_{2peak}$.

3.2.6.5 Compound action potentials (M-waves) measurement

M-wave signals were recorded from the *vastus lateralis* (VL) and *vastus medialis* (VM) muscles of the right thigh using bipolar electrodes (Blanc and Dimanico 2010) (Figure 3.3). Prior to the electrode placement, the skin was prepared by shaving then rubbing with an abrasive pad and cleaning with alcohol. The surface electrodes were placed in a bipolar configuration over the middle of the muscle belly, with the reference electrodes placed on an electrically neutral site, the anterior iliac spine; the interelectrode distance was 2 cm (Amann

and Dempsey 2008). The VL electrode placement was the lower 25% between Anterior Iliac Spine (AIS) and the Gerdy prominence (Blanc and Dimanico 2010). The VM electrode placement was the lower 25% between AIS and knee joint space in front of the anterior border of the medial collateral ligament (Blanc and Dimanico 2010). The vastus medialis electrode placement was a rectangle delimited by tangents to the medial side and the upper border of the patella with the knee in full extension then in flexion 90° (Blanc and Dimanico 2010). Skin impedance, skin resistance to conduct electrical current, was kept below 2 kΩ. To ensure low levels of movement artefact, electrode cables were fastened to the subjects' body with medical adhesive tape and wrapped in a net.

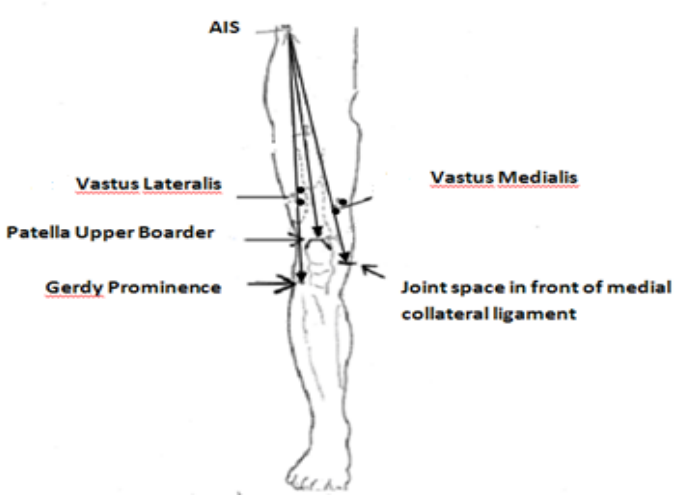

Figure 3.3 Minimal cross talk area (MCA) and surface electrode placement of the quadriceps; indicated by dots. To limit or avoid crosstalk from neighbouring muscles of the quadriceps surface electrodes were placed using landmarks. Vastus lateralis: lower 25% between AIS and Gerdy prominence. Vastus medialis vertical part: lower 25% between AIS and knee joint space in front of the anterior border of the medial collateral ligament. Vastus medialis horizontal part: a rectangle delimited by tangents to the medial side and the upper border of the patella with the knee in full extension then in flexion 90° (from Blanc and Dimanico 2010).

The M-waves were recorded with bipolar electrodes (preamplifier gain 375 x) (Mega Electronics Ltd, Kuopio, Finland). The M-wave signal was sampled at 1000 Hz, band pass filtered between 8 and 500 Hz, amplified (analogue differential amplifier, common mode rejection ratio > 110 dB, total gain 412, noise < 1.6 pV), analogue-to-digital converted (12-bit) and stored in a personal computer for analysis. The M-wave peak-to-peak, amplitude, duration and integral (Figure 3.4) were to establish reductions in membrane excitability and to examine M-wave parameters during recovery (Amann, Eldridge et al. 2006, Amann, Romer et al. 2006, Amann, Proctor et al. 2009). The M-waves were recorded in VM and VL as VM is more likely to be recruited in cycling, VL is typically studied for muscle biopsies.

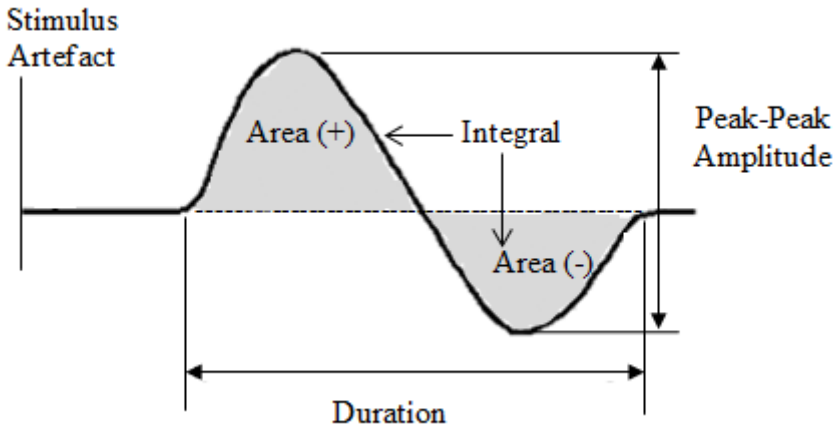

Figure 3.4 M-wave characteristics measured included peak to peak amplitude (mV), integral (positive plus negative area (mV.s)) and duration (ms).

3.2.7 Statistical analysis

A linear mixed model analysis of variance was used to calculate differences between 2L and 1L trials, with the Least Significant Difference test used for post-hoc analysis for time and trial (2L vs. 1L) main effects. Time by trial interactions are reported only when significant. Student's paired *t*-test was used to calculate differences between trials for $\dot{V}O_{2peak}$, heart rate, ventilation, power output and time to fatigue, including resting data for twitch and M-wave characteristics. Statistical significance was accepted at $P < 0.05$. Data are presented as mean ± standard deviation (SD). Statistical analyses were calculated using SPSS version 22 (SPSS Inc., Champion, IL).

3.3 RESULTS

3.3.1 Incremental cycling cardiorespiratory measures

The incremental cycle test $\dot{V}O_{2peak}$, $\dot{V}_{Epeak}$ and HR_{peak} were all greater during 2L than 1L ($P < 0.05$, Table 3.1).

Table 3.1 Peak cardiorespiratory values for 2L and 1L incremental cycle tests

		2L	1L
$\dot{V}O_{2peak}$	($L.min^{-1}$)	4.19 ± 0.76 *	3.09 ± 0.28
$\dot{V}_{Epeak}$	($L.min^{-1}$)	140.5 ± 37.0 *	91.9 ± 17.7
HR_{peak}	($b.min^{-1}$)	181 ± 8 *	169 ± 113

Data expressed as mean ± SD; n=10, * 2L greater than 1L, $P < 0.05$

3.3.2 Intermittent cycling tests

3.3.2.1 Power output

The power output during cycling at 80 and 90% $\dot{V}O_{2peak}$ was 245 ± 63 vs 142 ± 34 W and 273 ± 70 vs. 159 ± 37 W, for 2L vs. 1L respectively, being greater in 2L than 1L ($P < 0.05$).

3.3.2.2 Exercise time to fatigue

The time to fatigue in the final EB at 90% $\dot{V}O_{2peak}$ did not differ between trials (210 ± 40 vs. 205 ± 45 s, for 2L and 1L, respectively, $P = 0.56$).

3.4.4 Oxygen consumption

Pulmonary $\dot{V}O_2$ during cycling at 80% $\dot{V}O_{2peak}$ and 90% $\dot{V}O_{2peak}$ was greater for 2L than 1L ($P < 0.05$, Table 3.2).

Table 3.2 Pulmonary oxygen consumption during cycling at 80% $\dot{V}O_{2peak}$ and to fatigue at 90% $\dot{V}O_{2peak}$

		2L	1L
80% $\dot{V}O_{2peak}$	($L.min^{-1}$)	3.45 ± 0.76 *	2.65 ± 0.41
90% $\dot{V}O_{2peak}$	($L.min^{-1}$)	4.14 ± 0.76 *	3.09 ± 0.58

Data expressed as mean ± S.D; $n = 10$, * 2L greater than 1L, ($P < 0.05$); values reported as an average of the last minute of 80% $\dot{V}O_{2peak}$ and to fatigue at 90% $\dot{V}O_{2peak}$.

3.4.5 Heart rate and RPE during exercise

Neither the HR nor the RPE during exercise differed between 1L and 2L trials (Table 3.3).

Table 3.3 Effects of 2L and 1L cycling on heart rate (beat.min^{-1}) and rating of perceived exertion (RPE) pre-exercise, during intense intermittent cycling comprising six, 2-min bouts at 80% $\dot{V}O_{2peak}$ and a final bout to volitional fatigue at 90% $\dot{V}O_{2peak}$.

	Pre-exercise	80% V̇O2 peak						90% V̇O2 peak
HR (beat.min^{-1})		Exercise Bout Number						
		1	2	3	4	5	6	Fatigue
2L	62±5	138±16	144±18	149±17	154±16	156±18	158±17	175±11
1L	62±5	140±13	150±15	156±13	157±14	161±13	163±13	169±13
RPE								
2L		9.5±1.7	12.0±1.7	13.3±1.7	15±1.9	15.8±1.8	17.5±1.7	18.8±1.7
1L		10.3±1.5	11.7±1.6	13.3±1.2	14.2±0.7	15.0±1.1	16.8±1.1	19.6±0.5

All HR greater than pre-exercise, ($P < 0.05$, time main effect). Values are mean ± SD, $n = 10$.

3.4.6 Arterial and venous plasma [K^+]

Plasma $[K^+]_a$ increased to ~5.1 mM during the first exercise bout (EB1), remained elevated for each subsequent EB and during the final EB from 21.5 min, at fatigue as well as at 1-2 min recovery (time main effect, $P < 0.05$), returning to rest levels thereafter (Figure 3.5). The $[K^+]_a$ was higher in 2L than 1L (trial main effect, $P < 0.05$). There was a trial x time interaction ($P < 0.05$), with a greater $[K^+]_a$ during the final EB at 23 min and at fatigue for 2L than 1L (6.1 ± 0.6 vs. 5.6 ± 0.4 mM, respectively).

Plasma $[K^+]_v$ increased during EB1, remained elevated during EB2 – EB6, and during the final EB from 21.5 min onwards to fatigue; and at 1-30 min recovery (time main effect, $P < 0.05$, Figure 3.5). There was no significant difference between trials (main effect). There was a significant trial x time interaction ($P < 0.05$), with $[K^+]_v$ being less during 2L than 1L during EB1 (4.5 ± 0.3 and 4.7 ± 0.4 mM, respectively) and at the first 30 s of the final EB, at 21.5 min (Figure 3.5).

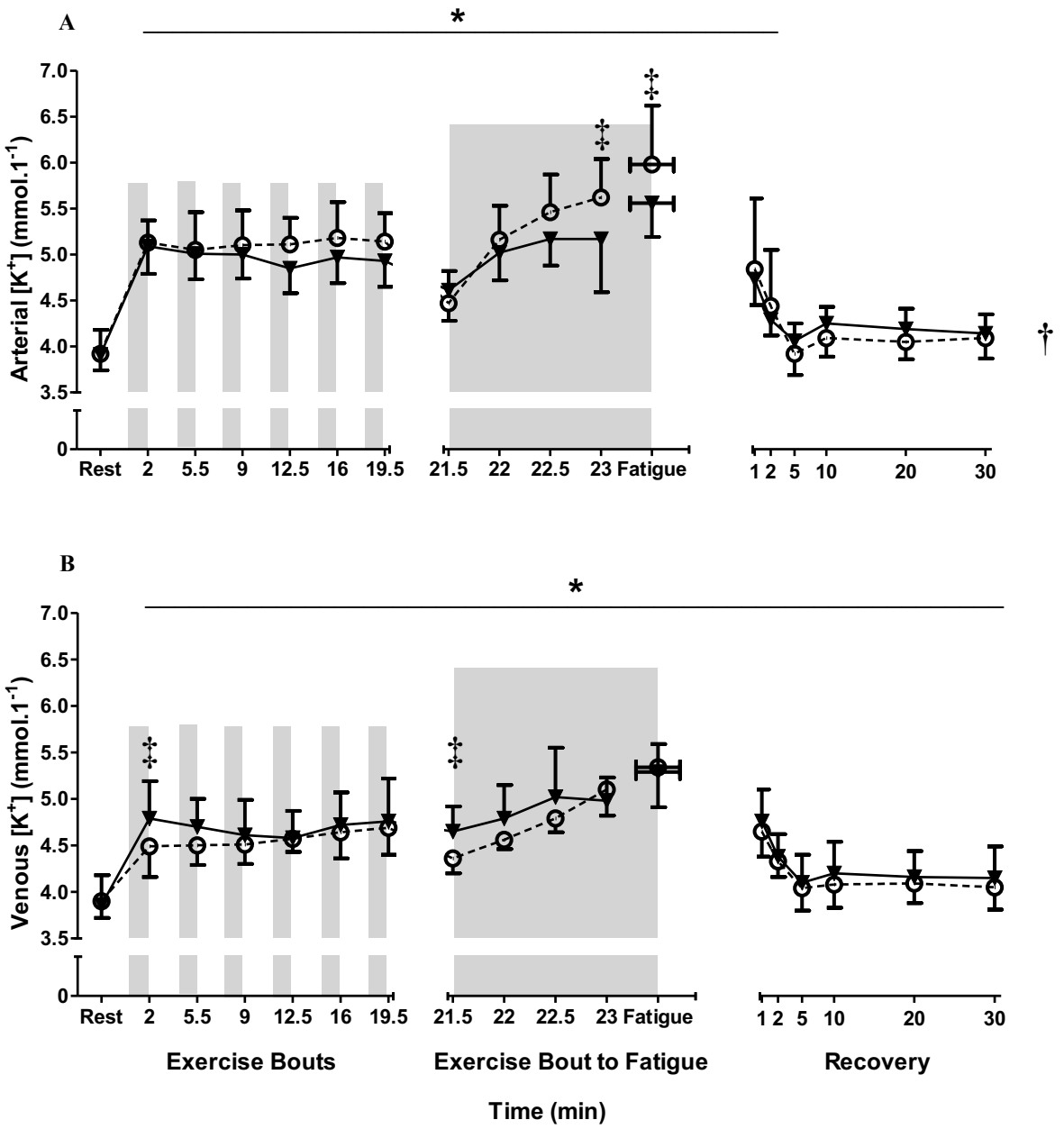

Figure 3.5 Effects of 2L (○) and 1L (▼) cycling on arterial (A) and venous (B) plasma [K^+] at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. n = 10, values expressed as mean ± S.D; horizontal bars indicate SD of time to fatigue. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), † Different between trials (trial main effect 2L > 1L, $P < 0.05$), ‡ 2L greater than 1L (trial x time interaction, $P < 0.05$).

3.4.7 Arterio-venous [K^+] difference across the forearm

The plasma $[K^+]_{a\text{-}v}$ was greater than rest during EB1 and for each subsequent EB; and during the final EB from 22 min to fatigue ($P < 0.05$, time main effect, Figure 3.6); the $[K^+]_{a\text{-}v}$ had returned to rest values at 1 min recovery. There was a higher $[K^+]_{a\text{-}v}$ during 2L than 1L ($P < 0.05$, trial main effect) and a significant time x trial interaction ($P < 0.05$), with greater $[K^+]_{a\text{-}v}$ in 2L than 1L during EB1 and during the final EB at 22 min through to fatigue.

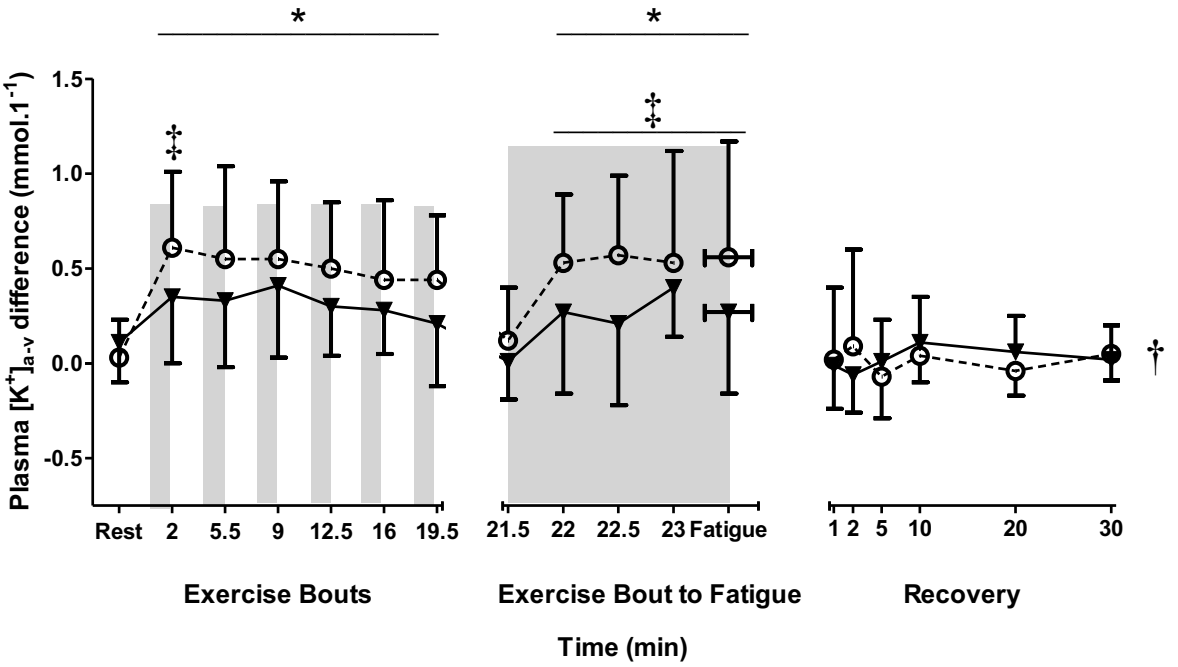

Figure 3.6 Effects of 2L (○) and 1L (▼) cycling on arterial-venous plasma $[K^+]_{(a\text{-}v)}$ at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), † Different between trials (trial main effect, $P = 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

3.4.8 Change in arterial and venous plasma [K^+] from rest

To account for any small intra-individual $[K^+]_a$ differences between 2L and 1L trials, the change from rest in plasma $[K^+]_a$ ($\Delta[K^+]_a$) and $[K^+]_v$ ($\Delta[K^+]_v$) were calculated at each time point. The plasma $\Delta[K^+]_a$ was elevated during all EB and at 1 and 2 min recovery (time main effect, $P < 0.05$; Figure 3.7). There was no difference between trials for $\Delta[K^+]_a$ (main effect) but there was a significant trial x time interaction ($P < 0.05$), with $\Delta[K^+]_a$ greater in 2L than 1L during the final EB at 23 min and at fatigue. There was a significant trial x time interaction ($P < 0.05$) with $\Delta[K^+]_a$ during 2L greater than 1L at fatigue.

The plasma $\Delta[K^+]_v$ was elevated after each EB and during recovery (time main effect, $P < 0.05$), but with no difference between trials (Figure 3.7).

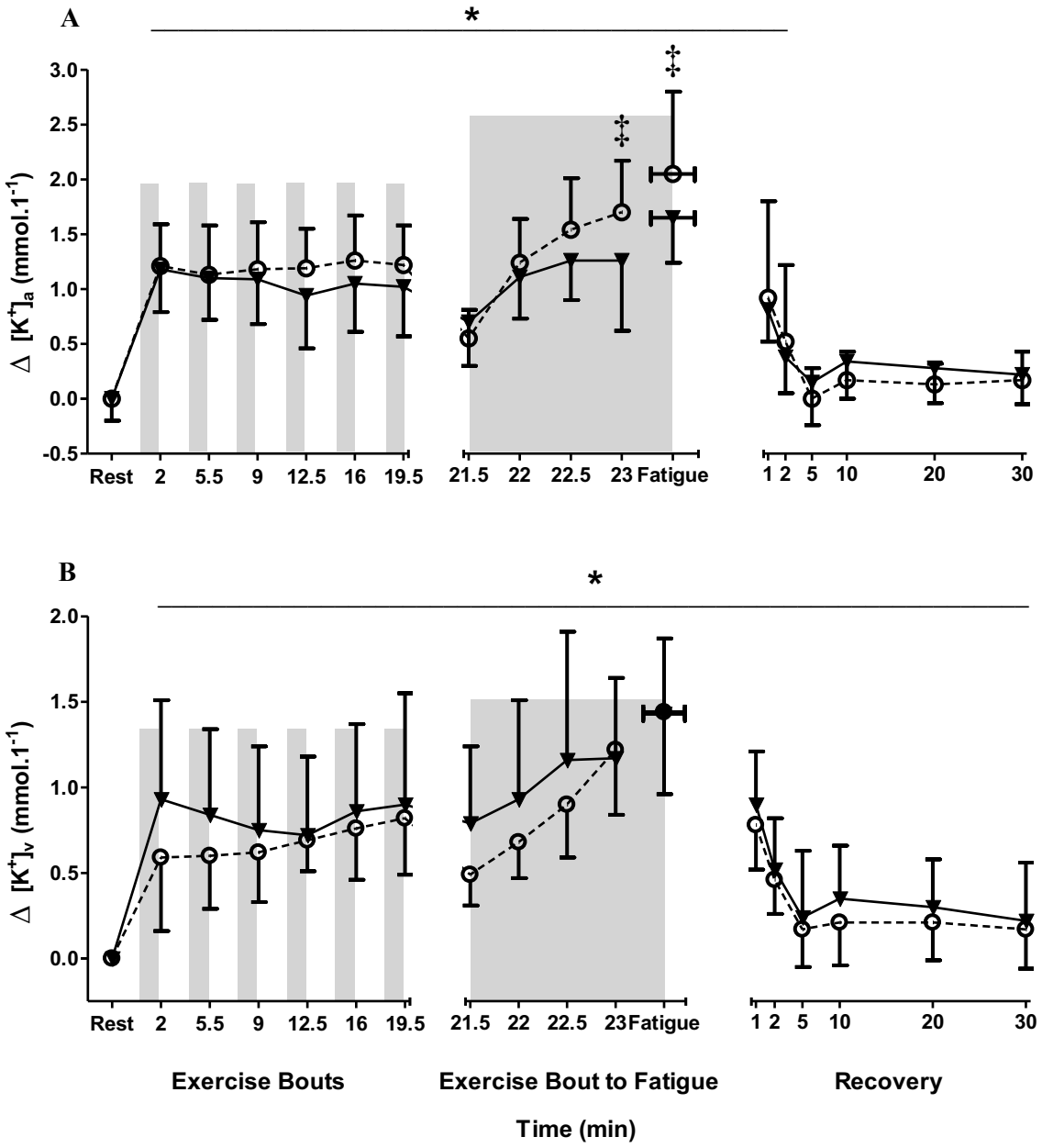

Figure 3.7 Effects of 2L (○) and 1L (▼) cycling on changes in plasma $[K^+]_a$ (A) and $[K^+]_v$ (B) at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are means ± S.D: n = 10. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

3.4.9 Δ $[K^+]_a$ /work Ratio

The ratio of $\Delta[K^+]_a$ to work during the final bout to fatigue at 90% $\dot{V}O_{2peak}$ was less during 2L than 1L (51.1 ± 14.0 vs. 69.3 ± 20.5 $nmol.L^{-1}.J^{-1}$ respectively, P = 0.05, Figure 3.8). This reflected the higher power output and thus work in 2L than 1L.

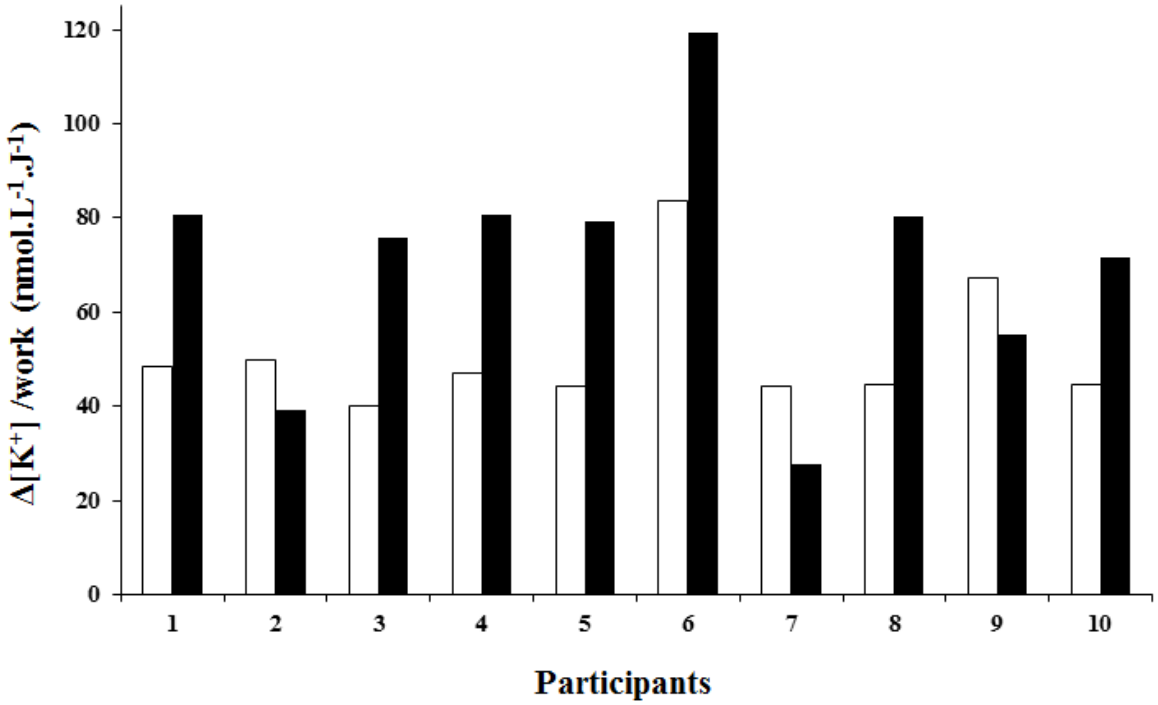

Figure 3.8 Rise in plasma $[K^+]_a$ above rest relative to work done ($\Delta[K^+]_a$.work ratio) for each participant during the final bout to fatigue at 90% $\dot{V}O_{2peak}$ for 2L (open bar) and 1L (shaded bar) cycling. n = 10; values reported as the $\Delta[K^+]$ relative to work during the EB to fatigue ($nmol.L^{-1}J^{-1}$).

3.4.10 [Hb] and Hct

The $[Hb]_a$ and $[Hb]_v$ increased during EB1 and remained greater for each subsequent EB to fatigue ($P < 0.05$) and at 1-20 min recovery (time main effect, $P < 0.05$). There were no significant differences between trials or time x trial interactions for $[Hb]_a$ or $[Hb]_v$ (Appendix F, Tables A3.7 - 3.10).

The Hct_a and Hct_v increased during EB1 and remained greater for each subsequent EB to fatigue ($P < 0.05$), as well as at 1 - 20 min recovery (time main effect, $P < 0.05$). There were no differences between trials or any trial x time interaction for Hct_a or Hct_v (Appendix F, Table A3.11 and 3.14).

3.4.11 Changes in blood volume

The change in blood volume (BV) measured in arterial and venous decreased from rest during EB1 and remained depressed for each subsequent EB to fatigue and at 1 - 20 min during recovery (time main effect, $P < 0.05$, Figure 3.9). There were no differences between trials for arterial or venous ΔBV. There was no trial x time interaction for ΔBV_a, but there was a significant trial x time interaction for ΔBV_v ($P < 0.05$), with ΔBV_v for 2L more negative than 1L at 30 min recovery.

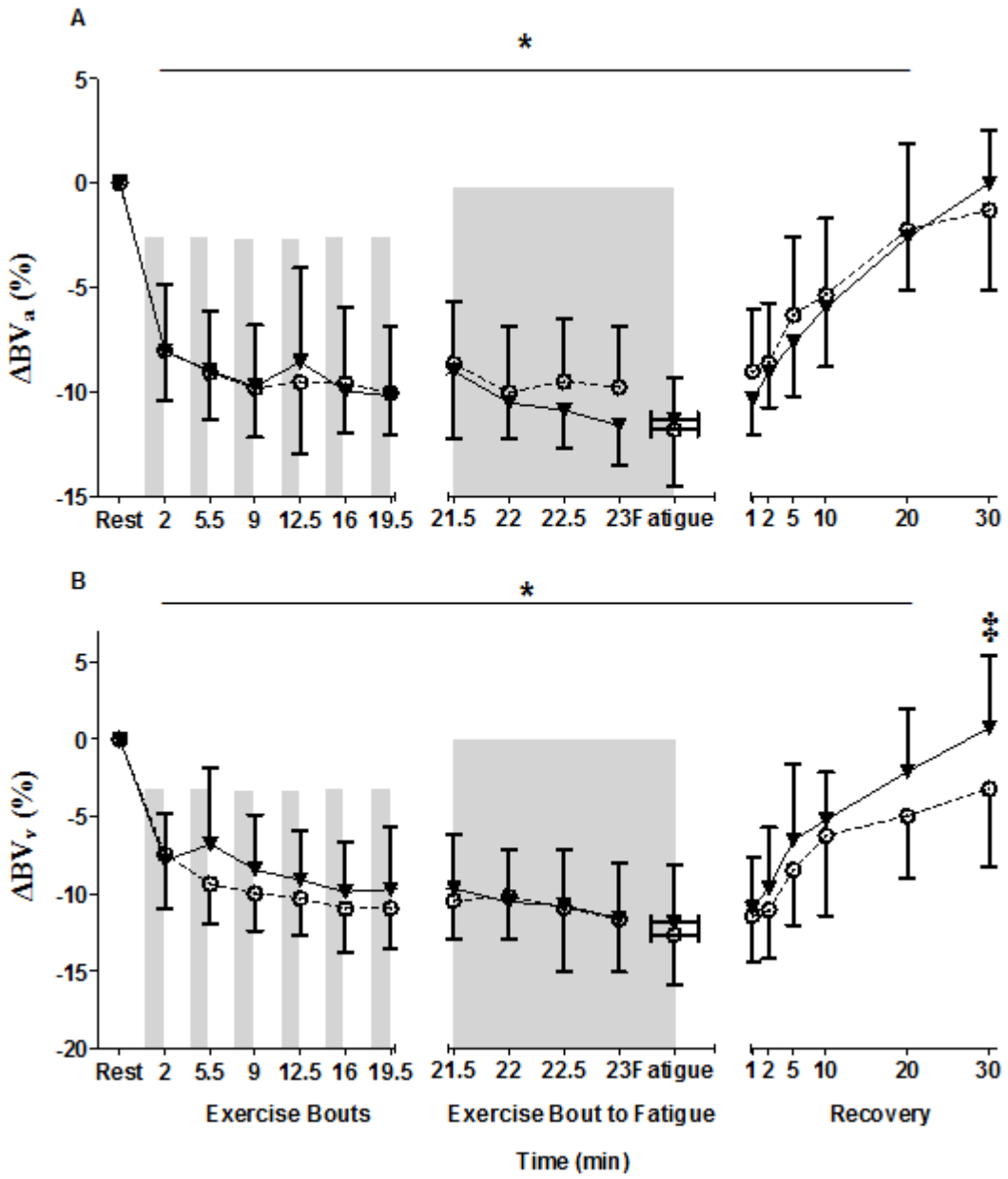

Figure 3.9 Effects of 2L (○) and 1L (▼) cycling on changes in arterial (A) and venous (B) blood volume from rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: n = 10. Shaded bars represent exercise bouts. * Less than rest (time main effect, $P < 0.05$), ‡ 2L less than 1L, (trial x time interaction, $P < 0.05$)

3.4.12 Plasma [Na^+]

The plasma $[Na^+]_a$ and $[Na^+]_v$ increased from rest during EB1 and remained elevated for each subsequent EB to fatigue; as well as during recovery at 1–5 min for $[Na^+]_a$ and 1 – 10 min for $[Na^+]_v$ (time main effect, $P < 0.05$), returning to rest levels thereafter (Figure 3.10). There were no significant differences between trials. However, there was a significant trial x time interaction for $[Na^+]_a$ ($P < 0.05$) with the $[Na^+]_a$ greater for 2L than 1L during the final EB to fatigue at 22.5 min only ($P < 0.05$).

3.4.13 Plasma [Ca^{2+}]

Plasma $[Ca^{2+}]_a$ and $[Ca^{2+}]_v$ increased during EB1 and remained elevated for each subsequent EB including to fatigue, and at 1 and 2 min recovery for $[Ca^{2+}]_a$ and at 1-5 min for $[Ca^{2+}]_v$ (time main effect, $P < 0.05$, Figure 3.11). There were no significant differences between trials. However, there was a significant trial x time interaction for $[Ca^{2+}]_a$ ($P < 0.05$) being greater in 2L than 1L during EB4 only ($P < 0.05$, Figure 3.11).

3.4.14 Plasma [Cl^-]

Plasma $[Cl^-]_a$ increased slightly during EB1 and remained elevated through to EB6, and during EB to fatigue from 22 min to fatigue, and at 1 to 20 min during recovery ($P < 0.05$, time main effect). There were no significant differences between trials for $[Cl^-]_a$ (Figure 3.12). In contrast, $[Cl^-]_v$ decreased slightly to be lower than rest during EB1 and EB2, at 21.5 min during EB to fatigue, and from 5 to 20 min recovery ($P < 0.05$, time main effect). There were no significant differences between trials for $[Cl^-]_v$ (Figure 3.12).

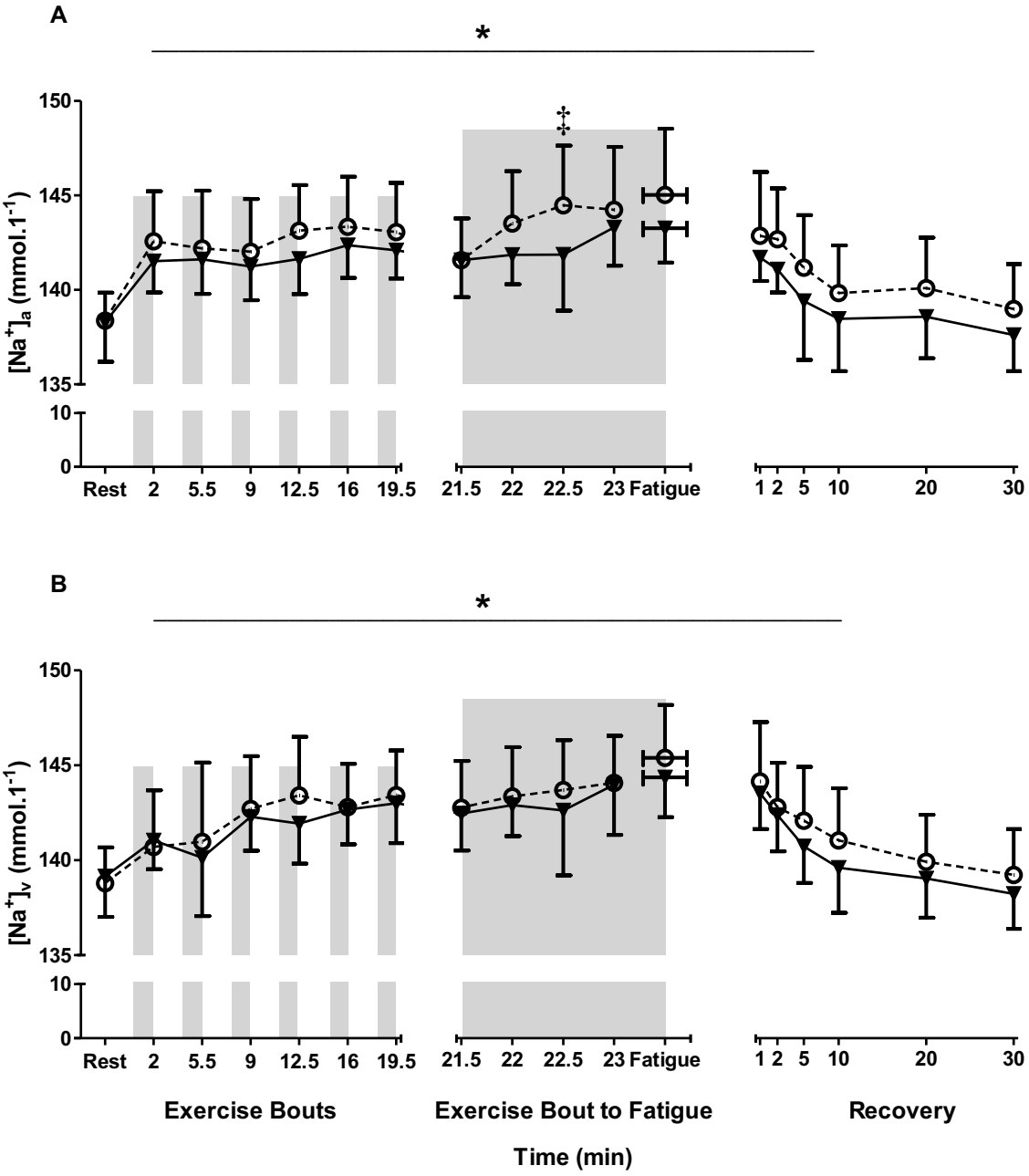

Figure 3.10 Effects of 2L (○) and 1L (▼) cycling on arterial (A) and venous (B) plasma [Na^+] at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

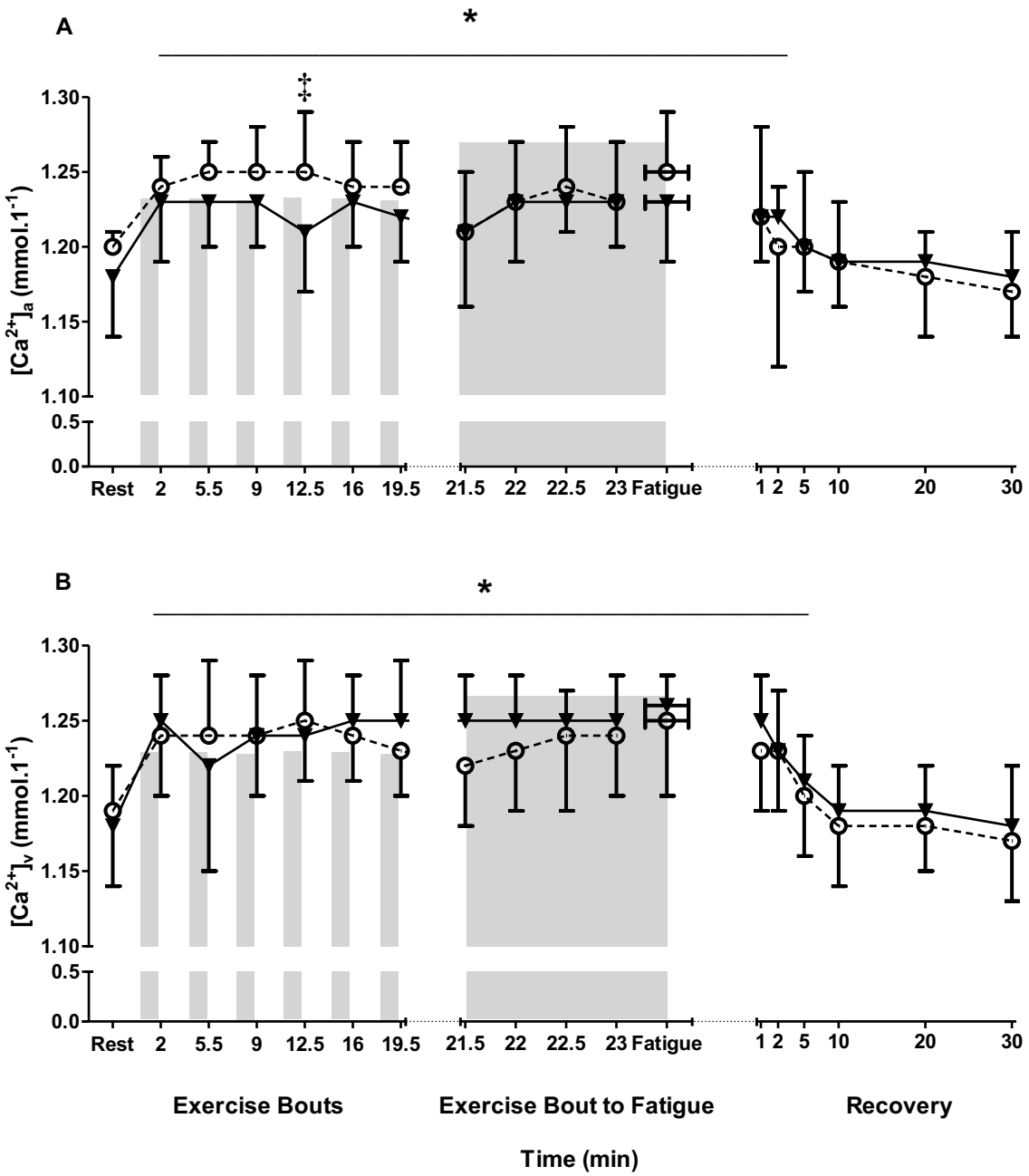

Figure 3.11 Effects of 2L (○) and 1L (▼) cycling on $[Ca^{2+}]_a$ (A) and $[Ca^{2+}]_v$ (B) at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

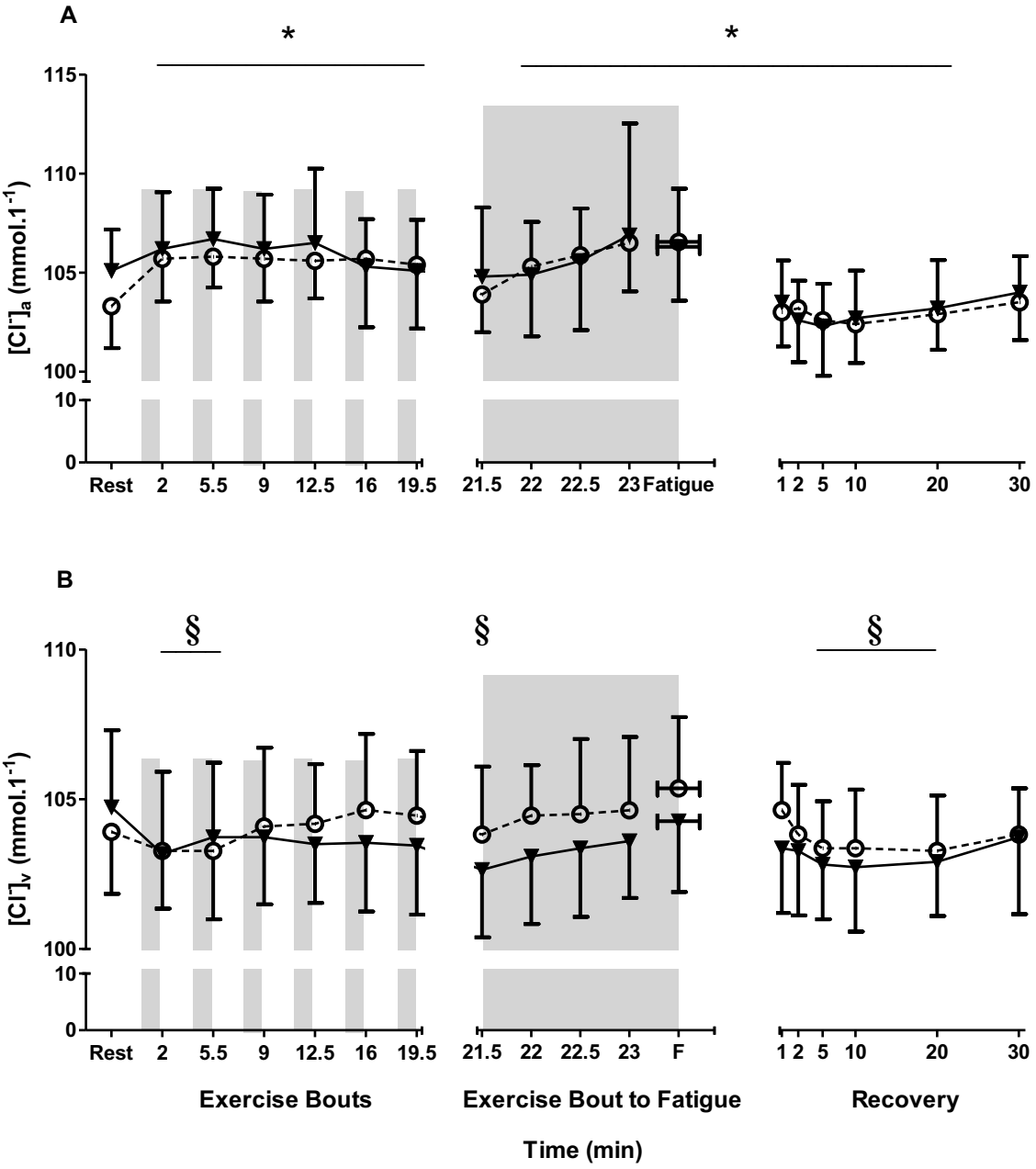

Figure 3.12 Effects of 2L (○) and 1L (▼) cycling on $[Cl^-]_a$ (A) and $[Cl^-]_v$ (B) at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), § Less than rest (time main effect, $P < 0.05$).

3.4.15 Plasma [Lac^-]

Plasma $[Lac^-]_a$ and $[Lac^-]_v$ each increased during EB1 and remained elevated for each subsequent EB including the EB to fatigue, as well as throughout recovery ($P < 0.05$, time main effect, Figure 3.13). There was no trial main effect for $[Lac^-]_a$. However, there was a significant trial x time interaction for $[Lac^-]_a$ ($P < 0.05$,) being greater in 2L than 1L during recovery at 2 - 30 min post-exercise (time by trial interaction, $P < 0.05$, Figure 3.13). However, there were no significant differences between trials or a significant trial x time for $[Lac^-]_v$ (Figure 3.13).

3.4.16 Plasma pH

Plasma pH_a and pH_v each decreased during EB1 and remained depressed for each subsequent EB including the EB to fatigue as well as throughout recovery ($P < 0.05$, time main effect). There was no trial main effect for either plasma pH_a or pH_v. The trial x time interaction for pH_a was significant ($P < 0.05$); pH_a was less in 2L than 1L during EB to fatigue and in recovery at 1, 2, 5 and 10 min post-exercise (Figure 3.14). Similarly, pH_v during 2L was less than 1L during recovery at 1, 2, 5 and 10 min post-exercise (trial x time interaction, $P < 0.05$, Figure 3.14).

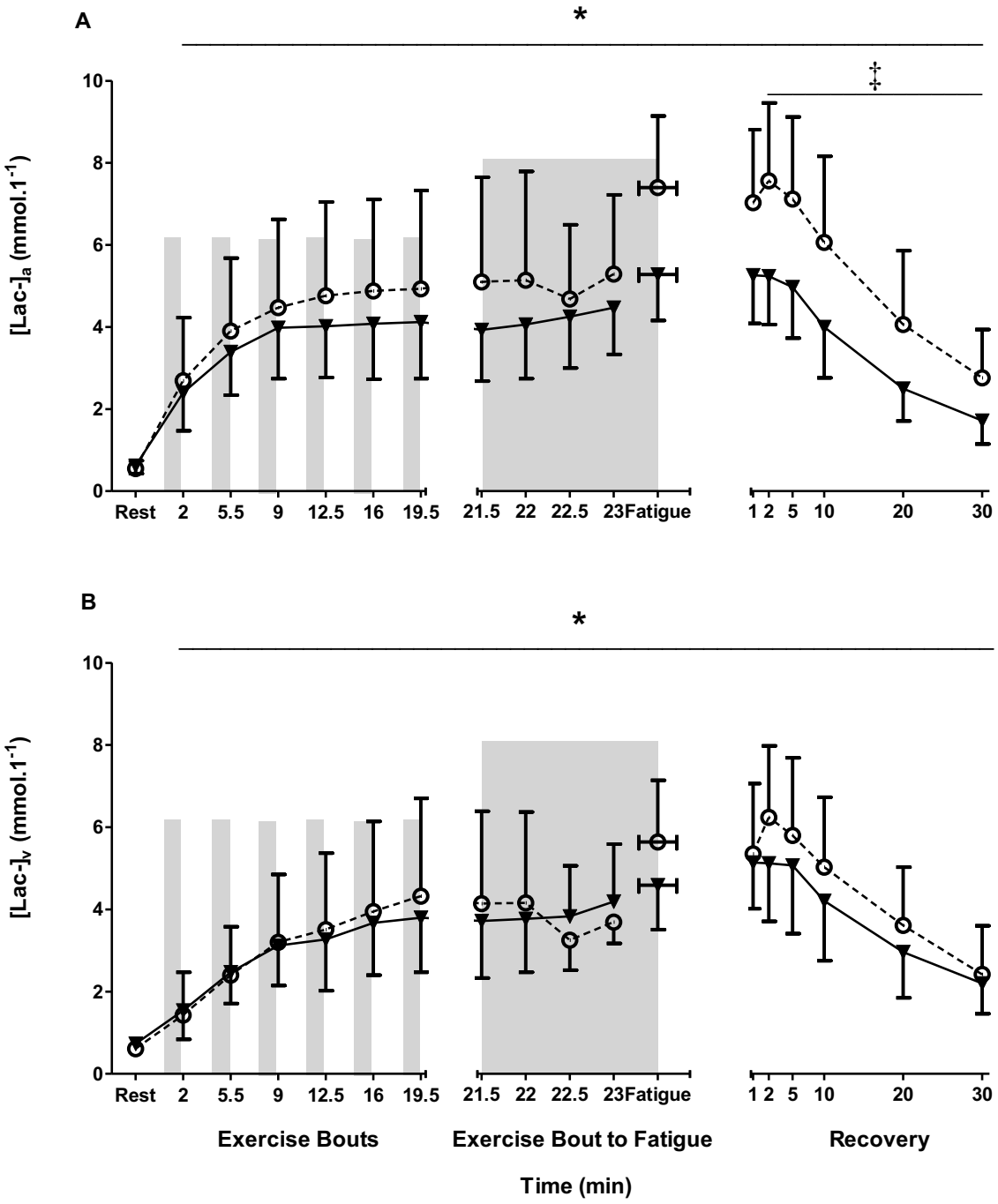

Figure 3.13 Effects of 2L (○) and 1L (▼) cycling on $[Lac^-]_a$ (A) and $[Lac^-]_v$ (B) at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

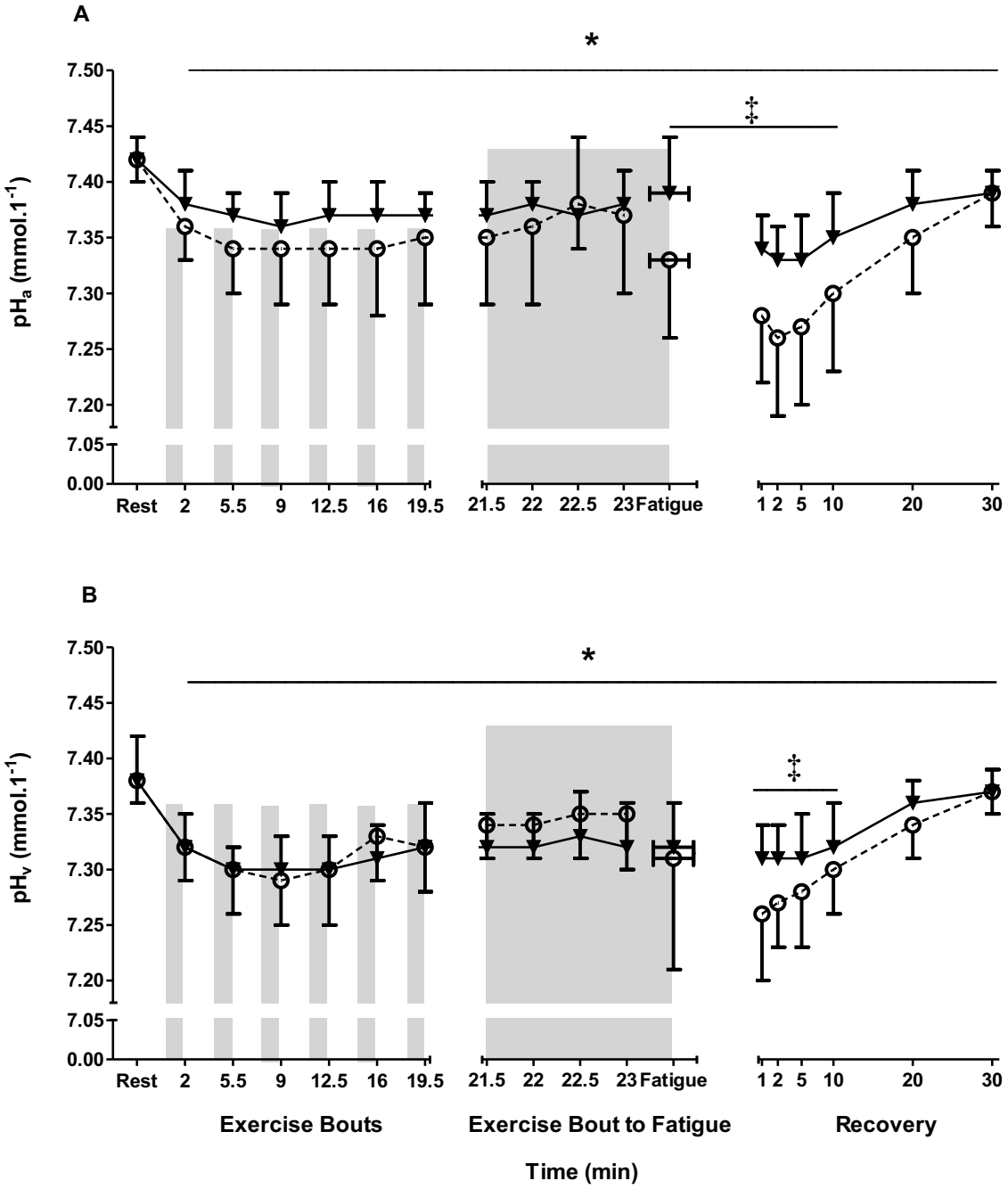

Figure 3.14 Effects of 2L (○) and 1L (▼) cycling on pH_a (A) and pH_v (B) at rest, during intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Greater than rest (time main effect, $P < 0.05$), ‡ 2L less than 1L, (trial x time interaction, $P < 0.05$).

3.4.17 Quadriceps maximal voluntary contractions (MVC)

The MVC pre-exercise values did not differ between trials (148 ± 63 vs. 144 ± 57 Nm, for 2L and 1L, respectively). The MVC was expressed as a percentage of pre-exercise values; this was decreased after each of EB1, EB3, EB6, and the final EB to fatigue, as well as at 10- and 30-min during recovery (time main effect, $P < 0.05$, Figure 3.15). There was no significant trial main effect. There was a significant trial x time interaction ($P < 0.05$) with MVC being greater in 2L than 1L after EB6 (i.e. lesser decrease).

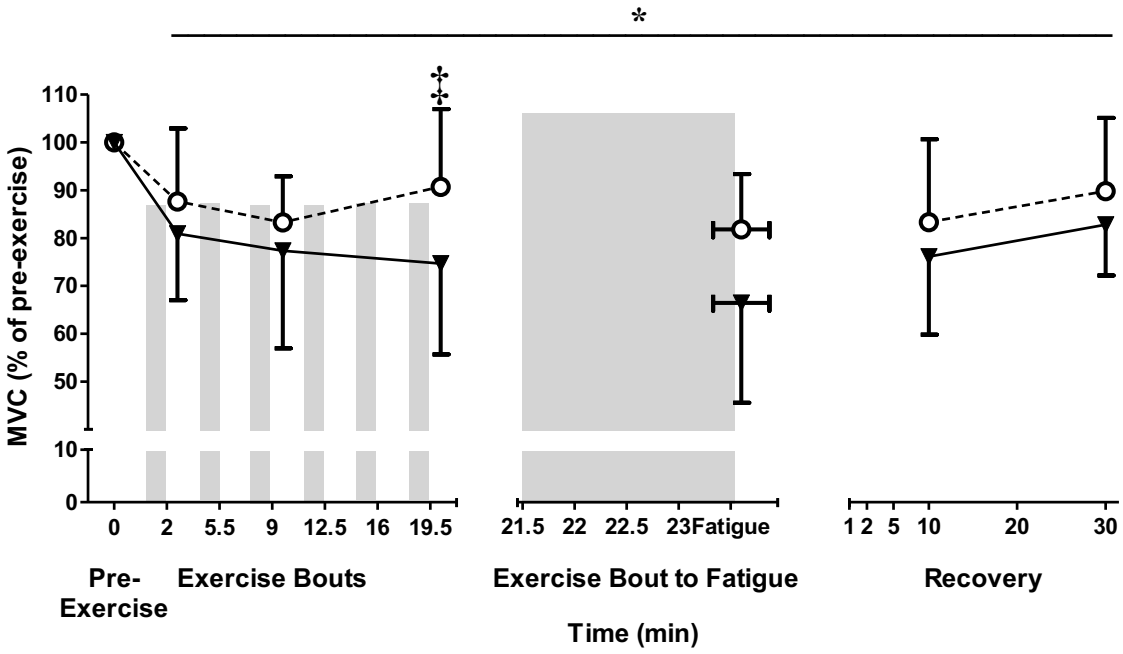

Figure 3.15 Effects of 2L (○) and 1L (▼) cycling on MVC expressed as a percentage of pre-exercise values, after bouts 1, 3 and 6 of intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, after high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and at 10- and 30-min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Less than pre-exercise (time main effect, $P < 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

3.4.18 Reliability for Q_{twpot} interday and intraday

During the ramp protocol, Q_{twpot} values did not significantly differ between 80 – 100% for both intra and interday trials (Table 3.4). The reliability of Q_{twpot} for both intraday (CV% <3.6) and interday (CV% <5.2) was considered good (Appendix F, Table A 1.0).

Table 3.4 Intraday and interday values when magnetic stimulation was applied to the femoral nerve during the ramp protocol.

Stimulation	80%	90%	100%
Trial		Twitch (Nm)	
Famil	18.5 ± 9.0	20.3 ± 10.5	20.8 ± 10.7
2L	16.9 ± 10.0	18.5 ± 10.6	19.4 ± 10.9
1L	17.7 ± 10.4	18.9 ± 10.7	25.7 ± 11.5

Data expressed as mean ± S.D; n = 10.

3.4.19 Quadriceps potentiated twitch (Q_{twpot})

The Q_{twpot} pre-exercise values did not differ between trials (23.4 ± 13.4 vs. 23.0 ± 14.5 Nm, for 2L and 1L, respectively). The Q_{twpot} was expressed as a percentage of pre-exercise values; this was decreased after each of EB1, EB3, EB6, EB to fatigue and at 10- and 30-min recovery (time main effect, $P < 0.05$). There was no significant trial main effect. There was a significant trial x time interaction ($P < 0.05$) with Q_{twpot} being greater in 2L than 1L at 30 min recovery ($P < 0.05$, Figure 3.16).

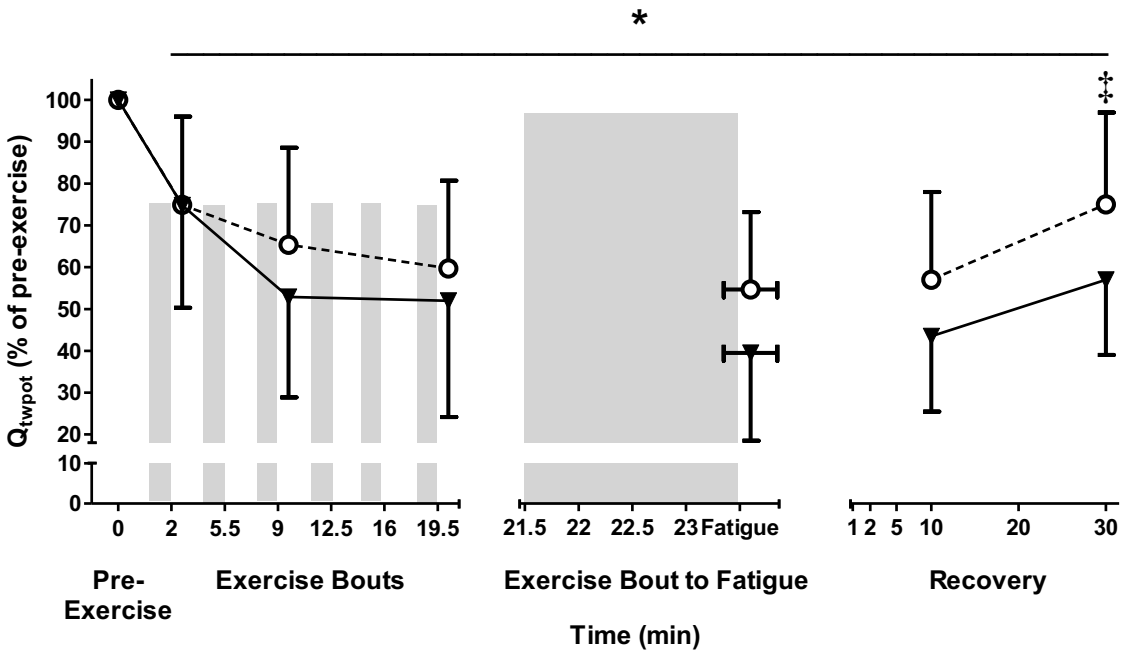

Figure 3.16 Effects of 2L (○) and 1L (▼) cycling on Q_{twpot} expressed as a percentage of pre-exercise values, after bouts 1, 3 and 6 of intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, after high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and at 10- and 30- min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Less than pre-exercise (time main effect, $P < 0.05$), ‡ 2L greater than 1L, (trial x time interaction, $P < 0.05$).

3.4.20 Quadriceps potentiated paired twitch (Doublet)

The Doublet torque pre-exercise values did not differ between trials (49.5 ± 31.6 vs. 46.0 ± 25.5 Nm, for 2L and 1L respectively). The doublet torque was expressed as a percentage of pre-exercise values; this was decreased after each of EB1, EB3, EB6, EB to fatigue and at 10- and 30- min during recovery (time main effect, $P < 0.05$, Figure 3.17). There was no significant trial main effect.

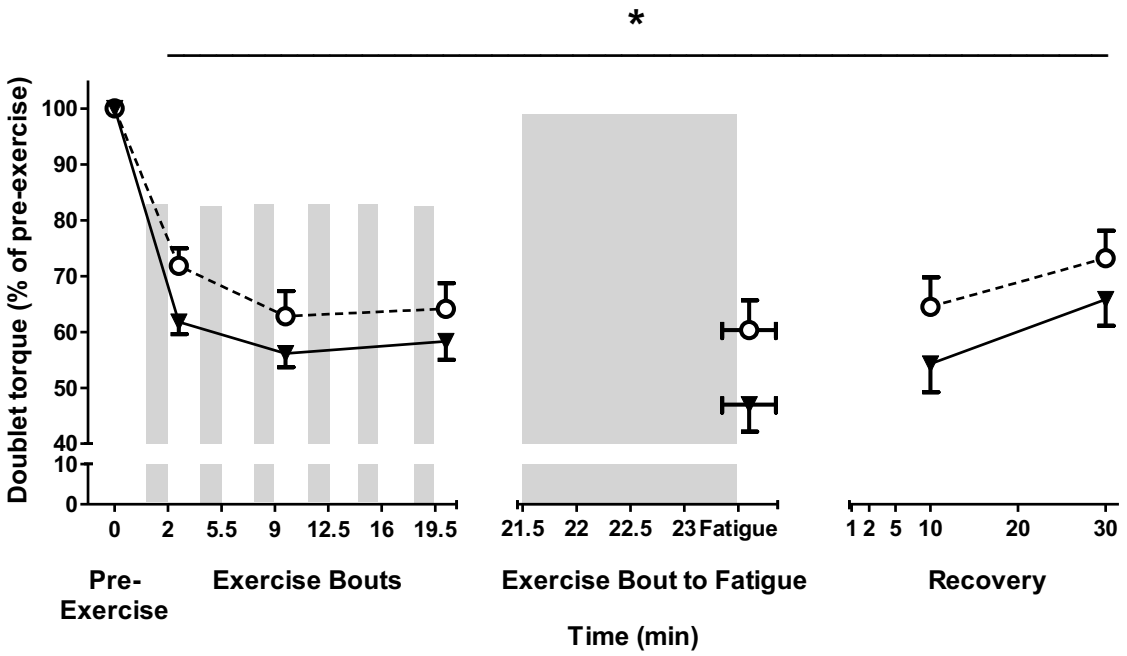

Figure 3.17 Effects of 2L (○) and 1L (▼) cycling on doublet torque expressed as a percentage of pre-exercise values, after bouts 1, 3 and 6 of intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, after high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and at 10- and 30- min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Less than pre-exercise (time main effect, $P < 0.05$).

3.4.21 Quadriceps potentiated 20 Hz tetani

The 20 Hz tetani torque pre-exercise values did not differ between trials (109.9 ± 44.7 vs. 95.7 ± 49.3 Nm, for 2L and 1L, respectively). The 20 Hz tetani torque, expressed as a percentage of pre-exercise values, decreased after EB6, EB to fatigue and during recovery (time main effect, $P < 0.05$, Figure 3.18). There was no significant trial main effect.

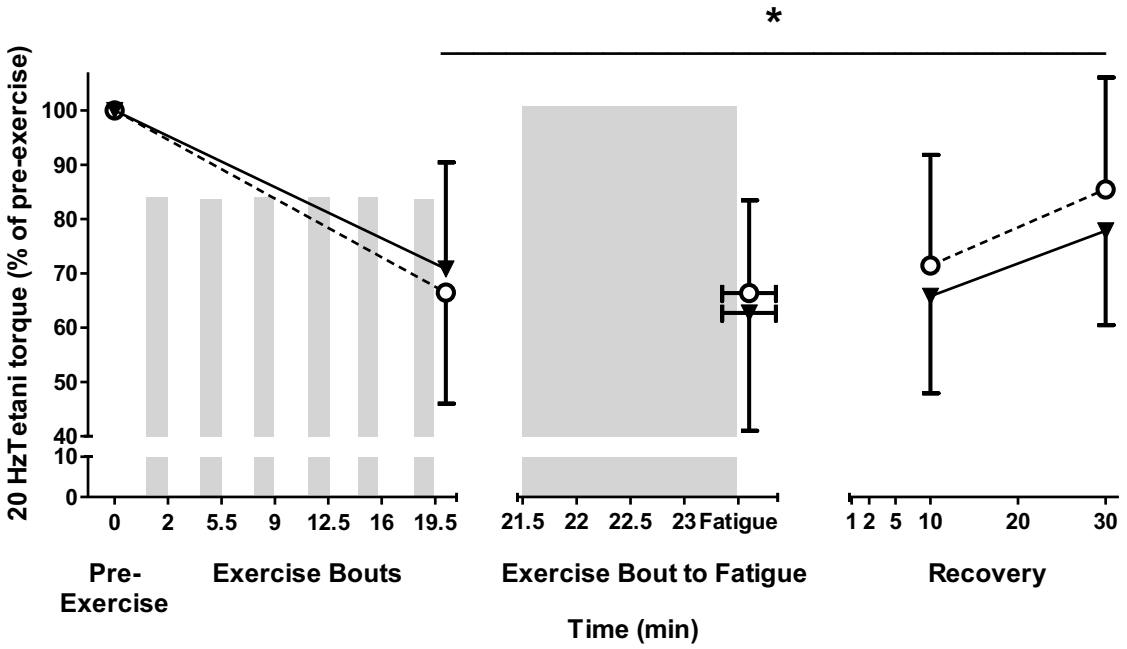

Figure 3.18 Effects of 2L (○) and 1L (▼) cycling on Tetani torque, expressed as a percentage of pre-exercise values, after bouts 1, 3 and 6 of intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, after high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and at 10- and 30- min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Less than pre-exercise (time main effect, $P < 0.05$).

3.4.22 Quadriceps Muscle M-wave During the Evoked Twitch

3.4.22.1 M-wave amplitude

The VM muscle pre-exercise M-wave amplitude values did not differ between trials (2.8 ± 2.1 vs. 3.6 ± 2.5 mV, for 2L and 1L, respectively) or the VL (3.5 ± 2.4 vs. 2.7 ± 2.3 mV for 2L and 1L, respectively). For both VM and VL the M-wave amplitude expressed as a percentage of pre-exercise values was decreased following EB1, EB6, EB to fatigue and during recovery (time main effect, $P < 0.05$, Figure 3.19). However, there was a significant trial x time interaction for VM ($P < 0.05$), with amplitude in 2L less than 1L after EB3 and for VL ($P < 0.05$), with amplitude in 2L less than 1L during recovery at 30 min (Figure 3.19). There was no significant difference between trials.

3.4.22.2 M-wave duration

The pre-exercise M-wave duration did not differ between trials for VM (29.6 ± 16.4 vs. 30.2 ± 14.4) or for VL (33.1 ± 11.6 vs. 28.5 ± 13.0 ms) for 2L vs. 1L, respectively. For VM the M-wave duration, expressed as a percentage of pre-exercise, was increased at 1 min following EB time to fatigue and at 10 min recovery (time main effect, $P < 0.05$, Figure 3.21). For VL the M-wave duration increased after EB time to fatigue (time main effect, $P < 0.05$). There were no significant differences between trials, or significant trial x time interaction, for M-wave duration for either VM or VL muscles (Figure 3.20).

3.4.22.3 M-wave area

The pre-exercise M-wave area did not differ between trials for VM (20 ± 8 vs. 25 ± 10 mV.s) or for VL (26 ± 16 vs. 23 ± 16 mV.s) for 2L vs. 1L, respectively. For VM the M-wave area, expressed as a percentage of pre-exercise, decreased at 1 min following EB time to fatigue and at 10 min recovery (time main effect, $P < 0.05$, Figure 3.21). For VL, the M-wave area,

expressed as a percentage of pre-exercise, there was no change with time (main effect). There were no significant differences between trials, or significant trial x time interaction, for M-wave area for either VM or VL muscle (Figure 3.21).

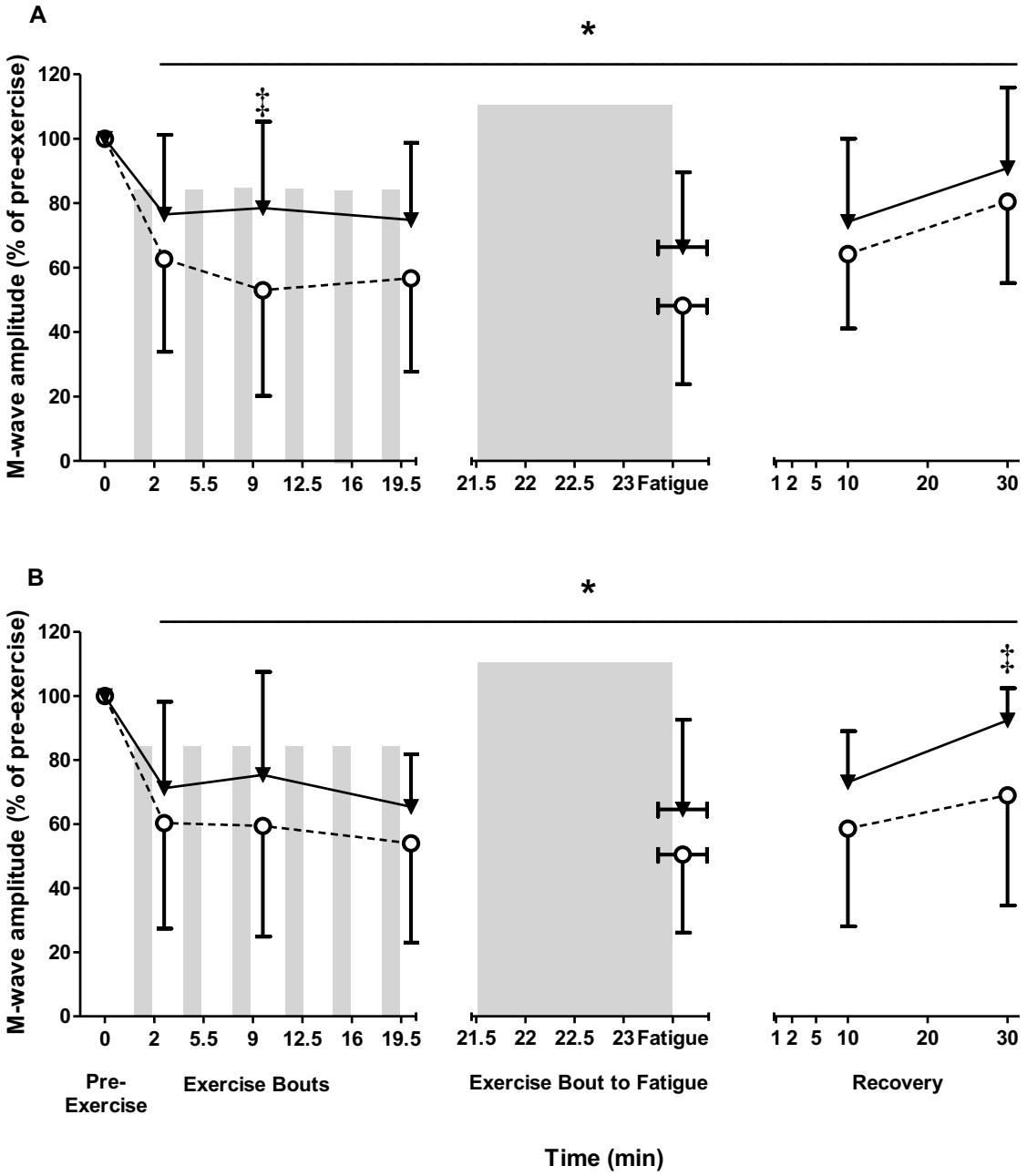

Figure 3.19 Effects of 2L (○) and 1L (▼) cycling on M-wave amplitude during an evoked quadriceps twitch for VM (A) and VL (B), expressed as a percentage of pre-exercise values, after bouts 1, 3 and 6 of intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, after high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and at 10 and 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. * Less than pre-exercise (time main effect, $P < 0.05$), ‡ 2L less than 1L (trial x time interaction, $P < 0.05$).

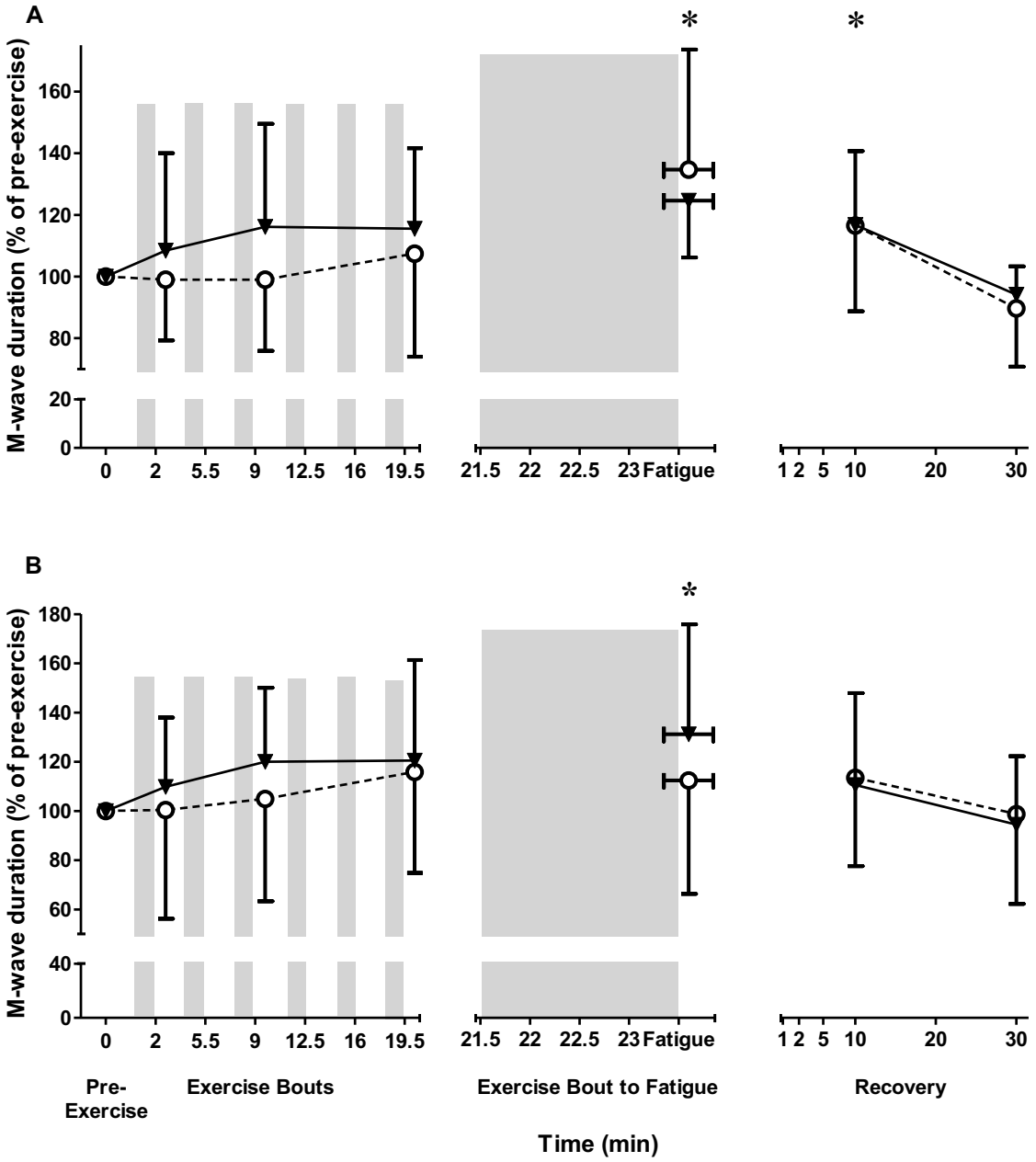

Figure 3.20 Effects of 2L (○) and 1L (▼) cycling on M-wave duration during an evoked quadriceps twitch for VM (A) and VL (B), expressed as a percentage of pre-exercise values, after bouts 1, 3 and 6 of intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, after high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and at 10 and 30 min recovery. Values are mean ± S.D: n = 10. Shaded bars represent exercise bouts. ***** Greater than pre-exercise (time main effect, $P < 0.05$).

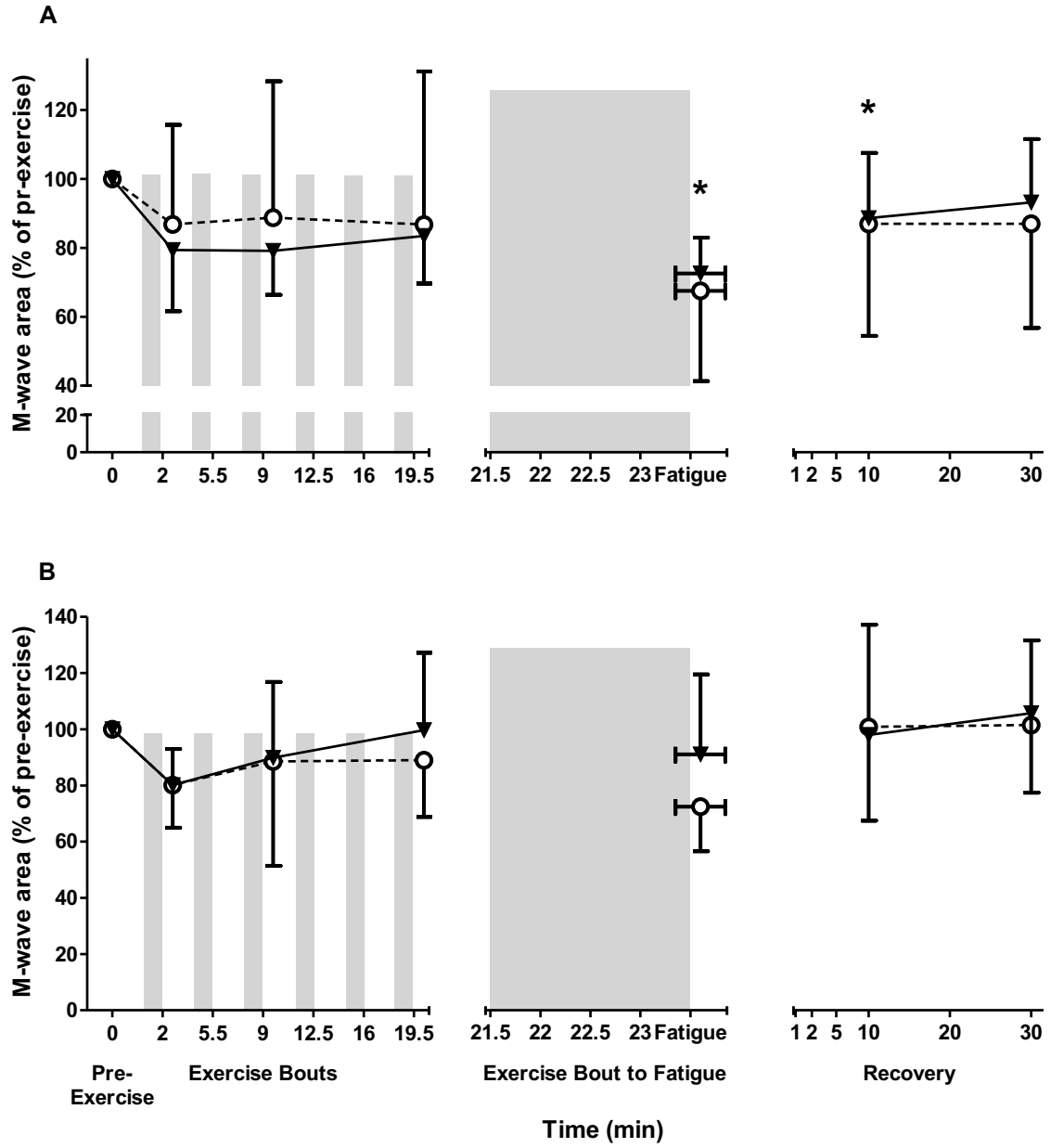

Figure 3.21 Effects of 2L (○) and 1L (▼) cycling on M-wave area during an evoked quadriceps twitch for VM (A) and VL (B), expressed as a percentage of prior to exercise, after intermittent exercise comprising six 2 min repetitions at 80% $\dot{V}O_{2peak}$, at high intensity exercise at 90% $\dot{V}O_{2peak}$ continued to fatigue and for 30 min recovery. Values are mean ± S.D: $n = 10$. Shaded bars represent exercise bouts. *Less than pre-exercise ($P < 0.05$).

3.4.23 Quadriceps muscle M-wave during the evoked doublet

3.4.23.1 M-wave amplitude

The pre-exercise M-wave amplitude was greater for 1L than 2L for VM (3.1 ± 2.1 vs. 4.6 ± 2.8 mV) and for VL (3.7 ± 1.8 vs. 5.7 ± 3.7 mV), for 2L vs. 1L, respectively ($P < 0.05$). For VM and VL the M-wave amplitude, expressed as a percentage of pre-exercise, was decreased following EB1, EB3, EB6 and EB to fatigue (time main effect, $P<0.05$). There were no significant differences between trials, or significant trial x time interaction, for M-wave amplitude, for either VM or VL muscles (Appendix F, Tables A 1.34 and A 1.38).

3.4.23.2 M-wave duration

The pre-exercise M-wave duration did not differ between trials, for VM (28.5 ± 11.6 vs. 28.5 ± 10.8 ms) or for VL (29.7 ± 13.4 vs. 27.7 ± 7.9 ms), for 2L vs. 1L respectively. The M-wave duration, expressed as a percentage of pre-exercise was increased at 1 min following EB to fatigue for VM (time main effect, $P < 0.05$). For the VL muscle, M-wave duration, expressed as a percentage of pre-exercise, was increased following each of EB1, EB3, EB6, EB time to fatigue and at 10- and 30- min during recovery (time main effect, $P < 0.05$, Appendix F, Tables A 1.36 and A 1.40).

3.4.23.3 M-wave area

The pre-exercise M-wave area did not differ between trials, for VM (15.9 ± 14.7 vs. 22.6 ± 17.0 mV.s) or for VL (30.4 ± 23.9 vs. 30.2 ± 23.8 mV.s), for 2L and 1L respectively. The M-wave area, expressed as a percentage of pre-exercise, was decreased following EB1 and EB6 in the 2L (time main effect, $P < 0.05$ Appendix F, Tables A 1.35 and A 1.39); whilst in the 1L the M-wave area was increased following EB1 (time main effect, $P < 0.05$), then decreased after EB6 (time main effect, $P < 0.05$). There was a trial x time interaction ($P < 0.05$) for VM

with a greater decrease in 2L than 1L after EB1 ($P < 0.05$). For the VL muscle, the M-wave area, expressed as a percentage of pre-exercise, was decreased after EB1, EB6, EB to fatigue, and at 10- and 30- min during recovery (time main effect, $P < 0.05$, Appendix F Tables A 1.35 and A 1.39).

3.4.24 Quadriceps muscle M-wave during the evoked 20 Hz tetani

3.4.24.1 M-wave amplitude

The pre-exercise M-wave amplitude did not differ between trials, for VM (5.4 ± 4.1 vs. 4.1 ± 1.9 mV) or VL (6.1 ± 4.4 and 4.5 ± 2.2 mV), for 2L and 1L, respectively. The VM muscle M-wave amplitude, expressed as a percentage of pre-exercise, was decreased at 1 min following EB to fatigue and at 10 min during recovery (time main effect, $P < 0.05$), then returned to pre-exercise values. The VL muscle M-wave amplitude, expressed as a percentage of pre-exercise, decreased following EB to fatigue and during recovery (time main effect, $P < 0.05$). There was a trial x time interaction ($P < 0.05$), with 2L less than 1L at 30- min recovery (Appendix F, Tables A 1.42 and A 1.46).

3.4.24.2 M-wave duration

The pre-exercise M-wave duration did not differ between trials, for VM (22.9 ± 4.7 vs. 21.6 ± 8.8 ms) or VL (26.7 ± 6.9 vs. 23.7 ± 8.6 ms), for 2L and 1L, respectively. The VM muscle M-wave duration, expressed as a percentage of pre-exercise was increased at 1 min following EB to fatigue, and at 10- and 30- min during recovery (time main effect, $P < 0.05$). For the VL muscle, expressed as a percentage of pre-exercise, increased following EB time to fatigue and at 10- min during recovery (time main effect, $P < 0.05$, Appendix F, Tables A 1.44 and A 48).

3.4.24.3 M-wave area

The pre-exercise M-wave area did not differ between trials, for VM (25.8 ± 18.8 vs. 22.1 ± 9.0 mV.s) or for VL (27.8 ± 21.0 vs. 27.5 ± 12.4 mV.s), for 2L and 1L respectively. The M-wave area, expressed as a percentage of pre-exercise, was decreased at 1 min following EB to fatigue, and at 10- and 30- min during recovery for VM (time main effect, $P < 0.05$, Figure 3.28). For the VL muscle, the M-wave area, expressed as a percentage of pre-exercise, was decreased at 1 min following EB to fatigue and at 10- min during recovery (time main effect, $P = 0.05$, Appendix F, Tables A 1.43 and A 1.47).

3.5 Discussion

This study compared the effects of a large versus smaller contrasting muscle mass, using two- versus one-legged cycling, on arterial and venous plasma [K^+] and other electrolytes, exercise time to fatigue following high-intensity cycling and on post-exercise quadriceps muscle function measured by MVC, and evoked muscle twitch, doublet and 20Hz tetani, induced via magnetic stimulation of the femoral nerve, with measures of torque (Nm) and M-wave characteristics (amplitude, duration and area). The cycling exercise was performed at the same relative intensities for 2L vs. 1L trials, with no difference in RPE and HR between 2L and 1L exercise, indicating that the exercise intensities evenly matched for both the 2L and 1L cycle work-rate.

Exercise with the larger muscle mass resulted in higher arterial plasma [K^+] during high-intensity intermittent cycling exercise and in recovery. Since the exercise was performed at the same relative intensities during both trials (80% and 90% $\dot{V}O_{2peak}$), these findings confirm that the contracting muscle mass during exercise is an important determinant in regulating $[K^+]_a$. Since the absolute work rate during the 2L trial was close to double that of the 1L trial, one would also expect a substantially higher [K^+] proportional to the muscle mass trial. Therefore, the difference between trials is much less than might be predicted. The greater $[K^+]_{a-v}$ together with larger $\Delta[K^+]_{work}{}^{-1}$ ratio in 2L than 1L suggests a larger K^+ clearance also occurred from blood during exercise with the large muscle mass. However, the greater $[K^+]_a$ with 2L was not associated with greater decrements in muscle function with fatigue, with no major differences in exercise duration, voluntary (MVC) and evoked torque (twitch, doublet, 20 Hz) or M-wave characteristics, with the exception of a larger decrease in MVC at 1 min following EB to fatigue and at 30 min during recovery for 1L than 2L. The small difference in [K^+] between trials is consistent with [K^+] being tightly regulated during exercise and probably explains why no or limited differences in muscle function and exercise performance were found between trials.

3.5.1 Larger contracting muscle mass increases arterial plasma $[K^+]$ and $[K^+]_{a-v}$ during high-intensity cycling

The $[K^+]_a$ attained during cycling at 90% $\dot{V}O_{2peak}$ was ~6 mM, consistent with other findings of hyperkalaemia during high-intensity exercise (Medbo and Sejersted 1985, Medbo and Sejersted 1990, Vøllestad, Hallén et al. 1994, McKenna, Heigenhauser et al. 1997). The large increase in plasma $[K^+]$ with intense exercise may be attributed to a greater rate of K^+ release into plasma from active muscle than the K^+ reuptake by active muscle and K^+ clearance by inactive muscle and other tissues, in agreement with previous studies (Juel, Bangsbo et al. 1990, Green, Chin et al. 1993). Non-contracting tissues assists in maintaining concentration gradients for the net movement of K^+ into the venous circulation from interstitial fluids in active muscle (Lindinger, McKelvie et al. 1995). The rapid increase in plasma $[K^+]$ during high-intensity intermittent exercise probably reflects a lag in the activation of the Na^+,K^+,-ATPase in muscle at the beginning of exercise, with the excess K^+ cleared when exercise ceases (Medbo and Sejersted 1990, Verburg, Hallén et al. 1999). K^+ loss from skeletal muscle also results in K^+ accumulation in the muscle interstitium (Street, Nielsen et al. 2005), with previous microdialysis studies shown $[K^+]$ values between 10 – 13 mM in interstitial space of contracting muscle, considerably greater than arterial and venous $[K^+]$ (Green S, Langberg H et al. 2000, Juel, Pilegaard et al. 2000)). The initial rapid loss of K^+ from the exercising muscle to the circulation is primarily regulated by the balance between K^+ efflux rate from the muscle cells and the reuptake rate (Vøllestad, Hallén et al. 1994).

A higher $[K^+]_a$ and a greater $\Delta[K^+]_a$ were observed in 2L compared to 1L during the during the high-intensity cycling bout to fatigue, which lasted for a similar duration in the two trials. This suggests that a greater overall K^+ efflux from contracting muscles occurred during the 2L than 1L cycling. Hence it is likely that a greater K^+ clearance also accompanied the 2L exercise,

minimising differences in $[K^+]_a$ between trials. Intermittent exercise is therefore an effective model allowing for K^+ clearance between exercise bouts. As 2L cycling requires a larger active muscle mass, there is also a proportionally lesser amount of inactive muscle to assist in the clearance of K^+ during exercise. It was therefore anticipated that plasma $[K^+]$ may have been larger than 6 mM as considerably larger values have been previously reported during various exercise models utilising a large muscle mass (Medbo and Sejersted 1990, Sejersted and Sjøgaard 2000).

The increase in plasma $[K^+]$ with intense exercise may be attributed to a greater rate of K^+ release into plasma from active muscle than the K^+ reuptake by active muscle and K^+ clearance by inactive muscle and other tissues, which agrees with previous studies (Juel, Bangsbo et al. 1990, Green, Chin et al. 1993). Subsequently, regulation of the plasma compartment by non-contracting tissues assists in maintaining concentration gradients for the net movement of $[K^+]$ into the venous circulation from interstitial fluids of active muscle (Lindinger, McKelvie et al. 1995).

In contrast to the greater $[K^+]_a$ with 2L cycling, quite different results were found when $[K^+]$ was measured in antecubital blood, which drains the forearm muscles, which were largely inactive. The $[K^+]_v$ was less in the 2L than 1L trial during two of the intermittent exercise bouts, including during the EB to fatigue. Importantly, the arterio-venous $[K^+]_{a-v}$ difference across the forearm was greater in 2L than 1L throughout the trial and particularly during the EB to fatigue. It is likely that Na^+, K^+-ATPase activity in inactive muscles may have lowered the rise in K^+ during exercise, suggesting the 2L has a greater K^+ uptake than 1L. The catecholamines adrenaline and noradrenaline play an important role in regulating Na^+-K^+-ATPase, increasing the rate of active Na^+, K^+- transport in skeletal muscle (Clausen and Everts 1989, Clausen 1996). Circulating catecholamines are higher during large muscle mass, and thus, via activating muscle Na^+, K^+-ATPase may reduce circulating $[K^+]$ during exercise (Lockwood, Lum et al.

1974, DeFronzo, Bia et al. 1981, Katz, Sahlin et al. 1985). Hence, the greater $[K^+]_a$ and $\Delta[K^+]_a$ during intense exercise involving large muscle mass suggest K^+ release from active muscles may have been attenuated by a greater adrenergic outflow; a similar mechanism probably also explains greater clearance of K^+ by inactive muscles. However, it is important to acknowledge that both the radial arterial and antecubital venous $[K^+]$ would substantially underestimate muscle interstitial $[K^+]$ during exercise.

In summary these findings support the hypothesis that $[K^+]_a$ was greater during two- than one-legged intense cycling, indicating the contracting muscle mass directly affects $[K^+]_a$ during high-intensity cycling bouts. The greater arterio-venous K^+ difference across the inactive forearm in 2L probably reflects greater K^+ clearance during high-intensity exercise, due to increased overall activation of Na^+, K^+-ATPase. However, there is the possibility that differences in the forearm blood flow might have occurred between trials; this would affect K^+ uptake since this equates to the product of $[K^+]_{a-v}$ difference x blood flow. The slightly elevated plasma $[K^+]_a$ suggests that muscle interstitial $[K^+]$ might also be higher during the 2L exercise, although this was not measured here.

3.5.2 **Muscle excitability function and fatigue during and following high-intensity cycling bouts**

The effects of muscle mass were also investigated on exercise time to fatigue and on voluntary and evoked muscle torque and M-wave characteristics (amplitude, duration and area). Exercise time to fatigue did not differ between 2L and 1L. High-intensity cycling exercise performed by both two- and one-leg to exhaustion elicited fatigue of the quadriceps muscles, evidenced by considerable reductions in MVC, $Q_{tw,pot}$ and Q_{20HZ}. After 2L cycling, post-exercise MVC torque decreased by ~19%, $Q_{tw,pot}$ by ~45% and Q_{20HZ} by ~34%, whilst after 1L, MVC torque decreased by ~34%, $Q_{tw,pot}$ by ~54% and Q_{20HZ} by ~34%. These declines are similar to previous reported declines of between ~28 and ~60% after knee extensor MVC, tetanic and twitch forces (Polkey, Kyroussis et al. 1996, Amann, Eldridge et al. 2006, Rossman, Venturelli et al. 2012, Cairns, Inman et al. 2017).

The non-significant trial main effects indicates no major differences between 2L and 1L for any of MVC, $Q_{tw,pot}$ and Q_{20HZ}, although greater reductions were seen for 1L in MVC at 1 min after fatigue and in $Q_{tw,pot}$ at 30 min recovery. It has been suggested that when the source of skeletal muscle afferent feedback is confined to a small contracting muscle mass, the central nervous system tolerates a greater magnitude of peripheral fatigue and likely greater intramuscular metabolic disturbances (Rossman, Venturelli et al. 2012). The similar percentage declines of MVC, $Q_{tw,pot}$, doublet, 20Hz tetani and M-wave in 2L and 1L occurred despite greater $[K^+]_a$ and presumably also higher muscle interstitial $[K^+]$ in 2L without invoking greater muscle fatigue. This may point to dissociation between elevated $[K^+]$ and fatigue. However, since microdialysis has shown $[K^+]_I$ of 10 – 13 mM in contracting skeletal muscle, considerably above arterial $[K^+]$ (Green S, Langberg H et al. 2000, Juel, Pilegaard et al. 2000, Nordsborg, Mohr et al. 2003), $[K^+]_a$ will substantially underestimate $[K^+]_I$. Measuring $[K^+]_I$ during exercise would have provided more insight to the effects of muscle mass on fatiguability. It is possible

that greater disturbances in muscle $[K^+]_I$ may also have been tolerated with the 2L trials. The interstitial space has a substantial capacity for accumulating K^+ and the K^+ efflux across the sarcolemma would only be evident in the venous effluent from contracting muscles (Sejersted and Sjøgaard 2000). Thus, the apparent dissociation between impacts of different muscle mass on arterial $[K^+]$ measures and muscle contractile function do not necessarily allow firm conclusions to be drawn on the role of K^+ in skeletal muscle fatigue.

The M-wave with elicited muscle twitch exhibited considerable changes with fatigue, with each of decreased peak-to-peak amplitude, increased duration and decreased total area. Some differences in responses were seen in M-wave with different stimulation paradigms. This might reflect a lack of sensitivity in the M-wave area measurement. Bigland-Ritchie, Jones et al. (1979) observed increased M-wave area after a 60 s MVC because of a slowing of conduction velocity, most likely as a result of increased duration without loss of amplitude (Bigland-Ritchie, Jones et al. 1979). During maximal stimulation for up to 60 s the action potential was prolonged and area increased (Bigland-Ritchie, Jones et al. 1979). Furthermore, after stimulation at high frequencies the surface action potentials and rectified EMG increased dramatically during the first 10–15 s then decreased, probably as a result of failure of electrical propagation (Bigland-Ritchie, Jones et al. 1979). There were no significant trial order and few interaction effects detected for M-wave characteristics for amplitude and area after exercise; a finding consistent with previous studies (Rossman, Venturelli et al. 2012, Rossman, Garten et al. 2014). During continuous or repeated muscle activation whilst the neural stimulation rate decreases considerably, it remains adequate for complete force production because the metabolic activity involved in the contractions change the muscle properties; reducing the rate of relaxation and the fusion frequency (Bigland-Ritchie and Woods 1984, Balog, Thompson et al. 1994). Therefore, the observed M-wave area decline, in the present study, may be explained by a slight decrease in amplitude. Interestingly, stimulating the muscle at one-minute post-

exercise may be influenced by a hyper-polarising effect, due to an electrogenic effect of increasing Na^+,K^+,-ATPase activity, which probably diminished any membrane depolarisation effects and fatigue (Hicks and McComas 1989). The exercise-induced increase in Na^+, K^+-ATPase activity acts to restore the transmembrane [Na^+] and [K^+] in the muscle cell and through its electrogenic effect, it was proposed to enable muscles to remain excitable during continuous contractile activity (Hicks and McComas 1989). This superimposed on fatigue effect may explain the less consistent decrease in M-wave area. The observed changes in M-wave characteristics are consistant with the changes in membrane excitability, presumably reflecting K^+ shifts across the muscle membrane. However, these occurred irrespective of size of active muscle mass during exercise. The counterbalancing Na^+,K^+-ATPase stimulation effect on fatiguing muscle may explain the less consistent decrease in M-wave data.

3.5.3 RPE, HR, time to fatigue and oxygen consumption responses to high-intensity cycling

A novel finding was that cycling time to fatigue, RPE and HR during EB to fatigue were not different between trials during high-intensity cycling using the same participants and muscle action. Findings from previous studies have found higher RPE during large muscle mass exercise compared to a small muscle mass (Green 2004). The very high RPE at the end of exercise indicate significant psychophysiological stress, and suggest participants were exercising at close to their capacity. As RPE was taken only at one specific time point and so can only relate to the K^+ at that point. Also, the measure was arterial K^+ whereas interstitial K^+ might be anticipated to be more closely linked.

Furthermore, heart rate responses elicited by partial flow restriction during leg cycling suggest the muscle metaboreflex principally elevates heart rate by increasing cardiac sympathetic activity, and only following dynamic exercise with a large muscle mass (Fisher, Adlan et al.

2013). The greater $\dot{V}O_2$ for 2L than 1L cycling, is expected as due to the higher absolute peak output.

3.5.4 Plasma ion concentrations during high-intensity cycling

Studies in this laboratory have typically examined the range of electrolyte and acid-base disturbances with exercise and effects of varying interventions. These measures were therefore done routinely. Furthermore, changes in electrolytes are likely to be involved in fatigue. This study investigated K^+ and muscle function recovery post-exercise. Therefore, it was important to also study recovery of other electrolyte and acid-base disturbances.

The arterial plasma [Na^+], [Ca^{2+}], [Cl^-], [Lac^-] all increased and pH decreased with high-intensity cycling exercise, for both 2L and 1L. Similar directional responses were seen in antecubital venous plasma, with the exception of $[Cl^-]_v$ which was reduced with exercise. There were no significant trial main effects, indicating no systematic differences between trials; although there was a trial by time interaction effect with 2L greater than 1L for $[Na^+]_a$, $[Ca^{2+}]_a$, $[Lac^-]_a$ and pH_a. This strongly suggests that regulation of these electrolytes and acid-base state is more heavily influenced by relative exercise intensity than the amount of contracting muscle mass. Therefore, the observed ionic and metabolic disturbances in the present study may have been too small to contribute to fatigue. During the present study $[Cl^-]_a$ increased, consistent with the possibility that a normal plasma [Cl−] range from 96 to 106 mM prior to exercise may protect against fatigue. When extracellular [Cl^-] was reduced from 128 to 10 mM in non-fatigued muscles, force was initially depressed but subsequently recovered fully (Cairns, Ruzhynsky et al. 2004). Prior observations of low [Cl^-] have been suggested to be caused by a greater K^+ efflux (Cairns and Dulhunty 1995, Dutka, Murphy et al. 2008) or greater K^+ induced depolarisation (Cairns, Ruzhynsky et al. 2004). It is likely a small increase in these ion concentrations would be expected with a decrease in plasma volume, although these effects

were not calculated here. However, little is known about the effects of HIIT on plasma volume variations and its likely link to increased muscle performance. These effects were not calculated for plasma volume as the automated analysers measuring Hb and Hct have recently been shown to provide artefactual analyses of Hct and thus changes in plasma volume (Watson and Maughan 2014), therefore it was not considered a reliable calculation and was not included here. The greater $[Lac^-]_a$ in 2L during recovery at 2 to 30 min is consistent with a greater work output during 2L because of the much higher absolute power output. It has previously been shown that a rapid rise in $[Lac^-]_a$ and subsequent Lac^- uptake across inactive forearm muscle occurs after intense leg cycling exercise (Kowalchuk, Heigenhauser et al. 1988), demonstrating the importance of inactive muscle, as well as contracting muscle and other tissues, as a regulator of Lac^- in the arterial circulation.

During intense exercise numerous ion concentrations may change simultaneously in the interstitial, transverse tubular and intracellular compartment, and therefore require consideration (Cairns and Lindinger 2008). During muscle contractions, high $[K^+]_I$ may not cause a depolarisation sufficient to impair force production, due to protection by active Na^+, K^+-ATPase (Clausen 2003a) or because other ions such as Ca^{2+} , Cl^- , H^+ antagonise $[K^+]_I$ effects. The elevated $[Na^+]_I$ may also stimulate the Na^+, K^+-ATPase (Clausen 2003a), whilst interaction between lowered Na^+ and K^+ gradients reduce muscle excitability (Overgaard, Nielsen et al. 1999). This which may be explained by lowered $[Na^+]_I$ reducing the driving force for Na^+ (Cairns and Lindinger 2008). Cairns, Hing et al. (1998) recently showed that severe Ca^{2+} depletion did not cause fatigue. However, lowered extracellular $[Ca^{2+}]$, exacerbating fatigue during repeated or continuous tetani, whilst raised $[Ca^{2+}]_O$ (5–10 mM), or availability of more Ca^{2+} entry pathways, attenuated fatigue (Cairns, Hing et al. 1998). Whilst plasma Ca^{2+}

increased minimally, ~0.05 mmol.1^{-1}, in the present study it is difficult to use this as a marker of interstitial [Ca^{2+}]. Therefore, it is difficult to suggest such a slight increase in Ca^{2+} is likely to cause fatigue.

Force was depressed by ~10% when extracellular [Cl^-] was reduced from 127 to 10 mM in non-fatigued muscle (Cairns, Ruzhynsky et al. 2004) although it fully recovered when Cl^- efflux repolarised the E_m (McCaig and Leader 1984). Therefore, it is possible that prior to exercise a normal $[Cl^-]_o$ and normal chloride conductance (gCl) may protect, but when a muscle is first depolarised, a lower $[Cl^-]_o$ or lower gCl becomes protective (Ricker, Haass et al. 1978). Thus, the slight increase in Cl^- of ~ 0.05 mmol.$1.^{-1}$ during exercise in the present study may not have been large enough to have contributed to the reduced force.

A decreased pH_i (increased $[H^+]_i$) associated with lactic acid accumulation and $[K^+]_i$ depletion (Lindinger and Heigenhauser 1991) has long been linked to the development of fatigue (Fitts 1994) although this has been questioned as a large acidosis has little detrimental effect on maximum force at body temperature (Cairns 2006, Allen, Lamb et al. 2008a). Neither a preconditioning extracellular acidosis (Mainwood and Cechetto 1980, Kristensen, Albertsen et al. 2005) nor alkalosis with raised [HCO^-] (Lindinger, Heigenhauser et al. 1990, Cairns 2006, Broch-Lips, Overgaard et al. 2007) had any influence on fatigue resistance in isolated muscles. However, a H^+–K^+ interaction has been shown since acidosis partially restored force at raised extracellular [K^+] in human skeletal muscle (Lehmann-Horn and Kuther 1987). It has also been found that acidosis restored excitability in K^+-depressed muscle (Nielsen, de Paoli et al. 2001, Pedersen, Nielsen et al. 2004, Pedersen, de Paoli et al. 2005) although it had minimal effect on action potentials in normal solutions (Pedersen, Nielsen et al. 2004, Pedersen, de Paoli et al.

2005). Therefore, it is possible that the increase in Lac- by ~6 mmol.1^{-1} and the decrease in pH by ~0.05 mmol.1^{-1}, during intense exercise are linked to the development of fatigue. Although [K^+] increased during exercise it is difficult to use this as a marker of interstitial [K^+]. Therefore, it would be problematical in determining any detrimental effect on muscle performance and force.

A mechanism by which acidosis restores excitability may involve intracellular H^+ effects mediated via inhibition of *g*Cl (Pedersen, Nielsen et al. 2004, Pedersen, de Paoli et al. 2005, Bennetts, Parker et al. 2007). This has been shown via H^+ –K^+ –Cl^- interaction simultaneously in skinned rat fast-twitch fibres with low $[K^+]_i$ using acidotic conditions in normal and Cl^--free conditions (Pedersen, de Paoli et al. 2005). An intracellular acidosis allows greater force production in K^+ -depolarized fibres at normal Cl^-. However, in Cl^--free conditions the protective effect of acidosis was not evident. If t-tubular *g*Cl is reduced by acidosis, it is likely that a reduced *I*Na will still invoke action potentials during trains (Pedersen, de Paoli et al. 2005). However, extracellular H^+ effects via reducing inactivation of voltage-dependent Na^+ channels was found when acidosis caused an increased *I*Na in voltage clamp depolarized fibres (Lehmann-Horn and Kuther 1987).

Therefore, it is likely that the observered differences between trials in the changes in each of plasma volume, plasma [Na^+], [Ca^{2+}], [Lac^-], pH during intense exercise may not have been large enough to induce a significant difference between trials for either time to fatigue or muscle performance.

3.6 Conclusions

Exhaustive high-intensity intermittent cycling invoked marked and sustained increases in arterial and antecubital venous plasma $[K^+]$, with greater $[K^+]_a$ and $[K^+]_{a-v}$ across the relatively inactive forearm musculature, during 2L than 1L. This indicates that the magnitude of active muscle mass likely affected both contracting muscle K^+ release and inactive muscle K^+ clearance, with both likely being greater in 2L cycling. However, the time to fatigue in the final EB at 90% $\dot{V}O_{2peak}$ did not differ between 2L and 1L, indicating that there is limited evidence that high-intensity cycling exercise had a greater physiological effect on muscle function during exercise with a large muscle mass (2L) than a small muscle mass (1L), at the same relative intensity. Whilst no major differences in voluntary and evoked muscle torque occurred between trials, both the MVC and evoked Q_{twpot} torque decreased less for 2L than 1L. Furthermore, the high-intensity intermittent cycling resulted in a smaller decrease in Q_{twpot} M-wave amplitude for 2L than 1L, whilst during recovery Q_{twpot} peak amplitude decrease was higher for 2L than 1L. The changes in M-wave characteristics after intense exercise, decreased amplitude, increased duration and decreased area, are consistant with the changes in membrane excitability. However, the M-wave changes were irrespective of the active muscle mass during exercise, suggesting the differences in K^+ shifts across the muscle membrane with this exercise model were insufficient to induce major changes in excitability and fatigue.

CHAPTER 4

The effects of an acute oral dose of digoxin on plasma K^+ regulation, muscle performance and muscle excitability during and following high-intensity cycling in healthy adults

4.1 INTRODUCTION

During exercise, K^+ shifts from muscle intracellular to extracellular spaces and then diffuses into the blood, increasing plasma [K^+] (Sejersted and Sjøgaard 2000). A rise in muscle extracellular [K^+] may be in part responsible for muscle fatigue by depolarising the sarcolemmal membrane and reducing the excitability of the muscle cells (Balog 1994, Sejersted and Sjøgaard 2000, McKenna, Bangsbo et al. 2008). In skeletal muscle, the Na^+,K^+-ATPase is essential for regulating Na^+ and K^+ gradients across the plasma and t-tubular membranes, via active K^+ re-accumulation and Na^+ extrusion and thus regulating membrane excitability (Clausen 2008). One approach to explore the importance of the Na^+,K^+-ATPase and K^+ regulation in muscle function and fatigue is to use an intervention that inhibits the Na^+,K^+-ATPase (Sundqvist, Berglund et al. 1983). The pharmacological agent digoxin is used clinically and is a specific Na^+,K^+-ATPase inhibitor (Gheorghiade, van Veldhuisen et al. 2006, Vivo, Krim et al. 2008, Ambrosy, Butler et al. 2014). A major clinical function of digoxin is in the myocardium, where it increases the force of contraction and increases stroke volume, which is of potential benefit to patients with heart failure (Levi, Boyett et al. 1994). This occurs as a result of digoxin inhibiting the Na^+,K^+-ATPase in the heart, thereby inhibiting Na^+ extrusion, elevating intracellular $[Na^+]_i$, with increased Na^+/Ca^{2+} exchange across the cell membrane causing increased Ca^{2+} availability for SR Ca^{2+} release inside the cell, thus directly

increasing myocardial contractility (Fozzard and Sheets 1985, Levi, Boyett et al. 1994, Armoundas, Hobai et al. 2003, Espinosa-Tanguma, Algara-Suárez et al. 2012). An inotropic effect of digitalis on skeletal muscle has also been demonstrated in animals (Smulyan and Eich 1976), but few studies have investigated the effects of digoxin on muscle strength in humans. Digoxin will however, also selectively inhibit the Na^+,K^+-ATPase in skeletal muscle, thus potentially impairing K^+ regulation during exercise and accelerating the onset of fatigue. After an intravenous bolus of digoxin (0.01 $mg.kg^{-1}$), antecubital venous plasma [K^+] did not increase during dynamic handgrip exercise, compared to placebo (Janssen, Lheureux et al. 2009). However, the 30 min between digoxin infusion and commencement of exercise may have been insufficient time for sufficient digoxin binding to skeletal muscle (McKenna 2003). In healthy participants, oral digoxin (0.25 $mg^{-1}day$) ingestion for 14 days, surprisingly, did not impair arterial [K^+] or muscle performance during high-intensity cycling (Sostaric 2012). However, muscle analyses revealed that during this 14 day period there was a 7% increase in the Na^+,K^+-ATPase content that effectively counter-balanced the 7% deficit that would otherwise have occurred due to this fraction being bound and inhibited by digoxin (Sostaric 2012). Thus, digoxin will inhibit some of the Na^+,K^+-ATPase in both the heart and skeletal muscle, where this effect is less well known in humans. This study investigated the effects of acute oral digoxin intervention on arterial [K^+] regulation, neuromuscular function and exercise performance in healthy adults. Acute intervention was designed to prevent any possible compensatory upregulation of the Na^+,K^+-ATPase. Muscle excitability, exercise performance and fatigue were measured to determine possible mechanical influences of digoxin, at rest and following high-intensity cycling. It was hypothesised that digoxin would; (i) increase arterial plasma [K^+] during and following high-intensity exercise and recovery; (ii) reduce time to fatigue during high-intensity cycling; (iii) exacerbate the reductions in voluntary and evoked torque and in changes in M-wave characteristics after fatiguing exercise.

4.2 METHODS

Ten healthy recreationally active participants, comprising 6 males and 4 females, gave written informed consent prior to participating in the study (age 25.8 ± 5.6 yr, height 180.2 ± 9.9 cm, body mass 76.4 ± 9.1 kg, mean ± SD). The study was approved by the Victoria University Human Research Ethics Committee and as a clinical trial by the Therapeutic Goods Administration of Australia (2013/0604).

4.2.1 Experimental design

Participants reported to the laboratory on five separate occasions. The initial visit was to screen participants for eligibility into the study. The second visit was designed to establish $\dot{V}O_{2peak}$, and time to fatigue, whilst the third visit was to determine the variability of the time to fatigue component of the exercise protocol in these participants; these visits were separated by 5-7 days and no invasive procedures were undertaken. The fourth and fifth visits comprised the experimental trials with either a digoxin or placebo intervention; trials were conducted in a randomised, crossover, double-blinded, counterbalanced design. The experimental trials were separated by one week for males to ensure complete washout of digoxin and by 28 days for females to enable testing during the same phase of the menstrual cycle. For ethical reasons, the attending medical practitioner was non-blinded. Participants avoided vigorous exercise on the preceding night and the morning of the trial and maintained their normal dietary habits. Participants were advised to avoid alcohol, caffeine, tobacco from midnight prior to the day of the trial. The effectiveness of the blinding to the treatment was not directly assessed; no participants reported any altered sensation with either of the treatments. This digoxin study was part of a larger study performed in collaboration with another PhD student, who measured muscle Na^+,K^+-ATPase content and isoforms (T. Atanasovska PhD thesis); the exercise performance and plasma [K^+] data are shared and included in both theses.

4.2.2 Pre-Screening

The following procedures were undertaken during the pre-screening visit: written consent, anthropometric measures, incremental fitness test to determine $\dot{V}O_{2peak}$, antecubital venous blood sample to determine serum electrolyte profile and kidney function; resting and exercise electrocardiogram (ECG) recording, and familiarisation of the experimental exercise protocol. Participants were excluded from participating if they presented with or suffered from any cardiovascular or respiratory condition/disease, bleeding disorder, eating disorders, skin or anaesthetic allergies or musculoskeletal injuries that may be aggravated by the exercise protocol. Participants with normal kidney function as determined by urea and creatinine concentrations were allowed to proceed with the study. Normal ranges for urea were defined as between 2.5 - 6.5 mM for females and 3.0 - 7.5 mM for males whilst for creatinine were between 45 - 85 μM for females and 60 – 110 μM for males (Melbourne Pathology, 2015). Participants were not on any medications, except for the contraceptive pill for females.

4.2.3 Incremental cycle test and cardiorespiratory measures

Cardiorespiratory measures were monitored continuously pre-exercise, during the incremental cycle test and during recovery (Figure 4.1), as previously described (Chapter 3.2.3.1).

4.2.4 Placebo and digoxin administration

The digoxin intervention comprised 0.50 mg (2 x 0.25 mg) delivered orally in tablet form (Sigmaxin, digoxin tablet 250 μg, Aspen Australia, Melbourne, Australia), whilst the placebo was also delivered orally via tablet form containing lactose only (Stenlake Compounding Pharmacy, NSW, Australia). Both interventions were administered 60 min prior to exercise. Clinically, digoxin is typically taken orally in tablet form, using either 0.25 mg or 0.50 mg tablets; this oral delivery mode is best understood clinically, most easily managed and with less room for error, and is considered safe in young healthy adults. Digoxin has a high bioavailability which results in a rapid rise to peak concentrations in the blood typically within 1-1.5 hrs post ingestion (Silva, Costa et al. 2009, Schmitt, Kaeser et al. 2010).

4.2.5 Cycle exercise protocol test

Participants exercised on a Lode cycle ergometer (Lode, Excalibur Sport V2.0, Groningen, The Netherlands). Participants were required to cycle continuously for 1 minute at an intensity of 60% $\dot{V}O_{2peak}$, 1 minute of 95% $\dot{V}O_{2peak}$ then a final bout of 95% $\dot{V}O_{2peak}$, at ~60-65 rev.min^{-1}, continued until volitional exhaustion, defined as an inability to maintain pedal cadence above 65 rev.min^{-1}. Although participants received verbal encouragement to maximise their effort during the trial, participants did not cycle above 65 rev.min^{-1}.

The intense continuous interval test was used because it is accompanied by a dramatic rise in plasma [K’] with each exercise bout and by marked muscular fatigue, evidenced by progressively declining work output.

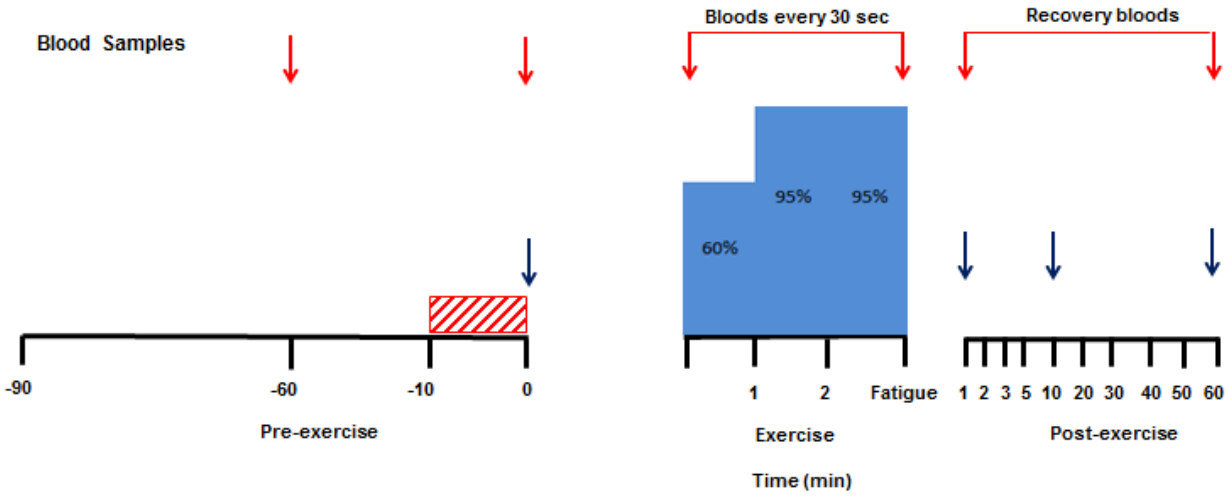

Figure 4.1 A schematic illustrating the cycle test protocol utilising both DIG and PLAC.

Legend

: ramp protocol (described in Chapter 3.2.6.2)

: Magnetic Stimulation (described in section 4.2.8.1)
: Blood Sampling (described in section 4.2.8)

4.2.6 Power outputs for cycling exercise

Participants performed the cycle exercise tests at power outputs corresponding to 60% $\dot{V}O_{2peak}$ and 95% $\dot{V}O_{2peak}$ power outputs.

4.2.7 Variability for cycling time to fatigue

Variability of test measures were determined for the two variability trials using the intraclass correlation coefficient (ICC) and typical error ± 90% confidence limits, expressed as a percentage (coefficient of variation, CV).

4.2.8 Arterial cannulation - Blood sampling and analyses

A cannula (Arrow Quick Flash, 20 gauge) was inserted anterograde into the radial artery of the left arm, then covered with an adhesive sterile patch (Tegaderm), and attached to a sterile extension tubing set (ITL Arterial Kit), which was affixed to the forearm and upper arm of the participant, under local anaesthesia (1% xylocaine). The arterial line was kept patent by a slow, sterile, isotonic saline (0.9% NaCl) infusion bag under pressure to enable rapid, repeated blood sampling during cycling. Participants rested supine for 20 min before resting blood samples were obtained prior to the commencement of each trial. This period allowed the stabilisation of posture-induced fluid shifts and minimise any fluctuations in $[K^+]$. Participants were then administered either placebo or digoxin and a second blood sample taken 60 min later, with participants remaining in supine posture. An additional blood sample (5 ml) was collected for the determination of serum digoxin concentration ([SDC]). Following a series of baseline MVC and magnetic stimulations, the participants then moved to the adjacent cycle ergometer, where a seated pre-exercise sample was taken (0 min) and then commenced the cycling test. Blood samples were then taken at 30 s intervals throughout exercise, with the final sample during the time to fatigue bout taken immediately prior to volitional fatigue. Recovery blood samples were collected at 1, 2, 3, 5, 10, 20, 30, 40, 50- and 60-min post-exercise with the participants lying in a supine position. Approximately 4.7 ml of blood was withdrawn on each occasion. Approximately 1.7 ml was drawn in a heparin-coated blood gas syringe (Radiometer, Safe Pico Aspirator) for analyses of plasma gas tension, acid-base balance and electrolyte concentration, as well as whole blood haematocrit (Hct) and haemoglobin ([Hb]), glucose and lactate concentrations for duplicate analyses. Duplicate analyses were conducted for the rest sample with single analysis for exercise and recovery samples. Arterial plasma pH, gas tensions (PCO_2, PO_2), electrolyte concentrations ($[K^+]$, $[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$), Hct, [Hb], blood glucose and lactate concentrations were analysed using an automated blood gas analyser (Radiometer,

ABL800 Flex analyser, Denmark). An additional 3 mL blood sample was collected to determine [SDC]; this was kept at room temperature for 15 min to allow for clotting then spun down for 10 min at 3500 rpm and analysed by an external pathology company using an automated immunoassay analyser (Roche, Cobas 602, Switzerland). SDC were reported in nM or as below the detection limit of 0.2 nM at pre-exercise only. To determine digoxin effects on post-exercise K^+ dynamics, the decline in $[K^+]_a$ from fatigue values were calculated in recovery ($-\Delta[K^+]_a$).

4.2.9 Quadriceps neuromuscular function

4.2.9.1 Maximal voluntary contraction and evoked muscle torques

The voluntary and evoked muscle torque (Nm) measurements and procedures were as previously described (Chapter 3.2.6.1).

4.2.9.2 Peripheral magnetic stimulation

The magnetic stimulation measures were performed as previously described (Chapter 3.2.6.2)

4.2.9.3 Magnetic stimulation protocol

To ensure full motor unit (MU) recruitment maximal twitch torque was achieved with the magnetic stimulator (i.e., plateau in twitch torque), a ramp test was performed at the beginning of each session. A twitch torque plateau during the ramp protocol confirmed full MU recruitment when the rise between the 80-100% stimulation intensities did not differ significantly.

The magnetic stimulation protocol comprised a 4 s MVC, then three $Q_{tw,pot}$, followed by a 4 s MVC then two doublet (20 Hz), and a final 4 s MVC, then 1 20 Hz tetani. These measures

were conducted pre-exercise at 60 min post-intervention, after exercise to fatigue (~1 min post-exercise) and at 10- and 60-min post-exercise.

4.2.9.4 Compound action potentials (M-waves) measurement

M-wave signals were recorded and analysed as previously described (Chapter 3.2.6.4)

4.2.10 Statistical Analysis

All data were analysed using a mixed linear model to detect differences for time and treatment main effects and for time x treatment interaction. When significant main effects or interactions were found, pairwise comparisons were made using the Least Significant Difference (LSD) post hoc test. Statistical significance was accepted at $P<0.05$. Treatment main effects or treatment x time interaction effects are reported only when significant. Data are presented as mean ± standard deviation (SD). Statistical analyses were calculated using SPSS version 22 (SPSS Inc., Champion, IL). The intraday (e.g., trial 1 vs. trial 2) and interday (e.g., DIG vs. CON) reliability of time to fatigue were estimated using the intraclass correlation coefficient [ICC (3,1)] (Hopkins 2000) and typical error ± 90% confidence limits, expressed as a percentage [coefficient of variation (CV)] (Hopkins 2000).

4.3 RESULTS

4.3.1 Exercise time to fatigue

Cycling time to fatigue at 95% $\dot{V}O_{2peak}$ had excellent reproducibility during variability trials (CV = 3.9, ICC 0.91). The time to fatigue cycling at 95% $\dot{V}O_{2peak}$ was 7.8% less for DIG than PLAC (224.2 ± 48.1 vs. 241.8 ± 56.8 s, respectively, P<0.05).

4.3.2 Cardiorespiratory measures during cycling

The $\dot{V}O_{2peak}$ cycle test cardiorespiratory measures were $\dot{V}O_2$ (3.87 ± 0.91 L.min^{-1}), $\dot{V}_E$ (133.3 ± 23.5 L.min^{-1}) and RER (1.22 ± 0.08). During the intense cycling bouts there were no significant differences between DIG and PLAC for peak values during time to fatigue for $\dot{V}O_2$ (3.43 ± 0.68 vs. 3.56 ± 0.81 L.min^{-1}, P = 0.19), $\dot{V}_E$ (148.1 ± 40.2 vs. 153.1 ± 36.7 L.min^{-1}, P = 0.31) and RER (1.27 ± 0.11 vs. 1.26 ± 0.10, P=0.49), respectively.

4.3.3 Serum digoxin concentration

Serum digoxin concentration at 60 min post-ingestion in DIG was 3.36 ± 0.80 nM (range 2.2 - 4.7 nM). In PLAC, the SDC was below the detection limit of 0.2 nM for all participants.

4.3.4 Plasma $[K^+]_a$

Plasma $[K^+]_a$ was greater than baseline throughout exercise, then decreased during early recovery to below baseline at 3-20 min post-exercise (time main effect, P < 0.05, Figure 4.2A). Plasma $[K^+]_a$ was greater for DIG than PLAC during exercise to fatigue (treatment main effect, P<0.05). The peak $[K^+]_a$ was 6.55 ± 0.57 vs. 6.31 ± 0.57 mM, for DIG and PLAC respectively). The $\Delta[K^+]_a$ became more negative during recovery compared to fatigue values, reaching -3.14 ± 1.10 mM at 5 min post-exercise, (time main effect, P<0.05, Figure 4.2B). The $-\Delta[K^+]_a$ was less negative for DIG than PLAC, (-2.90 ± 0.57 vs. -3.11 ± 0.41 mM, respectively, treatment main effect, P<0.05).

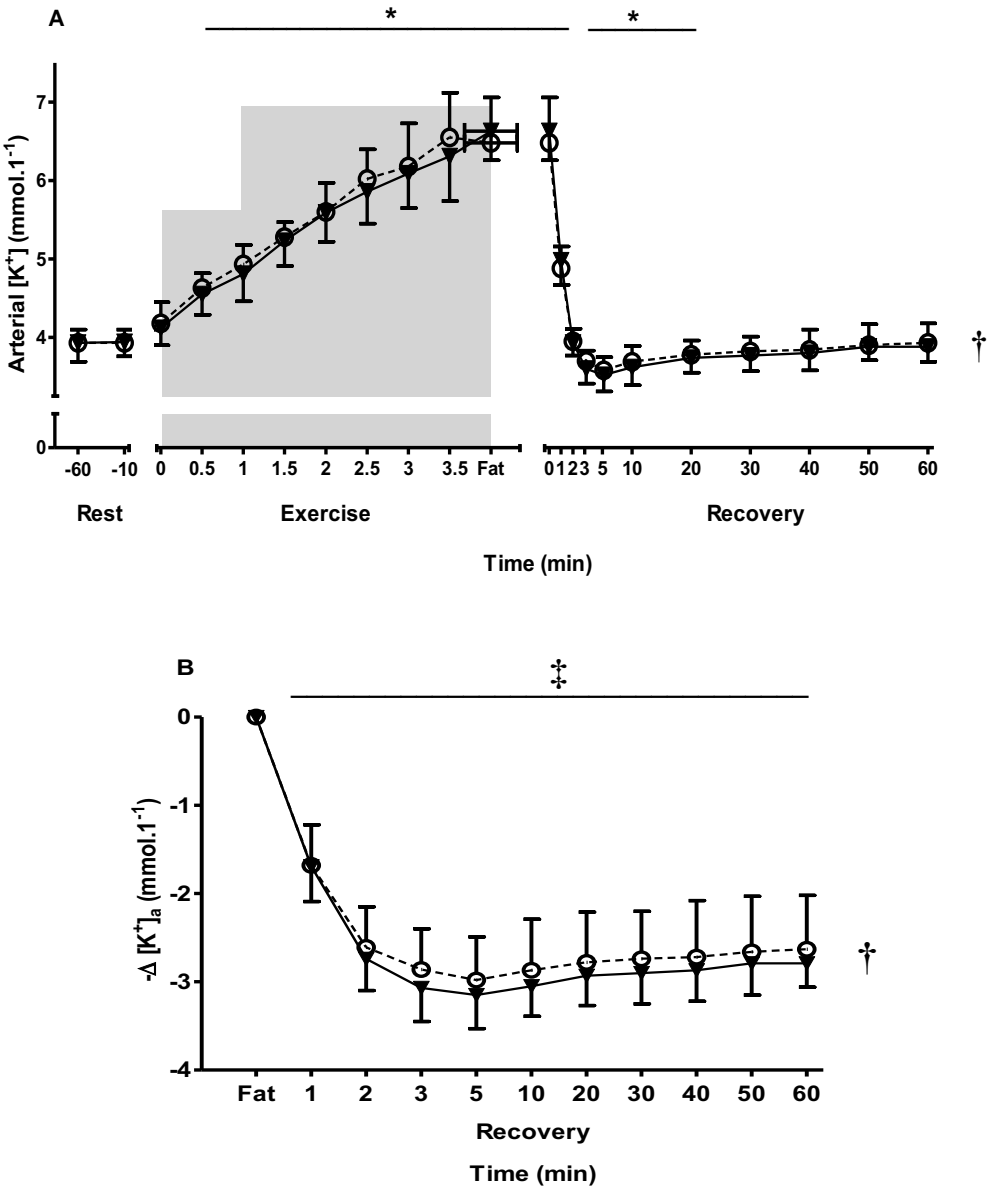

Figure 4.2 Plasma $[K^+]_a$ (A) for DIG (○) and PLAC (▼) at baseline, during and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue (Fat) at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Plasma $-\Delta[K+]_a$ (B) during 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. *n* = 10. Shaded bars represent exercise bouts. * Greater than baseline (time main effect, $P<0.05$); ‡ Less than Fatigue (time main effect, $P<0.05$); † DIG different to PLAC (treatment main effect, $P < 0.05$).

4.3.6 [Hb] and Hct

Arterial [Hb] was greater than baseline throughout exercise, reaching 15.2 ± 1.2 and 15.5 ± 1.0 gdL^{-1} at fatigue for DIG and PLAC respectively, then decreased during early recovery to below baseline by 40 min post-exercise (time main effect, $P<0.05$, Appendix J A 2.3). Arterial Hct was greater than baseline throughout exercise, reaching 46.4 ± 3.8 and 47.4 ± 2.9 at fatigue for DIG and PLAC, respectively, then decreased during early recovery to below baseline by 40 min post-exercise (time main effect, $P<0.05$, Appendix J A 2.4).

4.3.7 Changes in blood volume

Blood volume decreased below baseline throughout exercise, with ΔBV_a reaching -14.3 ± 1.3 % at fatigue, gradually returned to baseline during recovery at 30 and 40 min, and then exceeded baseline values at 50- and 60-min post-exercise (time main effect, $P < 0.05$, Figure 4.3). There was no significant main effect for DIG.

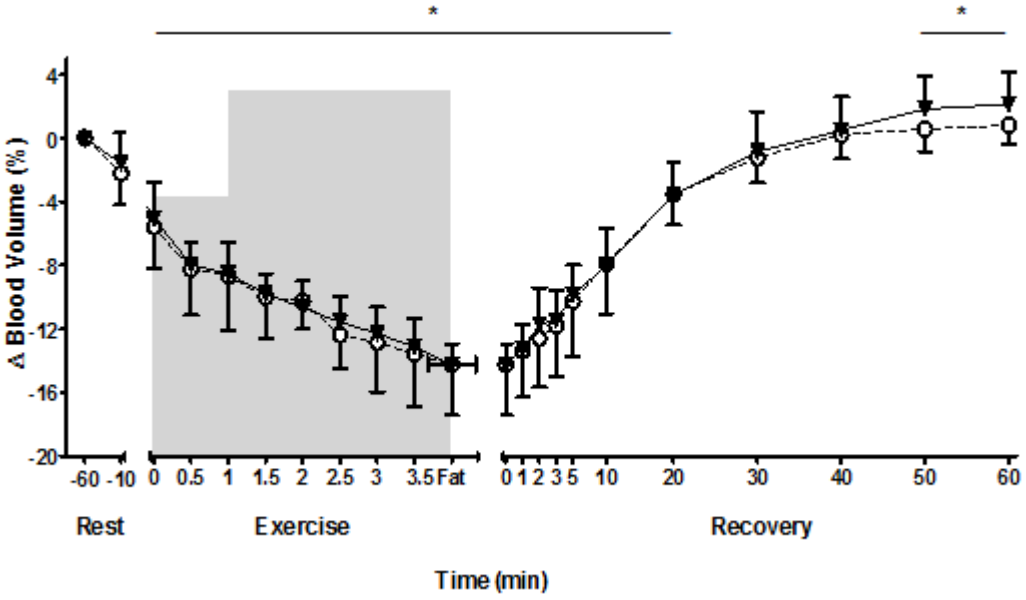

Figure 4.3 Changes in arterial blood volume from baseline for DIG (○) and PLAC (▼) during and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. n = 10. Shaded bars represent exercise bouts. *Greater than baseline (time main effect, P< .05).

4.3.8 Plasma $[Na^+]_a$, $[Cl^-]_a$ and $[Ca^{2+}]_a$

Plasma $[Na^+]_a$ was greater than baseline throughout exercise, increasing to 148.5 ± 1.8 mM at fatigue and then decreased during recovery, but remained above baseline, up to and at 5 min post-exercise (P < 0.05, time main effect, Figure 4.4 A).

Plasma $[Cl^-]_a$ was greater than baseline throughout exercise, increasing to 117.1 ± 2.1 mM at fatigue and decreased during recovery but remained above baseline up to and at 20 min post-exercise (time main effect, P < 0.05, Figure 4.4 B).

Plasma $[Ca^{2+}]_a$ was greater than baseline throughout exercise, increasing to 1.33 ± 0.04 mM at fatigue and decreased during recovery, but remained above baseline up to and at 10 min post-exercise (time main effect, P < 0.05, Figure 4.4 C).

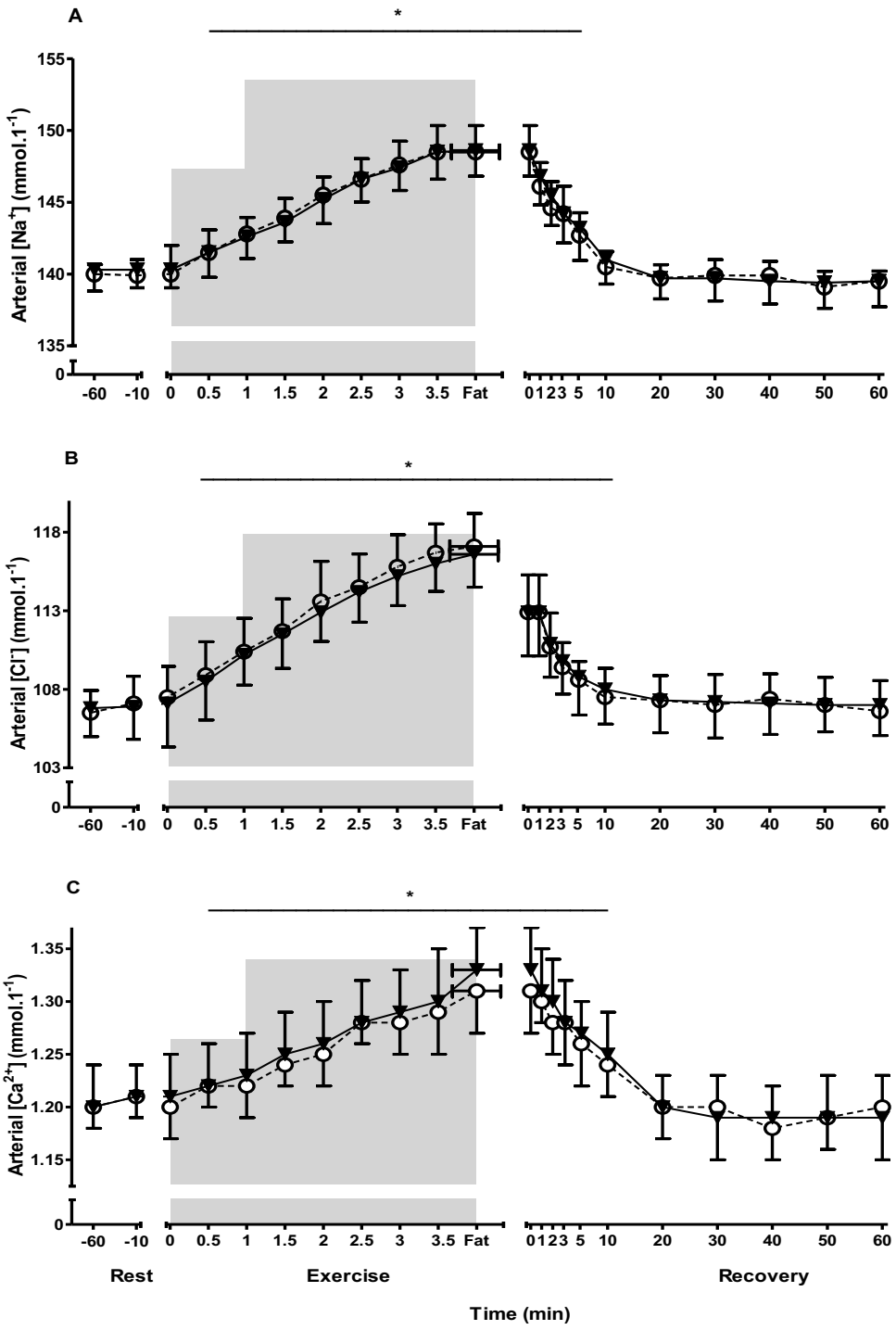

Figure 4.4 Plasma $[Na^+]_a$ (A), $[Cl^-]_a$ (B) and $[Ca^{2+}]_a$ (C) for DIG (○) and PLAC (▼) from baseline, during and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. n = 10. Shaded bars represent exercise bouts. *Greater than baseline (time main effect, $P < 0.05$).

4.3.9 Blood $[Lac^-]_a$ and Plasma pH_a

Blood $[Lac^-]_a$ was greater than baseline throughout exercise and in early recovery peaking at 17.4 ± 3.5 mM at 1 min post exercise; blood $[Lac^-]_a$ subsequently decreased during recovery but remained above baseline at 60 min post-exercise (time main effect, $P < 0.05$, Figure 4.5 B).

Plasma pH_a decreased below baseline from 1 min throughout exercise and in early recovery to 7.18 ± 0.05 mM at 5 min post-exercise; plasma pH_a subsequently increased during recovery but was still less than baseline at 40 min post-exercise (time main effect, $P < 0.05$, Figure 4.5 A).

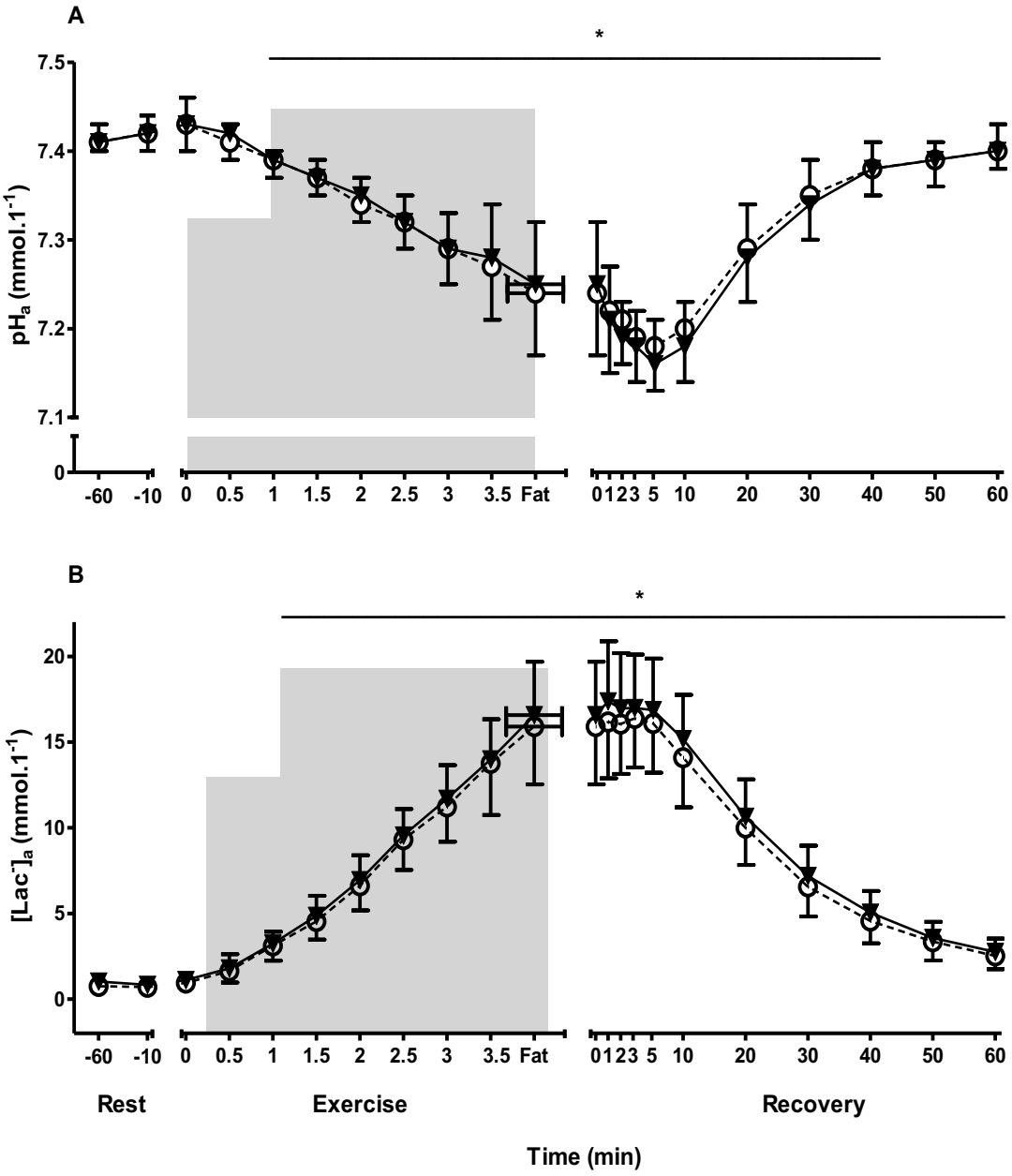

Figure 4.5 Plasma pH_a (A) and blood $[Lac^-]_a$ (B) for DIG (○) and PLAC (▼) at baseline, during and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. n = 10. Shaded bars represent exercise bouts. *Greater than baseline (time main effect, $P < 0.05$).

4.3.10 Muscle Contractile Responses

4.3.10.1 Maximal voluntary contractions (MVC)

The MVC torque values at baseline did not differ between trials (86.9 ± 29.7 vs. 84.0 ± 23.2 Nm, for DIG and PLAC, respectively). The MVC expressed as a percentage of pre-exercise decreased following exercise to fatigue and remained less than baseline at 60 min post-exercise (time main effect, $P < 0.05$, Figure 4.6).

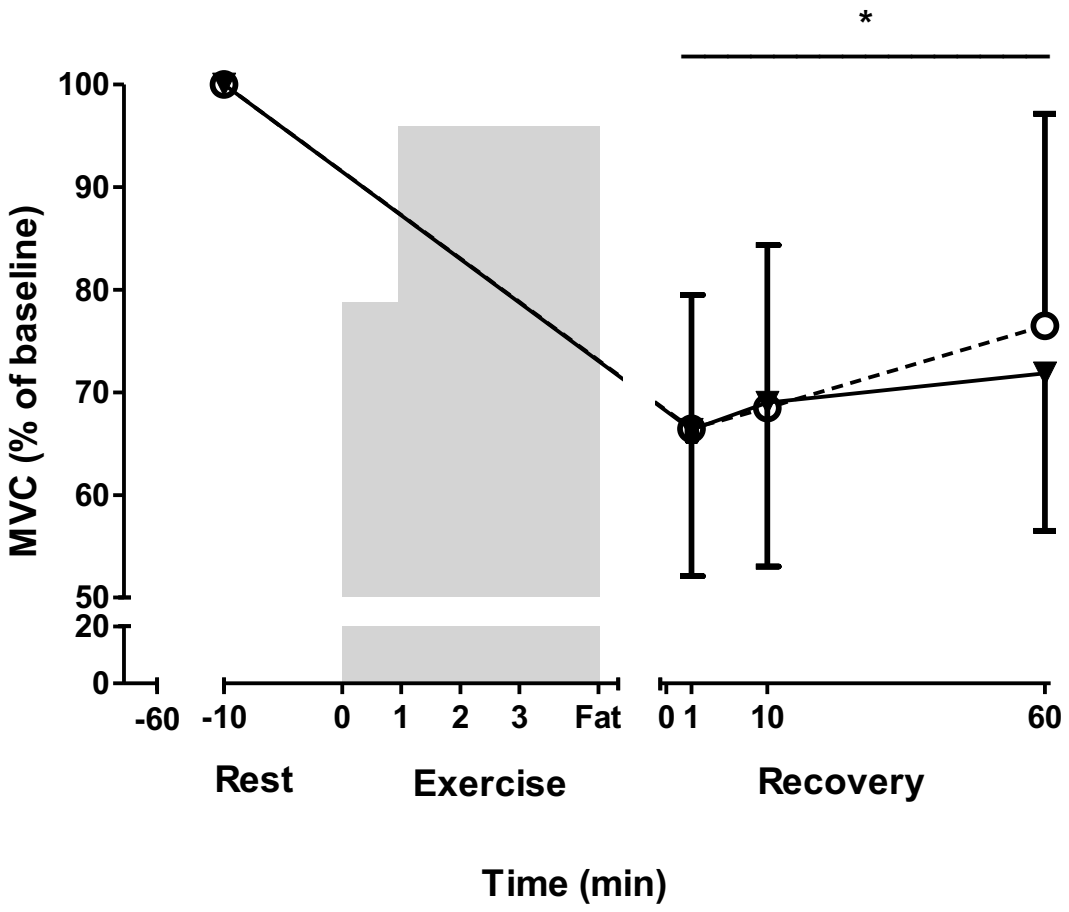

Figure 4.6 Effects of DIG (○) and PLAC (▼) on MVC torque, expressed as a percentage of baseline after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. $n = 10$. Shaded bars represent exercise bouts. *Less than baseline values (time main effect, $P < 0.05$).

4.3.10.2 Potentiated quadriceps twitch

The Q_{twpot} baseline did not differ between trials (20.2 ± 4.2 vs. 21.8 ± 6.4 Nm, for DIG and PLAC, respectively). The Q_{twpot} torque expressed as a percentage of baseline decreased following exercise to fatigue (1 min post-exercise) and did not subsequently recover by 60 min post-exercise (time main effect, $P < 0.05$, Figure 4.7).

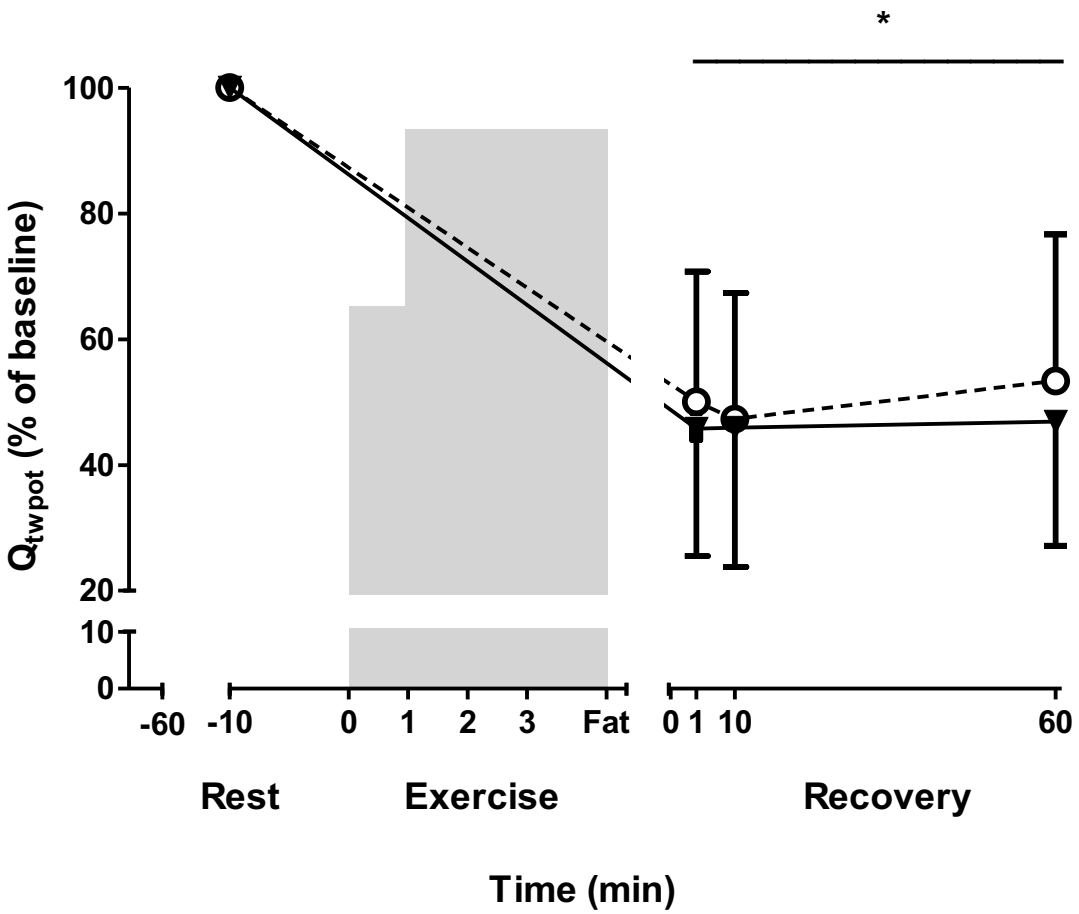

Figure 4.7 Effects of DIG (○) and PLAC (▼) on Q_{twpot} torque, expressed as a percentage of baseline after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. n = 10. Shaded bars represent exercise bouts. *Less than baseline values (time main effect, $P < 0.05$).

4.3.10.3 Potentiated quadriceps paired twitch (Doublet)

The doublet twitch torque baseline values did not differ between trials (37.7 ± 10.7 vs. 39.1 ± 9.4 Nm, for DIG and PLAC, respectively). The doublet twitch torque expressed as a percentage of baseline decreased following exercise to fatigue and did not subsequently recover by 60 min post-exercise (time main effect, $P < 0.05$, Figure 4.8). There was no significant treatment main effect or treatment x time interaction.

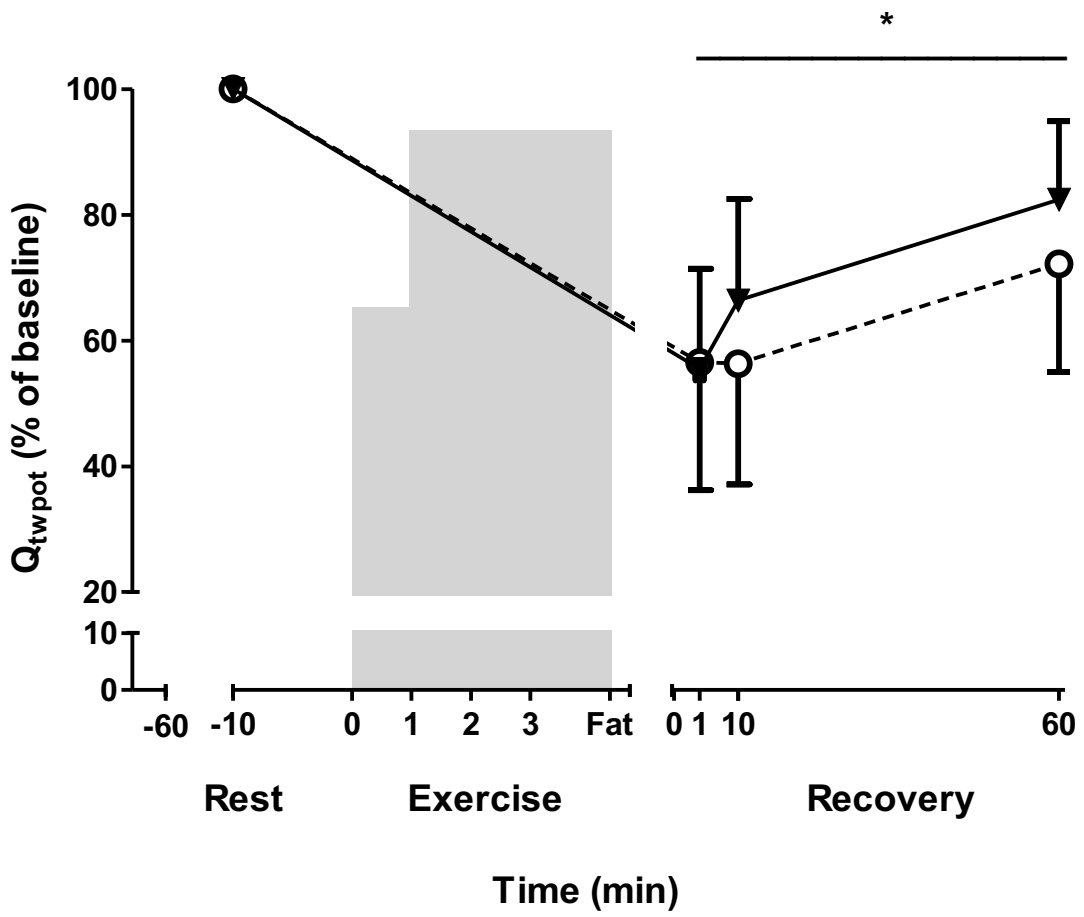

Figure 4.8 Effects of DIG (○) and PLAC (▼) on paired twitch torque expressed as a percentage of baseline after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. n = 10. Shaded bars represent exercise bouts. *Less than baseline (time main effect, $P < 0.05$).

4.3.10.4 Potentiated quadriceps 20 Hz tetani

The 20 Hz tetani torque values were significantly different for DIG vs. PLAC at baseline (51.5 ± 16.1 vs. 68.4 ± 9.3 Nm) and during recovery at 60 min (46.4 ± 12.9 vs. 63.2 ± 7.0 Nm), (treatment x time interaction, $P < 0.05$, respectively).

The 20 Hz tetani torque expressed as a percentage of baseline decreased following exercise to fatigue and did not subsequently recover by 60 min post-exercise (time main effect, $P < 0.05$, Figure 4.9). There was no treatment main effect or treatment x time interaction.

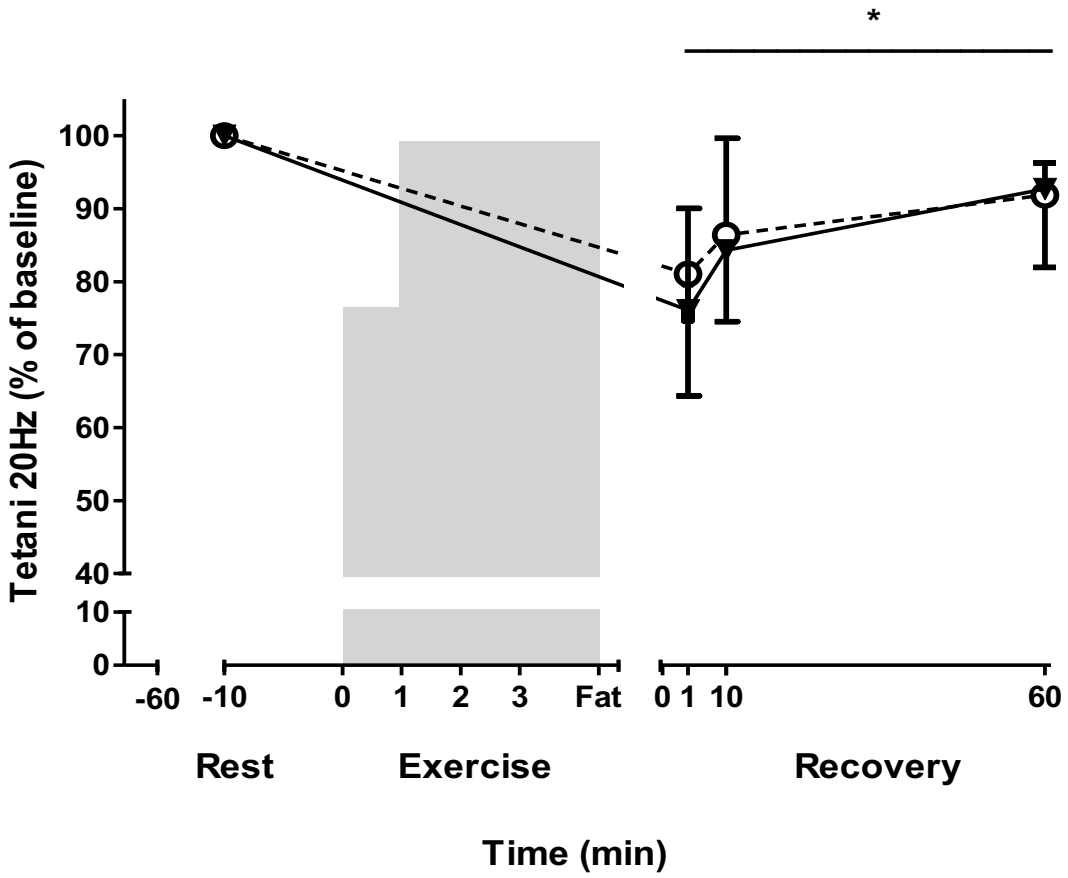

Figure 4.9 Effects of DIG (○) and PLAC (▼) on 20 Hz Tetani torque, expressed as a percentage of baseline after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; Horizontal error bars represent SD of time to fatigue. $n = 10$. Shaded bars represent exercise bouts. *Less than baseline (time main effect, $P < 0.05$).

4.3.11 Compound Muscle Activity (M-wave) During the Evoked Quadriceps Twitch

4.3.11.1 M-wave amplitude

The VM muscle M-wave amplitude (mV), expressed as a percentage of pre-exercise, was not significantly changed after exercise and did not differ between DIG and PLAC (Table 4.2). In contrast, the VL muscle M-wave amplitude, expressed as a percentage of pre-exercise, increased above baseline following exercise to fatigue and remained above baseline during recovery at 60 min post-exercise (time main effect, $P < 0.05$, Table 4.2).

4.3.11.2 M-wave duration

The VM muscle M-wave duration (ms), expressed as a percentage of pre-exercise, was not significantly different after exercise to fatigue, but was increased during recovery at 60 min post-exercise (time main effect, $P<0.05$). The VL muscle M-wave duration, expressed as a percentage of pre-exercise, was greater than baseline during recovery at 60 min (time main effect, $P < 0.05$, Table 4.2). There was a treatment main effect for VL M-wave duration with DIG greater than PLAC ($P < 0.05$) and a treatment x time interaction, with DIG greater than PLAC at fatigue ($P < 0.05$).

4.3.11.3 M-wave area

The VM muscle M-wave area (uV.s), expressed as a percentage of pre-exercise, was unchanged at exercise to fatigue (1 min post-exercise), but then increased above baseline at 60 min post-exercise (time main effect, $P<0.05$). The VL muscle M-wave area, expressed as a percentage of pre-exercise, increased above baseline at 10- and 60-min post-exercise (time main effect, $P < 0.05$, Table 4.2).

Table 4.2 Effects of DIG and PLAC on M-wave amplitude, duration and area, expressed as percentages of baseline values, during the evoked Q_{twpot} for VM and VL at baseline and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; *n* = 10. ‡Treatment main effect ($P < 0.05$), †Treatment x Time effect ($P < 0.05$), *Greater than baseline (time main effect, $P < 0.05$). VM: Vastus Medialis, VL: Vastus Lateralis

M-wave	Muscle	Treatment	Baseline	Fatigue	Recovery (min)	
					10	60
Amplitude (%)	VM	DIG	100	150.1 ± 85.3	132.7 ± 81.2	186.2 ± 134.2
		PLAC	100	122.8 ± 42.6	102.6 ± 59.8	110.3 ± 47.6
	VL	DIG	100	194.7 ± 123.6*	178.2 ± 153.2*	239.8 ± 245.9*
		PLAC	100	144.8 ± 93.8*	191.0 ± 136.4*	201.5 ± 173.7*
Duration (%)	VM	DIG	100	125.3 ± 45.4	126.3 ± 68.8	156.5 ± 67.7*
		PLAC	100	109.3 ± 37.1	105.4 ± 20.3	124.5 ± 33.7*
	VL‡	DIG	100	138.8 ± 89.4†	86.4 ± 42.0	136.9 ± 85.7*
		PLAC	100	105.0 ± 54.2	133.4 ± 88.4	157.5 ± 100.1*
Area (%)	VM	DIG	100	127.4 ± 63.7	124.2 ± 49.2	164.4 ± 42.7*
		PLAC	100	106.8 ± 37.1	111.5 ± 45.6	141.5 ± 51.4*
	VL	DIG	100	138.9 ± 89.4	86.4 ± 42.0*	136.9 ± 85.7*
		PLAC	100	105.0 ± 54.2	133.4 ± 88.4*	157.5 ± 100.1*

4.3.12 Compound Muscle Activity (M-wave) During the Evoked Quadriceps Doublet

4.3.12.1 M-wave Amplitude

The VM muscle M-wave amplitude (mV), expressed as a percentage of pre-exercise, were not significantly different between DIG and PLAC (Table 4.3), and there were no time or treatment main effects. The VL muscle M-wave amplitude, expressed as a percentage of pre-exercise, was significantly greater in DIG than PLAC ($P < 0.05$, Table 4.3). There was a treatment main effect for the VL muscle M-wave amplitude ($P < 0.05$), with DIG greater than PLAC.

4.3.12.2 M-wave Duration

The VM and VL muscle M-wave duration (ms), expressed as a percentage of pre-exercise, did not differ significantly between DIG and PLAC (Table 4.3), and there were no treatment or time main effects. For the VL muscle M-wave duration there was a significant treatment x time interaction with DIG greater than PLAC after exercise to fatigue ($P < 0.05$, Table 4.3).

4.3.12.3 M-wave Area

The VM and VL muscle M-wave area (uV.s), expressed as a percentage of pre-exercise, baseline values were not significantly different between DIG and PLAC (Table 4.3). The VM muscle M-wave area decreased below baseline at fatigue (time main effect $P < 0.05$); there was no treatment main effect or treatment x time interaction. The VL muscle M-wave area decreased below baseline during recovery at 10 min (time main effect, $P < 0.05$, Table 4.3); there was no treatment main effect or treatment x time interaction.

Table 4.3 Effects of DIG and PLAC on M-wave amplitude, duration and area, expressed as percentages, during the evoked doublet for VM and VL at baseline and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; n = 10. * Time main effect ($P < 0.05$), ‡ Treatment main effect ($P < 0.05$), † DIG greater than PLAC (treatment x time interaction $P < 0.05$). VM: Vastus Medialis, VL: Vastus Lateralis

M-wave	Muscle	Treatment	Baseline	Fatigue	Recovery (min)	
					10	60
Amplitude (%)	VM	DIG	100	97.8 ± 65.6	90.29 ± 32.2	90.3 ± 31.1
		PLAC	100	121.7 ± 25.8	100.4 ± 17.0	93.6 ± 23.6
	VL	DIG	100	109.1 ± 42.6	105.4 ± 48.0	98.1 ± 46.3
		PLAC	100	112.9 ± 37.4	102.1 ± 39.7	106.2 ± 30.3
Duration (%)	VM	DIG	100	96.6 ± 25.7	95.9 ± 5.8	110.5 ± 29.7
		PLAC	100	101.3 ± 23.1	96.9 ± 29.4	96.3 ± 38.1
	VL‡	DIG	100	112.4 ± 35.8†	104.1 ± 30.5	99.5 ± 23.3
		PLAC	100	104.7 ± 17.1	100.9 ± 35.1	95.5 ± 33.5
Area (%)	VM	DIG	100	108.4 ± 65.0*	101.9 ± 31.0	92.0 ± 36.4
		PLAC	100	122.1 ± 52.3	27.0 ± 18.8	20.5 ± 5.2
	VL	DIG	100	124.5 ± 59.5	110.9 ± 53.6*	97.3 ± 23.4
		PLAC	100	104.9 ± 35.3	102.1 ± 47.2	99.6 ± 38.4

4.3.13 Compound Muscle Activity (M-wave) During the Evoked Quadriceps 20Hz Tetani

4.3.13.1 M-wave amplitude

The VM and VL muscle M-wave amplitude (mV), expressed as a percentage of pre-exercise, were not significantly different between DIG and PLAC (Table 4.4). For the VM muscle M-wave amplitude there was no treatment or time main effect. The VL muscle M-wave amplitude was unchanged following exercise to fatigue, and then decreased below baseline at 10- and 60-min post-exercise (time main effect, $P < 0.05$, Table 4.4).

4.3.13.2 M-wave duration

For the VM muscle M-wave duration (ms), expressed as a percentage of pre-exercise, there was a treatment x time interaction ($P < 0.05$) with DIG greater than PLAC at baseline and following exercise to fatigue (Table 4.4). There was a treatment main effect ($P < 0.05$) for the VL muscle M-wave duration with DIG greater than PLAC. For the VL muscle M-wave duration there was a treatment x time interaction ($P < 0.05$) with DIG greater than PLAC at baseline, after exercise to fatigue and during recovery at 10 and 60 min ($P < 0.05$, Table 4.4). There was no time main effect for VM or VL muscle M-wave duration.

4.3.13.3 M-wave Area

The VM muscle M-wave area (uV.s), expressed as a percentage of pre-exercise, was not significantly different between DIG and PLAC (Table 4.4); there were no treatment or time main effects, or treatment x time interaction. The VL muscle M-wave area (uV.s), expressed as a percentage of pre-exercise, increased from baseline at fatigue and during recovery at 10 min post-exercise (time main effect, $P < 0.05$, Table 4.4); there was no treatment x time interaction.

Table 4.4 Effects of DIG and PLAC on M-wave amplitude, duration and area, expressed as percentages of baseline values, during the evoked tetani for VM and VL at baseline and after high-intensity cycling comprising 1 min at 60% $\dot{V}O_{2peak}$, 1 min at 95% $\dot{V}O_{2peak}$, then continued until volitional fatigue at 95% $\dot{V}O_{2peak}$ and for 60 min recovery. Values are mean ± S.D; *n* = 10. * Different to baseline (time main effect, $P < 0.05$), ‡ Treatment main effect ($P < 0.05$), † DIG greater than PLAC (treatment x time interaction $P < 0.05$). VM: Vastus Medialis, VL: Vastus Lateralis

M-wave	Muscle	Treatment	Baseline	Fatigue	Recovery (min)	
					10	60
Amplitude (%)	VM	DIG	100	115.9 ± 43.7	118.9 ± 64.2	93.1 ± 23.2
		PLAC	100	111.6 ± 42.4	120.7 ± 46.0	99.0 ± 30.0
	VL	DIG	100	101.4 ± 24.2	98.2 ± 29.3	82.7 ± 37.7*
		PLAC	100	100.8 ± 33.4	101.0 ± 38.3	88.0 ± 21.5*
Duration (%)	VM	DIG	100	103.6 ± 29.2†	94.8 ± 21.6	101.2 ± 36.7
		PLAC	100	100.8 ± 30.9	107.6 ± 26.6	105.2 ± 8.6
	VL‡	DIG	100	97.0 ± 28.3†	103.2 ± 31.0†	94.2 ± 22.1†
		PLAC	100	105.3 ± 32.7	104.7 ± 29.3	96.8 ± 14.5
Area (%)	VM	DIG	100	114.7 ± 30.3	106.1 ± 38.7	85.6 ± 21.0
		PLAC	100	113.7 ± 48.4	102.4 ± 21.3	101.9 ± 32.4
	VL	DIG	100	117.7 ± 19.1*	116.2 ± 34.4*	89.2 ± 23.1
		PLAC	100	105.0 ± 25.4	110.0 ± 26.9	100.2 ± 38.5

4.4 DISCUSSION

This study investigated the effects of an acute oral digoxin treatment on arterial plasma K^+ regulation, exercise performance, muscle excitability and fatigue during and following high-intensity cycling. The results indicate that an acute oral digoxin intake in healthy individuals increased plasma [K^+] during exercise and recovery, including impairing exercise performance, with an earlier onset of fatigue. However, despite this impairment, there were no differences between DIG and CON in the muscle contractile measures, measured by an MVC and using magnetic stimulation for the evoked twitch, doublet or tetani contractions. The post-exercise M-wave amplitude, duration and area results for the evoked quadriceps twitch, doublet and tetani varied and were inconsistent across contraction types; the effects of digoxin were also variable. Thus, despite elevated [K^+] and earlier fatigue with digoxin, there was not a corresponding greater impairment of membrane excitability.

4.4.1 Serum digoxin concentrations

An acute oral dose of 0.5 mg digoxin adequately increased arterial [SDC] to approximately 3.36 nmol.L^{-1} (~2.62 ng.ml^{-1}), marginally higher than the recommended therapeutic range of 0.5 to 2.0 ng.ml^{-1} (Denker, Morelli et al. 2009). To allow for a peak [SDC], a 60 min timeframe was used for the 0.5 mg dose to reach levels within a steady state, clinically relevant, range of 0.8 - 2 ng.ml^{-1} (Smulders, Kuipers et al. 2006, Denker, Morelli et al. 2009). Results indicate [SDC] of 2.62 ng.ml^{-1} was higher than the peak [SDC] of 1.87 ng.ml^{-1} reported 60 min after a single oral digoxin dose of 0.05 mg (Schmitt, Kaeser et al. 2010). During intense cycling exercise, digoxin concentration in the quadriceps muscle, increased by 29%, and [SDC] decreased by 39%, suggesting the increase in skeletal muscle digoxin concentration is related to the neuromuscular activation (Joreteg and Jogestrand 1984). The digoxin concentration in erythrocytes decreased by 12% during exercise, demonstrating the increased uptake of digoxin

also in other tissues (Joreteg and Jogestrand 1984). Cycling exercise at 140 – 180 W for 60 min increased skeletal muscle digoxin by 20% and decreased [SDC] by 40% following digoxin treatment for two weeks at 0.5 mg.day^{-1} (Joreteg and Jogestrand 1983). In atrial fibrillation patients the initial [SDC] were 0.0, 1.1 and 2.5 ng.ml^{-1} at zero, low and high doses of digoxin respectively, all within the therapeutic range (1.3 to 2.6 ng.ml^{-1}); during cycling exercise at 25, 50 and 75 W, plasma [K^+] was significantly elevated by up to 20% (Nørgaard, Bøtker et al. 1991). Steady state SDC of 1.0 ± 0.2 ng.ml^{-1} has been reported following the same dose as utilised here (Sundqvist, Berglund et al. 1983). Following ten days of oral digoxin at 0.5 mg.day^{-1} plasma [SDC] decreased by 39% and digoxin concentration in skeletal muscle increased by 8% during cycling exercise (Jogestrand and Sundqvist 1981, Joreteg and Jogestrand 1984), indicating increased digoxin uptake in contracting muscle influences SDC. Thus, SDC may have fallen during exercise in these participants, although this was not measured. Therefore, the rise in SDC was broadly similar to previous findings and should be consistent with inducing possible detrimental effects on potassium and muscle performance.

4.4.2 Acute digoxin treatment increases plasma $[K^+]_a$ and decreases exercise performance

The plasma [K^+] increased rapidly at the onset of exercise and peaked at ~6.5 mM. Similar plasma [K^+] of ~6 mM has been observed during high-intensity cycling (Medbo and Sejersted 1985, Vøllestad, Hallén et al. 1994, McKenna, Heigenhauser et al. 1997). This exercise-induced hyperkalemia was due to the outward K^+ current with muscle contractions exceeding the Na^+,K^+-ATPase-mediated K^+ clearance rate. As the Na^+,K^+-ATPase is activated with muscle contractions (Clausen 2003a), [K^+] decreases immediately upon cessation of exercise, returning to resting levels within a few minutes post-exercise (Juel 1986). Here plasma [K^+] was slightly increased with digoxin compared to placebo, but it is small enough that it seems

unlikely to have any major physiological importance. It was hypothesised that digoxin would increase $[K^+]_a$ and accelerate muscle fatigue during high-intensity cycling. Interestingly, an expected partial blockade of the skeletal muscle Na^+,K^+-ATPase with digoxin did not cause a more marked increase in $[K^+]$ during exercise. A previous study found no effect of digoxin on $[K^+]$ measured after handgrip exercise in antecubital venous blood, at 30 min after digoxin intake (Janssen, Lheureux et al. 2009). It is possible in that study that 30 min between digoxin ingestion and commencement of exercise was insufficient time for maximal digoxin binding to skeletal muscle; also venous $[K^+]$ markedly underestimates $[K^+]_a$. These current findings of elevated $[K^+]_a$ during exercise and early recovery are more consistent with previous studies that found increases in $[K^+]$ during exercise after digoxin (Nørgaard, Bøtker et al. 1991, Schmidt, Bundgaard et al. 1995, Sostaric, Goodman et al. 2009). A more appropriate measure would have been to determine digoxin effects on muscle interstitial $[K^+]$ before, during and after exercise. The small effect of digoxin on $[K^+]_a$ possibly reflects the large outward K^+ current during muscle contractions, which overwhelmed and obscured a minor skeletal muscle Na^+,K^+-ATPase digoxin-inhibition (Janssen, Lheureux et al. 2009).

During post-exercise recovery there was an undershoot in plasma $[K^+]_a$, suggesting continued muscle Na^+,K^+-ATPase activity, likely due to a combination of effects from circulating catecholamines (Nielsen and Harrison 1998), previous membrane excitation (Nielsen and Clausen 1997), and acute increases in intracellular $[Na^+]$ (Everts and Clausen 1994). Interestingly an undershoot was not observed in the previous studies, which may be explained by the higher exercise intensity used in this study as participants exercised close to their $\dot{V}O_{2peak}$. The decline in plasma $[K^+]$ ($-\Delta[K^+]$), following exercise was less for DIG compared to PLAC. This is consistent with an earlier finding that digitalisation reduced the decline in plasma $[K^+]$ during early recovery in congestive heart failure patients following incremental cycling bouts (Schmidt, Bundgaard et al. 1995). As digoxin occupied ~10% of skeletal muscle Na^+,K^+-

ATPase in these patients (Schmidt, Holm-Nielsen et al. 1993), this is likely to reflect the reduced capacity of the Na^+,K^+-ATPase for K^+ reuptake due to digoxin inhibition. The higher [K^+] during exercise to fatigue and early recovery is consistent with the 7.8% earlier onset of fatigue with digoxin. These findings are consistent with previous findings that found treadmill running time was reduced following acute high dose digoxin intake in healthy humans (Bruce, Lind et al. 1968). In contrast to the present findings, others reported that digoxin did not adversely affect muscle performance in healthy humans (Sundqvist, Berglund et al. 1983, Gong, Petersen et al. 2005, Sostaric 2012). A daily dose of digoxin of 0.50 g for two weeks decreased maximal isometric strength by ~4% (Bruce, Lind et al. 1968), whilst maximal isokinetic muscle strength was unchanged (Sundqvist, Berglund et al. 1983). The effects of digoxin on muscle strength and performance during exercise are therefore conflicting. The latter may be due to the exercise characteristics, where studies reporting adverse effects utilised high-intensity exercise, contrasting negative findings when exercise was of a lower intensity and longer duration. Further, digoxin administration using an acute high dose, as prescribed in the present study, compared to long term low dose may have contrasting effects on muscle performance due to possible adaptability of Na^+,K^+-ATPase in skeletal muscle when exposed to digoxin long-term.

Despite the shorter cycling time to fatigue and the slightly higher $[K^+]_a$ during digoxin compared to placebo, the MVC after exercise were not different between trials. It has been suggested that feedback from fatiguing muscle plays an important role in the determination of central motor drive and force output, so that the development of peripheral muscle fatigue is carefully regulated (Amann and Dempsey 2008). Therefore, it is possible that AP along the muscle membrane was inhibited in the present study and suggests the activation of contractile elements was most likely to account for peripheral fatigue. Interestingly, the feedback from

fatiguing muscles may have had little impact on the central motor drive and force output between the two trials.

Considerable variability was evident in the decline in MVC torque following fatiguing exercise. This may in part be explained by sex-related differences which result in profound differences in neuromuscular performance and fatigability (Baar 2014, Hunter 2014). Females usually fatigue less than males during isometric fatiguing contractions at similar intensities (Hunter 2014, Hunter 2016a, Hunter 2016b). The previous findings are consistent in the present study where MVC following fatiguing exercise tended to decrease less for females than males during both digoxin and placebo, although this was not significant (25.9 ± 12.8 vs. 38.6 ± 12.8 % (P=0.08) and 24.5 ± 15.1 vs. 40.3 ± 12.7 % (P=0.06), % baseline values, female vs. male respectively). Investigating responses in males and females separately may have allowed for better interpretation of data, as it has recently been found that females are usually less fatigable than men during single-limb isometric contractions, primarily because of sex-related differences in contractile mechanisms (Hunter 2014). It is however, unclear if these sex differences in muscle fatigue occur for dynamic fatiguing exercises. However, fatigability will be task specific due to different neuromuscular sites being stressed as the tasks alter, and the stress on these sites will possibly differ between men and women. Task variables that can alter the sex difference in fatigue include the type, intensity and speed of contraction, the muscle group assessed, and the environmental conditions (Alves, Alves et al. 2014). The physiological mechanisms responsible for these differences in muscle fatigue include; activation of the motor neuron pool from cortical and subcortical regions, synaptic inputs to the motor neuron pool via activation of metabolically-sensitive small afferent fibres in the muscle, muscle perfusion, and skeletal muscle metabolism and fibre type properties (Keenan, DeLisle et al. 2005, Alves, Alves et al. 2014, Baar 2014). It has been reported that as muscle force declines, an extra effort by subjects briefly increased force output, which was accompanied by a proportionately greater

increase in EMG activity (Bigland-Ritchie, Jones et al. 1978). It was hypothesised that digoxin would impair excitability and thus would be anticipated to exacerbate the decline in M-wave amplitude following cycling to fatigue. Whilst considerable variability was evident in M-wave measures for digoxin and placebo, it is possible that digoxin binding to the Na^+,K^+-ATPase inhibited the Na^+,K^+-ATPase-mediated Na^+ and K^+ fluxes across the sarcolemmal and t-tubular membranes, accounting for impaired action potentials and subsequent muscle contraction. Whilst the present study was unable to determine the difference in muscle [K^+], unpublished data show there was a ~8-9% inhibition in muscle Na^+,K^+-ATPase, which is quite substantial. Thus, arterial plasma concentration difference may not be a reliable comparison measure. However, if Na^+,K^+-ATPase were fractionally inhibited a loss of muscle contractility and endurance would be expected, and associated with M-wave changes such as a decline in amplitude and area and increase in duration, and thereby possibly contribute to the onset of fatigue. Detrimental effects of ouabain-induced Na^+,K^+-ATPase inhibition and subsequent impairment of muscle excitability and contractility were previously shown in isolated muscles (Sostaric 2012, Clausen 2013a). The most likely interpretation in these in-vitro experiments is that partially inhibiting the Na^+,K^+-ATPase would impair the AP propagation along the sarcolemmal and t-tubule membrane, preventing release of Ca^{2+} from the SR and causing the onset of fatigue. The M-wave characteristic is measured here were not however, worsened following exercise after digoxin. As cycling performance was impaired with digoxin, indicating that muscles fatigued earlier; however, it was not possible to detect any effect in the evoked contractile and M-wave characteristics.

It has been suggested that the EMG amplitude-force relationship reflects the concurrent increases in motor unit recruitment and firing rates that regulate muscle force output (De Luca, Foley et al. 1996), and that EMG amplitude-force relationships have been able to distinguish between motor unit recruitment or rate coding as the primary mechanism to modulate force

(Cooper 2013). As the present study did not investigate muscle motor unit recruitment and firing rates or rate coding it is not possible to suggest this as the primary mechanism of the reduced voluntary and evoked torque. Repetitive stimulations of the nerve have been found to deplete acetylcholine (Ach) in the presynaptic terminal causing a decrease in the amplitude of the excitatory postsynaptic potential (EPSP) (Silinsky 2013). However, under normal circumstances, due to a high safety factor, EPSPs are maintained above the threshold to provoke an AP. Hence, repeated stimulations do not change the M-wave as the somatic efferent neuron continues to excite every muscle fibre in the motor unit (Curtis and Eccles 1960). Finally, as the evoked torque and M-wave measures were quite variable, it is difficult to conclude the effect of exercise and digoxin on excitability. Thus, the effects of digoxin at therapeutic levels on muscle evoked contractile performance and excitability after fatiguing exercise in healthy young adults remains unclear.

4.5 Conclusions

Acute digoxin administration increased K^+ disturbances during and after high-intensity cycling exercise and worsened time to fatigue in young healthy adults. However, digoxin did not alter the exercise-induced reductions in MVC or in evoked torque during a twitch, doublet and 20 Hz tetani contractions. The effects of digoxin on the evoked torques and on associated M-wave characteristics were inconsistent for twitch, doublet and 20 Hz tetani twitch, due to these results being quite variable. However, acute digoxin intake did result in an increase in M-wave amplitude at 1 min post-exercise. As these measures were sampled approximately 1 min after exercise, the effects of recovery are also likely to be super-imposed on the effects of fatigue. The elevated SDC suggest digoxin would most likely have partially inhibited skeletal muscle Na^+,K^+-ATPase, which is consistent with and may explain the higher $[K^+]_a$ during exercise, the smaller decline in plasma $[K^+]$ post-exercise and possibly the earlier time to fatigue. These

results suggest digoxin treatment is possibly due to the inhibiting effect of digitalisation on skeletal muscle Na^+,K^+-ATPase function and earlier onset of fatigue during intense cycling exercise in healthy humans. Further studies are required to demonstrate whether these adverse effects of exercise and digoxin are mediated by disturbances in membrane excitability.

CHAPTER 5

Effects of sprint training on arterial and venous [K^+] during and following high-intensity interval cycling, as well as muscle excitability and fatigue

5.1 INTRODUCTION

A growing body of evidence proposes that low-volume; high-intensity interval training (HIIT) may represent a strategy to induce skeletal muscle adaptations normally associated with endurance training (Gibala 2007, Billaut and Buchheit 2013, Nalcakan 2014). High- intensity exercise training causes large and rapid changes in skeletal muscle, including increases in muscle creatine kinase (CK), phosphofructokinase (PFK), proportion of Type IIa fibers, buffer capacity (Costill, Coyle et al. 1979, Sahlin and Henriksson 1984, Hellsten, Apple et al. 1996), work capacity (Mohr, Krustrup et al. 2006), mitochondrial biogenesis (Little, Safdar et al. 2010), aerobic metabolism (Gibala 2007) and the development of fatigue (Sjøgaard 1990, Clausen 2003a). Furthermore, Low-volume, high intensity, repeated sprint training improved functional performance and identified improved ion regulation as potential mechanisms of enhancing muscle performance (McKenna, Schmidt et al. 1993, Harmer, McKenna et al. 2000, McKenna, Bangsbo et al. 2008).

Thus, it is crucial that the Na^+,K^+-ATPase activity in muscle is rapidly increased to counterbalance the possible loss of excitability, through prompt restoration of Na^+/K^+ gradients (Clausen 2003a). During high frequency stimulation of isolated muscles, excitation may activate all of the Na^+,K^+-ATPase available within 10 s, causing up to 22-fold increase in Na^+ efflux (Clausen 2003a). Previous studies have demonstrated that intense training also leads to improved plasma K^+ regulation, evidenced after training by a lowered ratio of rise in plasma

[K^+] relative to work output during exercise (McKenna, Schmidt et al. 1993, McKenna, Heigenhauser et al. 1997) and a reduced [K^+] in muscle interstitium during exercise (Nielsen, Mohr et al. 2004). These changes were suggested to occur via greater muscle re-uptake of K^+ due to increased muscle Na^+,K^+-ATPase activity, consistent with other reports of elevated muscle Na^+,K^+-ATPase content ([^{3}H]-ouabain binding site content) and activity (maximal K^+-stimulated 3-O-MFPase activity) after training (McKenna, Schmidt et al. 1993, Green, Dahly et al. 1999, Green, Goreham et al. 1999).

Muscle fatigue during intense exercise can occur as a result of many factors, but impaired muscle fibre membrane excitability has been considered a key component (Bigland-Ritchie 1981, Bigland-Ritchie, Johansson et al. 1983, Bigland-Ritchie and Woods 1984, Zijdewind, Zwarts et al. 2000). A concurrent decline in muscle performance and amplitude of the muscle EMG has been reported across sprint repetitions (Racinais, Bishop et al. 2007, Mendez-Villanueva, Hamer et al. 2008). Importantly, fatigue during exercise has been shown to be delayed by HIIT (Jones and Vanhatalo 2017). Surprisingly, no study has directly determined the effects of HIIT on plasma [K^+] during and following intense fatiguing cycle exercise taken together with measurement of the acute changes in muscle contractile performance and excitability measured via M-waves. Therefore, this study investigated the effects of HIIT on arterial and antecubital venous [K^+], muscle excitability, torque generating capacity and fatigue. The arterio-venous difference measures across the forearm muscles further allow examination of the effects of training on K^+ clearance in inactive muscle. The effects of HIIT on other plasma electrolytes and acid-base variables were also investigated. It was hypothesised that sprint training will: 1) reduce arterial and venous [K^+] during and after exercise compared to pre-training; and 2) this would be associated with each of a delayed fatigue-induced cessation of exercise, and reduced post-exercise decreases in muscle voluntary and evoked

torque and also excitability, demonstrated by lower declines in M-wave (amplitude and area) with fatigue.

5.2 METHODS

5.2.1 Participants

Sixteen healthy recreationally active young adults gave written informed consent prior to participating in the study. Participants were randomly allocated to a High Intensity Interval Training group (HIIT) that comprised 6 males and 2 females (age 25.8 ± 5.5 yr, height, 184.0 ± 11.1 cm, mass 81.0 ± 17.3 kg, mean ± SD) and a control group (CON), also comprising 6 males and 2 females (age 23.6 ± 4.9 yr, height, 182.3 ± 8.1 m, mass 79.5±12.5 kg, mean ± SD). Participants were required to attend all three training sessions per week for seven weeks. The study was approved by the Victoria University Human Research Ethics Committee and conformed to the Declaration of Helsinki.

5.2.2 Experimental design

Participants were initially familiarised with the muscle strength testing and peripheral magnetic stimulation. After 30 min of rest, they performed an incremental cycle exercise test to determine $\dot{V}O_{2peak}$, followed by a further 30 min rest; they then performed a single 30 s maximal cycling effort for familiarisation purposes. The pre- and post-exercise test consisted of participants cycling at a cadence of 60-70 rpm for 2 min at 60% $\dot{V}O_{2peak}$, followed immediately by 2 min at 80% $\dot{V}O_{2peak}$; following 2 min rest they then performed two 30 s maximal cycling efforts, separated by 90 s. Pre and Post-training measures were made at rest, during and following two bouts of 30 s maximal cycle sprint exercise; these comprised arterial and venous plasma [K^+], plasma electrolytes and acid base status, voluntary and

magnetically evoked knee extensor muscle torque, M-wave characteristics of the vastus lateralis and vastus medialis muscles, heart rate (HR) and rating of perceived exertion (RPE). Forty-eight hours after the initial visit, the high-intensity interval training program commenced. Training was conducted in a laboratory under supervision three times per week over 7 weeks, totalling twenty-one sessions. The control group continued in their recreational exercise but did not perform any high-intensity exercise during the 7 weeks between trials. Muscle biopsies were taken under resting conditions 30 min after catheter insertion and at ~1 min after the second 30 s maximal cycling bout, but measurements were not reported in this thesis. Participants were asked to refrain from vigorous exercise, and from consuming alcohol and caffeine for 24 h before all tests. Seventy-two hours following the last high-intensity interval training session all participants performed post-test measures (Figure 5.1).

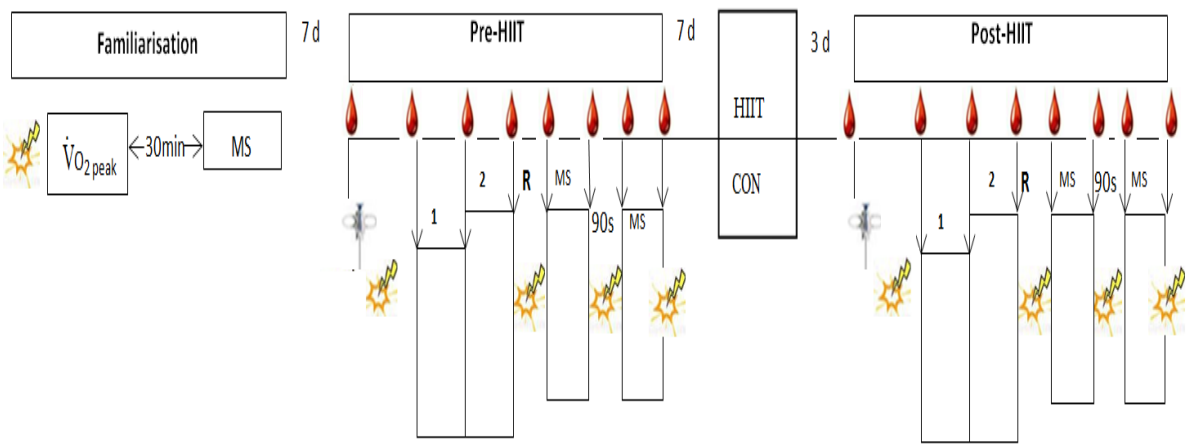

Figure 5.1 Schematic diagram of the testing schedule, blood sampling, magnetic stimulation and EMG undertaken during and following submaximal and intense exercise, before and after 7 weeks of High Intensity Interval Training (HIIT, n = 8) and Control group (CON, n = 8).

Legend:

- Peripheral Magnetic Stimulation;

- Arterial, Venous Blood samples

- Muscle Biopsy

MS (Max Sprint) 1 x 30s sprints;

Submaximal cycling 1**,** 2min at 60% $\dot{V}O_{2peak}$; 2, 2min at 80% $\dot{V}O_{2peak}$; R, 2min recovery;

$\dot{V}O_{2peak}$ is the peak oxygen consumption measured during the incremental exercise test.

5.3 EXERCISE TESTS

All cycling tests were conducted on an electromagnetically braked cycle ergometer (Lode, Groningen, Netherlands) (Chapter 3. 3.2.3.1).

5.3.1 Incremental Cycle Test and Cardiorespiratory Measures

Cardiorespiratory measures were undertaken during the pre-training incremental cycle test and during recovery, with all methods as previously described (Chapter 3. 3.2.3.2).

5.3.2 Pre and Post Training Cycle Exercise Test

5.3.2.1 Submaximal exercise test

Participants cycled at a cadence of 60-70 rev.min^{-1} for 2 min at 60% $\dot{V}O_{2peak}$ (HIIT 177 ± 45, CON 162 ± 22 W), followed immediately by 2 min at 80% $\dot{V}O_{2peak}$ (HIIT 229 ± 61, CON 215 ± 39 W). Cardiorespiratory measures were taken continuously during intermittent cycling with results reported for the last minute of each bout.

5.3.2.2 Maximal cycling efforts

Participants performed two 30 s maximal cycling efforts, separated by 90 s. Toe-clips were worn, exercise commenced from a stationary position and participants remained seated at all times during exercise, with the seat height and handlebar position standardised for pre and post-tests. Pedalling velocities were sampled at 83 Hz. Performance measures comprised peak power (PP), minimum power (MP), Average power (AP), time to PP (TTPP), fatigue index (FI), defined as the relative decline in power output from the PP attained in the first few pedal strokes to the final power output at the end of the maximal sprint bout, and cadence.

Cardiorespiratory measures were taken continuously during maximal cycling efforts with results averaged over each 15 s when data was reported by the metcart.

5.3.3 High intensity intermittent training (HIIT)

Participants performed High Intensity Interval Training (HIIT) which comprised repeated 30 s maximal sprint bouts (Figure 5.2) on a Velotron cycle ergometer (Dynafit Pro – RacerMate Cycle, Seattle, Washington) equipped with toe clips, 3 times per week for 7 weeks. Participants were previously familiarised with the maximal sprint bouts and verbally encouraged to produce their maximum effort. Power output was determined from pedalling velocity sampled at 83 Hz, with the PP and FI each calculated by a computer using Velotron Wingate Software (Version 1.0.2, RacerMate, Seattle). For HIIT, performance during the first four EB in the initial training session were also compared to the first four EB of the final training session. HIIT was used because such exercise is accompanied by a dramatic rise in plasma [K’] with each exercise bout and by marked muscular fatigue, evidenced by progressively declining work output. These pre and post cycling efforts are also similar to the efforts performed during the seven-week HIIT.

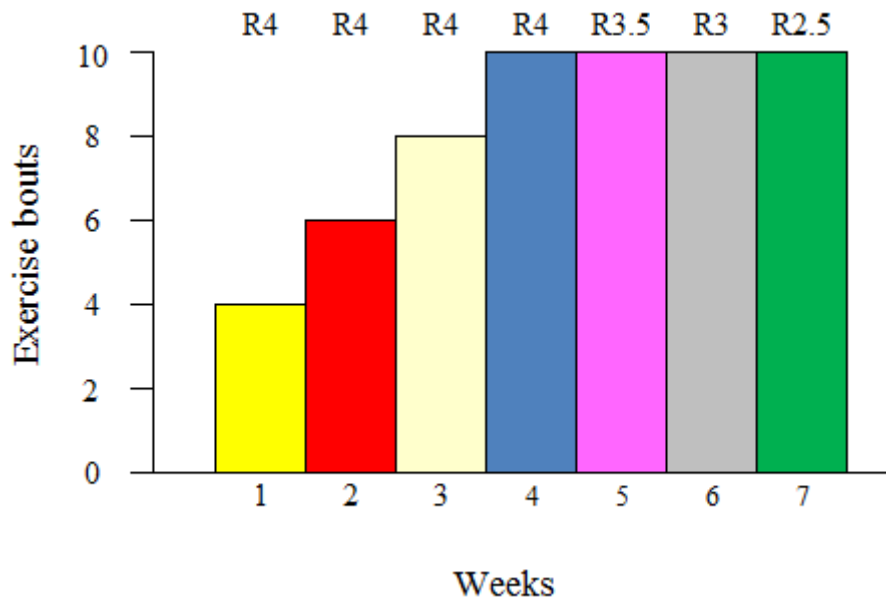

Figure 5.2 Schematic illustrating the seven-week High Intensity Intermittent Training protocol conducted three times per week. During week 1 each participant performed four 30s all out efforts with 4 min recovery between each effort. During weeks two, three and four the number of efforts increased by 2 each week with 4 min recovery between efforts. For weeks five, six and seven the number of bouts was maintained at 10 per session but recovery between each bout decreased by 30 s each week, in week 5 to 3.5 min, 3 min in week 6 and only 2.5 min in Week 7. Training program from McKenna et al (1993).

Legend:
R indicates recovery between each 30 s bout, 4 – 4 min, R3.5 – 3.5 min, R3 – 3 min, R2.5 – 2.5 min recovery.

5.3.4 Quadriceps neuromuscular function measures

All quadriceps voluntary and evoked measures, including MVC and magnetically evoked peripheral muscle torque and twitch torque ($Q_{tw,pot}$), doublet, 20Hz tetani, compound action potentials (M-waves), were all measured using protocols previously described (Chapter 3. 3.2.6). Interday and intraday reliability was calculated for the ramp test during each of the stimulator intensities (50%–100%) for torque using protocols previously described (Chapter 3.2.6.2). A plateau during the ramp protocol confirmed maximal stimulation when the rise between the 80-100% stimulation intensities did not significantly differ ($P > 0.05$).

5.3.5 Blood sampling and analysis

Catheters (20 or 22G, Arrow) were inserted retrograde into the deep antecubital vein (v) and anterograde into the radial artery (a) of the left arm, under local anaesthesia (1% xylocaine injection) then covered by a adhesive sterile patch (Tegaderm). Venous and arterial lines were kept patent by a slow, sterile, isotonic saline (0.9% NaCl) infusion bag under pressure. Participant's rested supine for 20 min with blood samples then obtained prior to the commencement of each trial. Participants then moved to the adjacent cycle ergometer, where a seated pre- exercise sample was taken (0 min). Blood samples were taken during the last 30 s of exercise of the 2 min cycling at both 60% and 80% $\dot{V}O_{2peak}$ and during the last 5 s of the two 30 s maximal sprints. During recovery, blood samples were collected at 1, 2, 5, 10, 20- and 30-min post- exercise. The first three recovery samples were taken with the participant seated on the ergometer; all subsequent samples were taken with the participant supine. Approximately 4.7 mL of blood was sampled and immediately measured using an automated blood gas analyser (Radiometer, ABL800 Flex analyser, Denmark) for plasma electrolyte concentrations ($[K^+]$, $[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$), gas tensions ($\mathbf{P}_{O2}$ and $\mathbf{P}_{CO2}$), O_2 saturation ($\mathbf{S}_{O2}$),

haemoglobin (Hb) and haematocrit (Hct), blood glucose, and acid–base status (pH, [Lac^-]). Duplicate analyses were conducted for the rest sample with single analysis for exercise and recovery samples.

5.3.6 Calculations for blood analyses

The change in blood volume (ΔBV) from rest was calculated as previously described (Chapter 3. 3.2.5). To account for any small intra-individual $[K^+]_a$ differences between pre and post-training within HIIT and CON, the change from rest in each of the plasma $[K^+]_a$ ($\Delta[K^+]_a$) and $[K^+]_v$ ($\Delta[K^+]_v$) were also calculated at each time point.

5.3.7 Statistical analysis

A linear mixed model analysis of variance was used to calculate any effects (time, trial and trial x time), with analyses performed separately within the HIIT and CON groups. To determine time differences within groups, statistical comparisons were made against the baseline (rest) measure. When significant effects were detected, pairwise comparisons were made using the Least Significant Difference test. Trial main effects or time x trial interaction effects were reported only when significant. Student's paired *t*-test was used to calculate differences between pre and post-training trials for cardiorespiratory measures and power output, including resting data for twitch and M-wave characteristics. Statistical significance was accepted at $P < 0.05$. Data are presented as mean ± standard deviation (SD). Statistical analyses were calculated using SPSS version 22 (SPSS Inc., Champion, IL).

5.4 RESULTS

5.4.1 Incremental cycling cardiorespiratory measures and peak power (pre-training)

The incremental cycling peak oxygen consumption ($\dot{V}O_{2peak}$), ventilation ($\dot{V}_{Epeak}$), heart rate (HR_{peak}) and peak power (PP) values at baseline did not differ significantly between HIIT and CON (Table 5.1).

Table 5.1 Peak cardiorespiratory and peak power values during the incremental cycle ergometer test conducted pre-training.

		HIIT	CON
$\dot{V}O_{2peak}$	($L.min^{-1}$)	3.40 ± 0.75	3.23 ± 0.59
$\dot{V}_{Epeak}$	($L.min^{-1}$)	130.4 ± 24.9	118.6 ± 31.4
HR_{peak}	($beat.min^{-1}$)	185 ± 8	183 ± 16
PP	(W)	295 ± 75	269 ± 37

Data expressed as mean ± SD; High intensity interval training; HIIT, ($n = 8$), Control group; CON, ($n = 8$).

5.4.2 Intermittent cycling cardiorespiratory measures

Within the HIIT group, each of the $\dot{V}O_2$, $\dot{V}_E$ and HR during exercise were not significantly different between Post- and Pre-training, whilst RPE values Post- were less than Pre-training for EB 1 and EB 2 ($P < 0.05$). Within the CON group, the $\dot{V}O_{2peak}$, $\dot{V}_E$, HR and RPE did not differ significantly between Pre- and Post-training.

Table 5.2 Cardiorespiratory measures obtained during two maximal 30 s cycle ergometer sprint bouts, conducted Pre and Post-training cycling for HIIT and CON

		HIIT		CON	
		EB 1	EB 2	EB 1	EB 2
$\dot{V}O_2$ (L.min^{-1})	Pre	2.50 ± 0.48	2.78 ± 0.49	2.46 ± 0.36	2.86 ± 0.62
	Post	2.49 ± 0.41	2.95 ± 0.56	2.18 ± 0.60	2.51 ± 0.73
$\dot{V}_E$ (L.min^{-1})	Pre	59.8 ± 16.3	78.1 ± 15.1	63.4 ± 13.26	81.8 ± 13.0
	Post	61.5 ± 14.3	81.1 ± 17.1	62.0 ± 22.4	77.6 ± 24.2
HR (beat.min^{-1})	Pre	149.8 ± 8	154.6 ± 8	149.1 ± 9	150.9 ± 16
	Post	147.6 ± 7	156.6 ± 7	149.4 ± 10	152.9 ± 11
RPE	Pre	15.3 ± 1.3	15.2 ± 1.0	12.9 ± 1.1	12.1 ± 0.8
	Post	12.2 ± 1.0 †	13.0 ± 0.5 †	13.9 ± 1.0	13.1 ± 0.6

Data expressed as mean ± SD; High intensity interval training, HIIT ($n = 8$), Control, CON ($n = 8$). Pre, Pre-training; Post, Post-training; EB, Exercise Bout. † Post < Pre ($P < 0.05$) for within groups.

5.4.3 Power outputs during sprint cycling bouts

The power output measures for HIIT and CON were not significantly different Pre vs Post-training (Table 5.3).

For HIIT, performances during the four EB in the initial training session were also compared to the first four EB of the final training session. There were no significant differences after training for any of mean power (589.79 ± 126.08 vs 566.15 ± 135.12 W), Total work (17.79 ± 4.7 vs 17.0 ± 4.0 kJ), Time to peak power (2.4 ± 1.4. vs 2.0 ± 1.5 s) and Fatigue index (57.7 ± 17.7 vs 58.0 ± 12.4 %), (all Pre- vs Post-train; respectively).

Table 5.3 Pre and Post-train cycling power during two, maximal 30 s sprint bouts for HIIT and CON

		HIIT		CON	
		EB 1	EB 2	EB 1	EB 2
Peak Power (W)	Pre	959 ± 306	907 ± 268	1035 ± 155	905 ± 172
	Post	1063 ± 330	984 ± 331	1062 ± 314	988 ± 282
Mean Power (W)	Pre	590 ± 138	537 ± 154	630 ± 96	535 ± 66
	Post	594 ± 167	578 ± 150	636 ± 109	516 ± 104
Minimum Power (W)	Pre	370 ± 147	330 ± 167	383 ± 66	330 ± 81
	Post	419 ± 149	375 ± 126	388 ± 117	286 ± 100
Total Work (kJ)	Pre	17.6 ± 4.1	16.0 ± 4.6	18.7 ± 2.9	16.0 ± 1.8
	Post	17.7 ± 4.9	17.1 ± 4.4	18.9 ± 3.3	15.4 ± 3.2
Time to Peak Power (sec)	Pre	2.8 ± 2.7	1.7 ± 0.8	3.3 ± 1.9	1.7 ± 1.3
	Post	1.8 ± 1.4	1.8 ± 1.5	3.1 ± 2.2	1.0 ± 0.4
Fatigue Index (%)	Pre	58.5 ± 18.2	61.9 ± 16.8	67.4 ± 15.0	66.8 ± 18.8
	Post	58.4 ± 16.8	62.5 ± 21.2	61.7 ± 12.7	70.3 ± 8.2

Data expressed as mean ± SD; High intensity interval training, HIIT, (n = 8), Control group, CON, (n = 8). EB, Exercise Bout.

5.4.6 Arterial plasma [K^+]

Plasma $[K^+]_a$ at rest did not differ significantly between HIIT or CON at Pre, or between Post compared to Pre in both groups. Plasma $[K^+]_a$ increased above rest during exercise and had returned to rest values at 2 min post-exercise, then increased slightly above rest at 10, 20 and 30 min post-exercise, for both HIIT and CON (time main effect, $P < 0.05$; Figure 5.3). For HIIT, there was a trial x time interaction with $[K^+]_a$ less during Post than Pre at 80% $\dot{V}O_{2peak}$ and at 1 min recovery ($P < 0.05$(Figure 5.3). No differences were seen in $[K^+]_a$ between Pre- and Post- trials in CON (Figure 5.3).

5.4.7 Venous plasma [K^+]

Plasma $[K^+]_v$ at rest did not differ significantly between HIIT or CON at Pre, or between Post compared to Pre in both groups. For HIIT, plasma $[K^+]_v$ increased above rest during exercise and had returned to rest values at 5 min post-exercise, but was slightly greater than rest at 10, 20 and 30 min post-exercise; similar changes were seen for CON except the increase in recovery occurred only at 20 and 30 min recovery (time main effect, $P < 0.05$; Figure 5.4). For HIIT, there was a trial x time interaction ($P < 0.05$) with $[K^+]_v$ during Post being greater than Pre at EB 4 ($P < 0.05$). For CON, there was a trial x time interaction ($P < 0.05$) with $[K^+]_v$ during Post being greater than Pre at 1 min post-exercise ($P < 0.05$).

5.4.8 Arterio-venous [K^+] difference

Plasma $[K^+]_{a-v}$ at rest were not significantly different between HIIT or CON at Pre, or between Post compared to Pre in both groups. Plasma $[K^+]_{a-v}$ was greater than rest (positive) during exercise at 60% $\dot{V}O_{2peak}$, 80% $\dot{V}O_{2peak}$, both EB 1 and EB 2 and was elevated at 1 min recovery, for both HIIT and CON ($P < 0.05$, time main effect, Figure 5.5).

5.4.9 **Change in arterial plasma [K^+] from rest**

The $\Delta[K^+]_a$ was greater than rest during 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, at each EB, and at 1 min recovery, for both HIIT and CON and additionally in CON at 10-30 min recovery (time main effect, $P < 0.05$; Figure 5.6). For HIIT, there was a significant trial x time interaction for $\Delta[K^+]_a$ ($P < 0.05$), being reduced Post compared to Pre at 80% $\dot{V}O_{2peak}$ ($P < 0.05$) For CON there was a significant trial x time interaction for $\Delta[K^+]_a$ ($P < 0.05$), being greater during Post compared to Pre at EB1 (Figure 5.6 B).

5.4.10 Change in venous plasma [K^+] from rest

The $\Delta[K^+]_v$ was greater than rest during exercise at 60% $\dot{V}O_{2peak}$, 80% $\dot{V}O_{2peak}$ and during each EB, and at 1 min and 2 min recovery for HIIT and CON; elevations in recovery were seen at 20-30 min for HIIT but only at1 min for CON (time main effects, $P < 0.05$; Figure 5.7).

5.4.11 Δ $[K^+]_a$ /work Ratio

The $\Delta[K^+]$ $work^{-1}$ ratio was 30.39 ± 22.54 vs. 28.94 ± 17.36 $nmol.1^{-1}$ J^{-1} for Pre- vs. Post-training respectively.

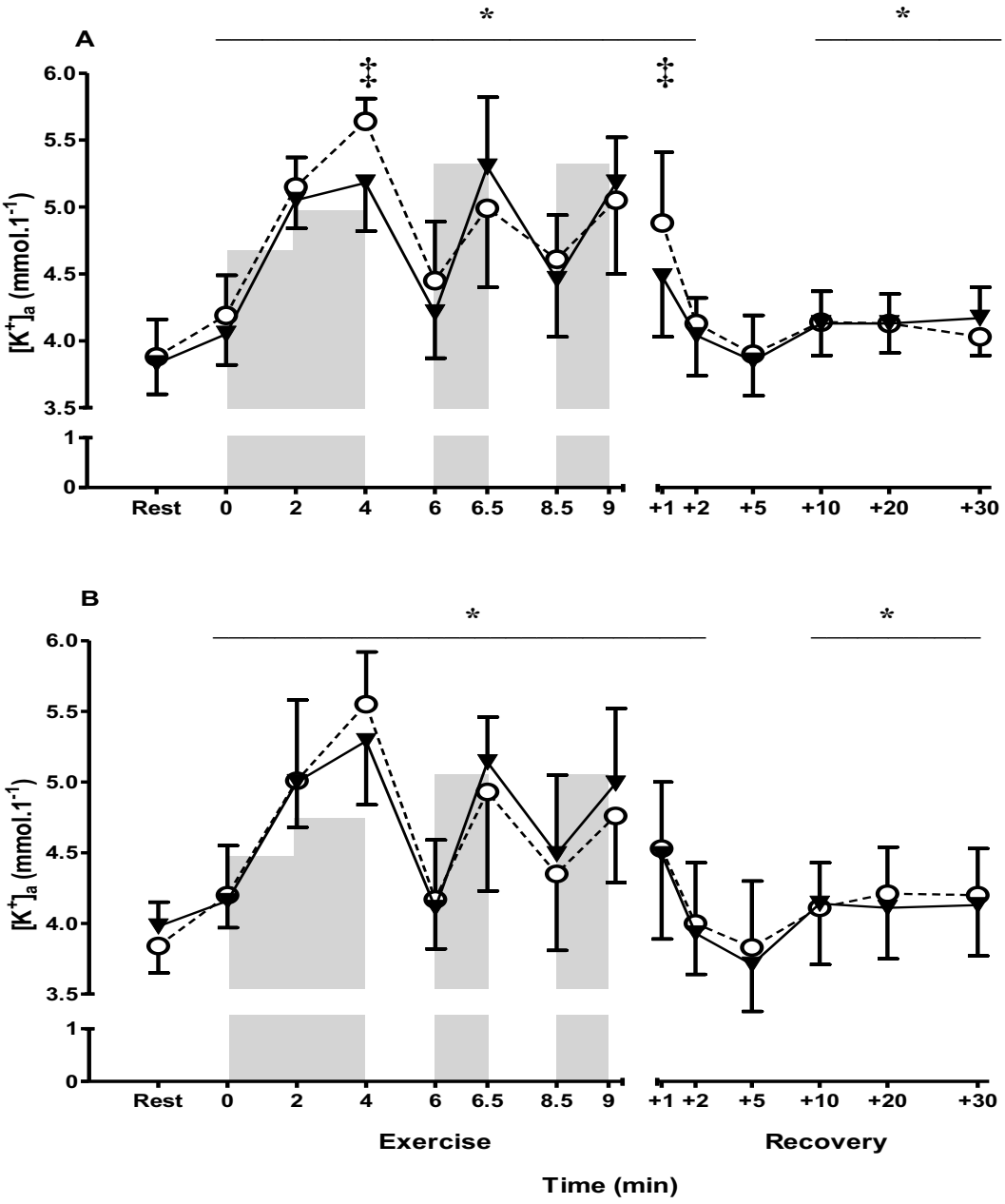

Figure 5.3 Plasma $[K^+]_a$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$). ‡ Pre > than Post for HIIT (trial x time interaction, $P < 0.05$).

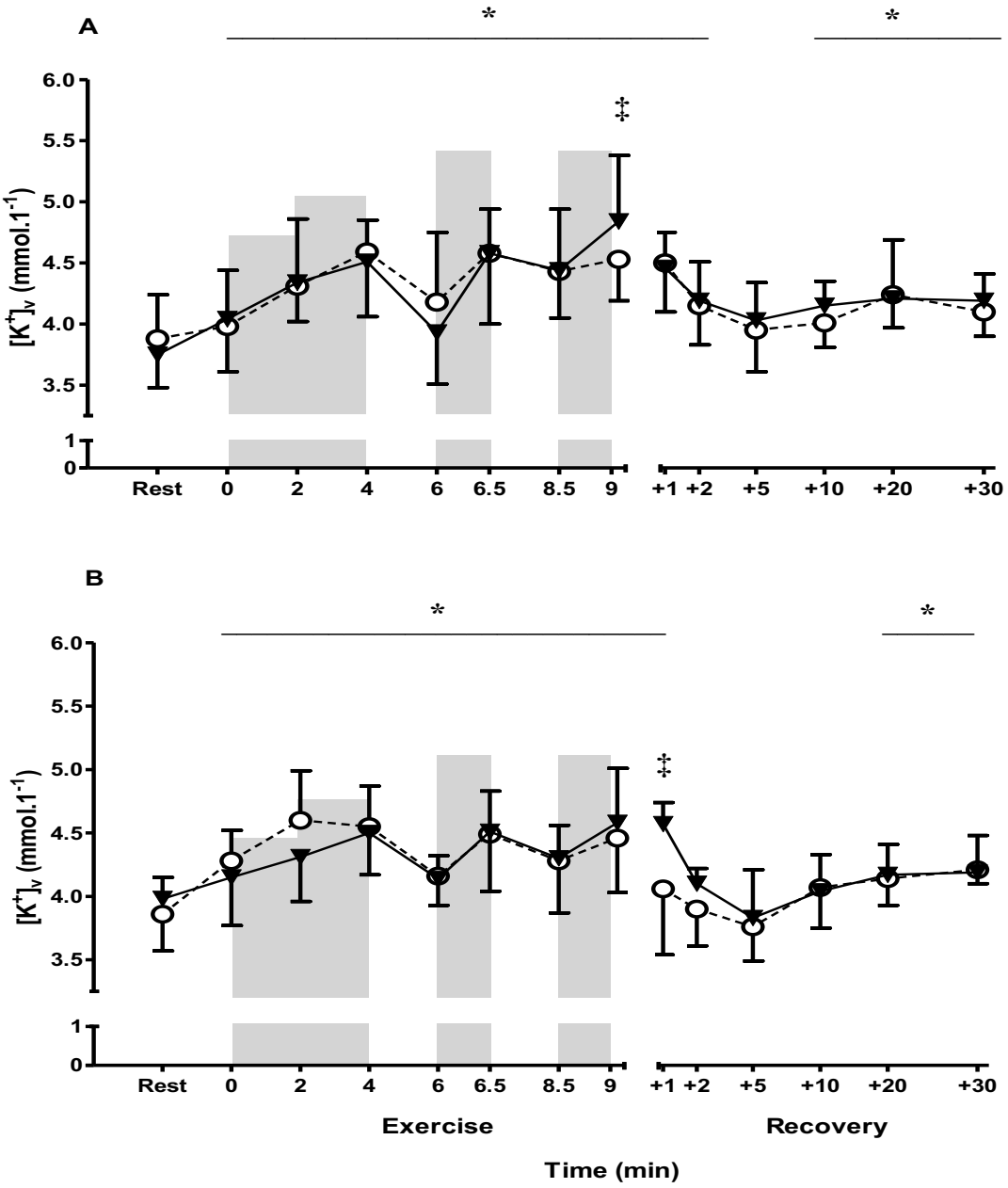

Figure 5.4 Plasma $[K^+]_v$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$, and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts, and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect. $P < 0.05$). ‡ Post > than Pre (trial x time interaction, $P < 0.05$).

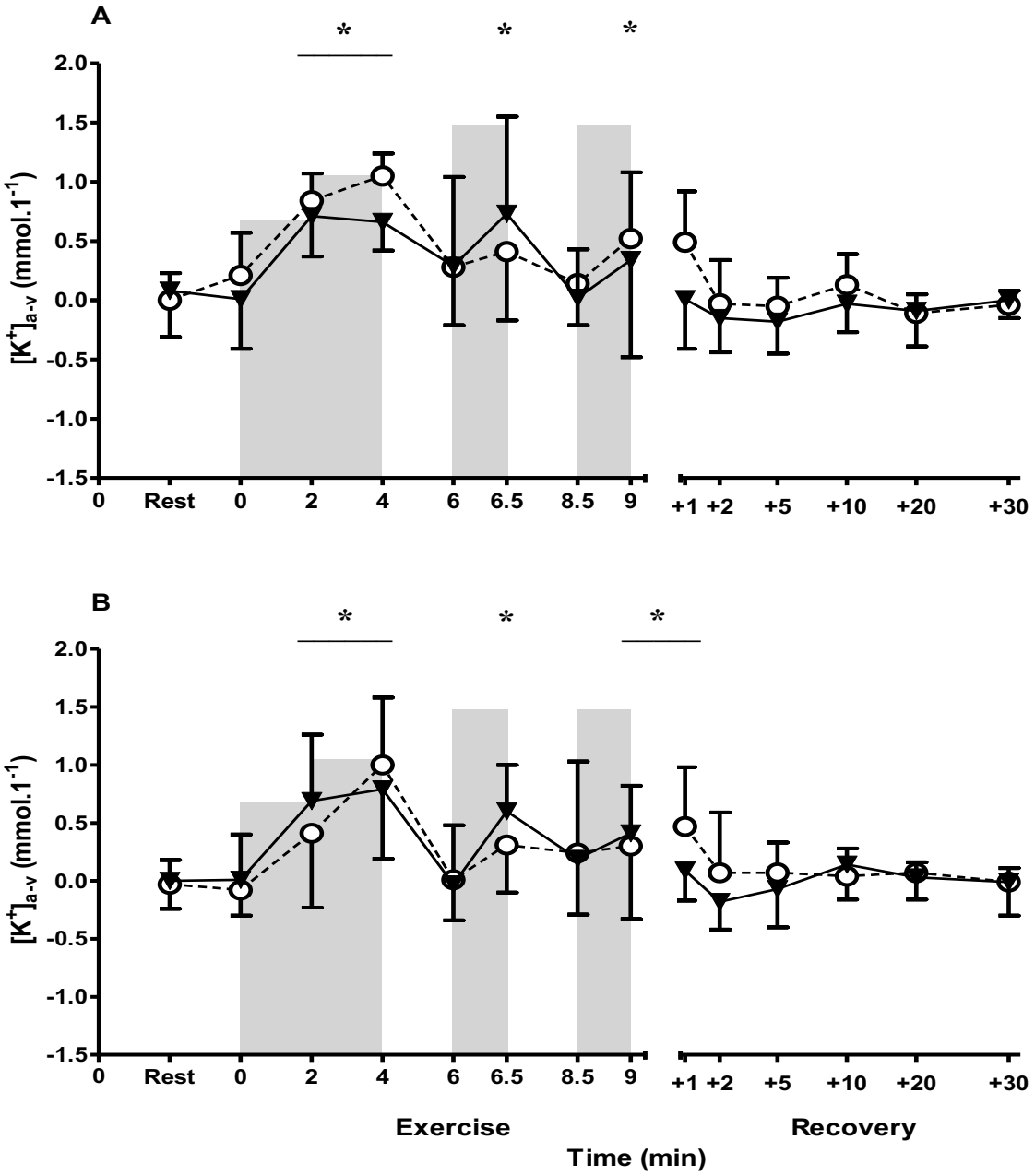

Figure 5.5 Plasma $[K^+]_{a\text{-}v}$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼).***** Greater than rest (time main effect, $P < 0.05$).

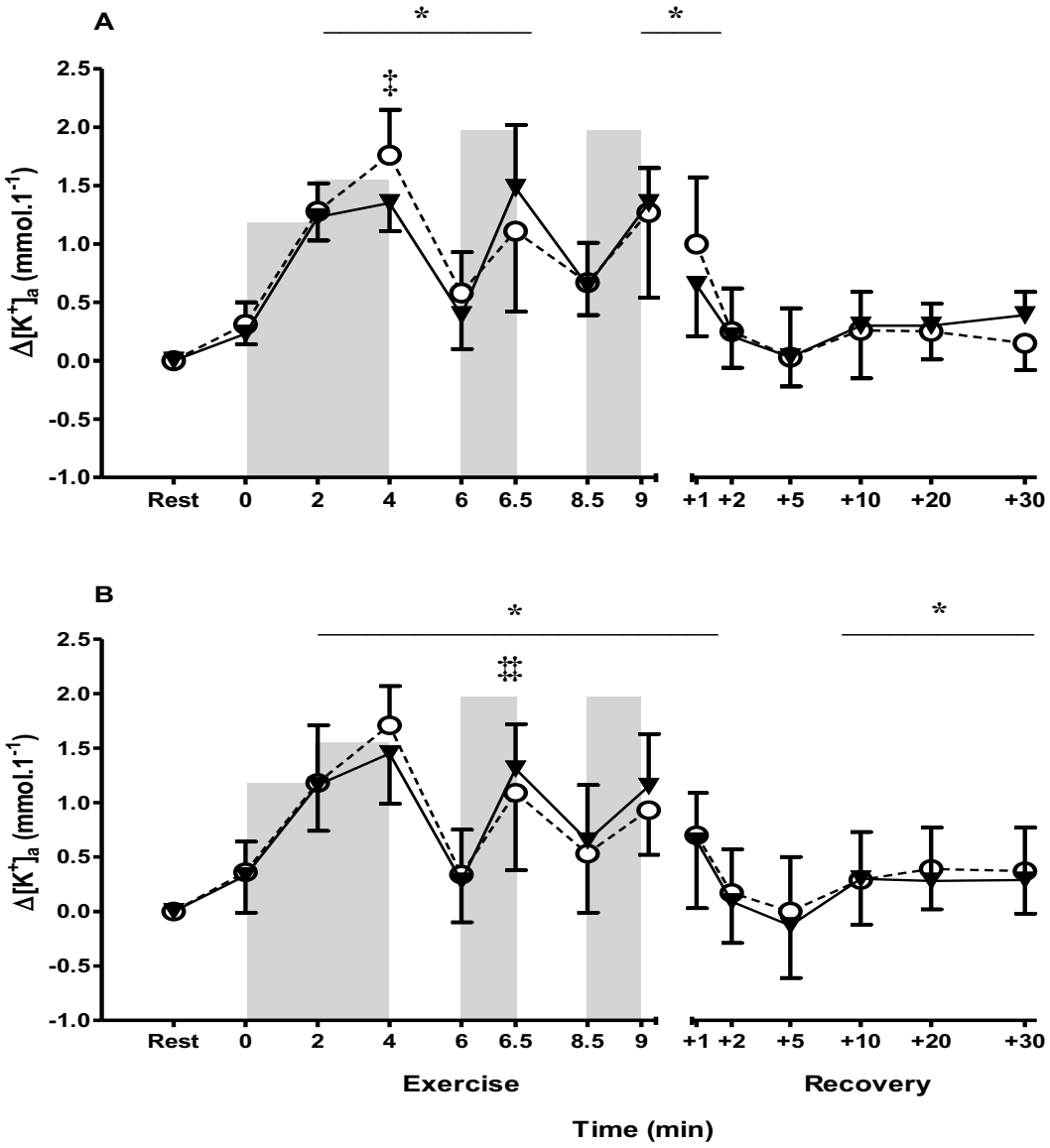

Figure 5.6 Change in plasma $[K^+]_a$ from rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$, and 80% $\dot{V}O_{2peak}$ immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$), ‡ Post < than Pre, (trial x time interaction, $P < 0.05$). ‡‡ Post < than Pre (trial x time interaction, $P < 0.05$).

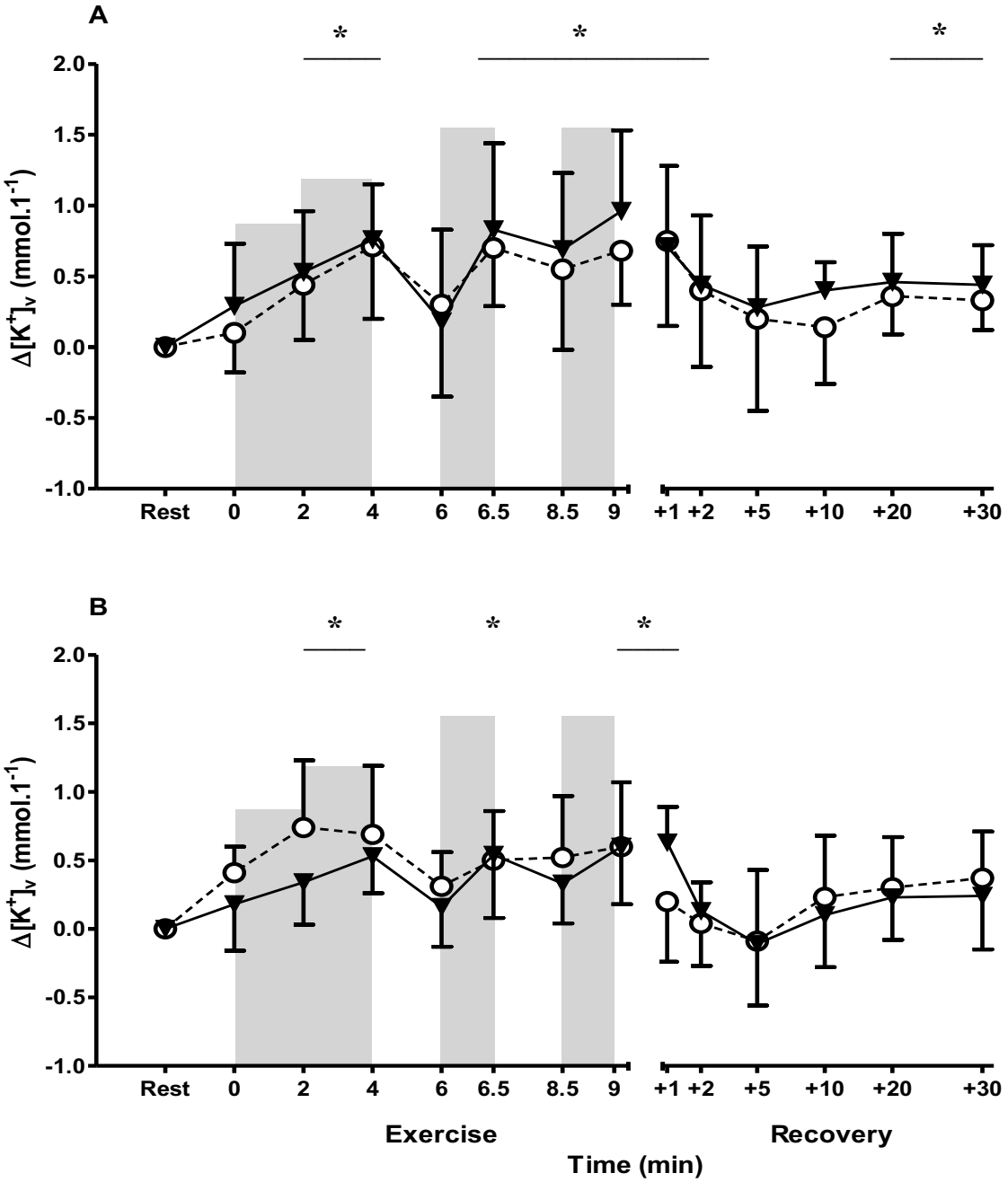

Figure 5.7 Change in plasma $[K^+]_v$ from rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$, and 80% $\dot{V}O_{2peak}$ immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$).

5.4.12 [Hb] and Hct

The $[Hb]_a$ and $[Hb]_v$ values at rest did not differ significantly between HIIT or CON at Pre, or Post compared to Pre in both groups. For HIIT and CON, $[Hb]_a$ and $[Hb]_v$ increased during 60% $\dot{V}O_{2peak}$ and remained above rest during exercise; during recovery $[Hb]_a$ remained above rest, whilst $[Hb]_v$ returned to rest at 30 min (time main effect, $P < 0.05$; Table 5.4).

The Hct_a and Hct_v, values at rest did not differ significantly between HIIT or CON at Pre, or Post compared to Pre in both groups. For HIIT and CON, Hct_a and Hct_v increased during 80% $\dot{V}O_{2peak}$ and remained greater than rest during exercise; during recovery Hct_a remained above rest, whilst Hct_v returned to rest at 30 min (time main effect, $P < 0.05$; Table 5.4).

Table 5.4 [Hb] and Hct values at rest, during exercise and recovery at 30 min

			Exercise			Recovery
HIIT		Rest	80% $\dot{V}o_{2peak}$	EB1	EB2	30 min
$[Hb]_a$	Pre	13.41 ± 1.10	14.92 ± 1.31	14.7 ± 1.37	15.10 ± 1.42	13.66 ± 1.34
	Post	13.63 ± 1.36	14.66 ± 1.23	14.91 ± 1.56	15.28 ± 1.50	13.87 ± 1.41
$[Hb]_v$	Pre	13.28 ± 1.33	14.31 ± 1.39	14.55 ± 1.07	14.88 ± 1.39	13.48 ± 1.39
	Post	13.52 ± 1.37	14.50 ± 1.21	14.42 ± 1.43	14.92 ± 1.46	13.46 ± 1.41
Hct_a	Pre	41.21 ± 3.37	45.80 ± 3.91	45.13 ± 4.09	46.27 ± 4.35	41.94 ± 4.01
	Post	41.81 ± 4.11	45.00 ± 3.77	45.75 ± 4.66	46.81 ± 4.59	42.63 ± 4.26
Hct_v	Pre	40.80 ± 4.00	43.88 ± 4.20	44.65 ± 3.18	45.57 ± 4.17	41.50 ± 4.21
	Post	41.46 ± 4.15	44.43 ± 3.64	44.31 ± 4.35	45.75 ± 4.36	41.35 ± 4.22
CON						
$[Hb]_a$	Pre	13.85 ± 1.35	15.38 ± 1.20	15.33 ± 1.26	15.48 ± 1.26	14.00 ± 1.41
	Post	14.13 ± 1.36	15.50 ± 1.45	15.71 ± 1.16	15.81 ± 1.52	14.26 ± 1.60
$[Hb]_v$	Pre	13.71 ± 1.36	14.69 ± 1.36	14.86 ± 1.27	15.09 ± 1.40	14.17 ± 1.37
	Post	13.98 ± 1.69	14.65 ± 1.60	14.85 ± 1.53	15.01 ± 1.59	14.01 ± 1.94
Hct_a	Pre	42.50 ± 4.04	47.11 ± 3.67	46.99 ± 3.84	47.46 ± 3.81	43.21 ± 4.34
	Post	43.61 ± 4.18	47.43 ± 4.31	48.11 ± 3.56	48.56 ± 4.61	43.78 ± 4.89
Hct_v	Pre	42.04 ± 4.13	45.04 ± 4.13	45.58 ± 3.86	46.20 ± 4.20	43.44 ± 4.09
	Post	44.24 ± 3.76	46.25 ± 3.76	46.64 ± 3.91	47.26 ± 3.77	44.61 ± 4.17

5.4.13 Changes in blood volume

For HIIT, the ΔBV_a decreased below rest during exercise, and was increased above rest prior to EB1 and during 10-20 min recovery (time main effect, $P < 0.05$; Figure 5.8). For CON, ΔBV_a decreased below rest during submaximal exercise, increased above rest prior to EB1 and was above rest during 5-30 min recovery (time main effect, $P < 0.05$; Figure 5.8). For HIIT, there was a significant trial x time interaction ($P < 0.05$) with ΔBV_a being greater during exercise at 80% $\dot{V}O_{2peak}$ and at 5 min recovery during Post compared to Pre-training.

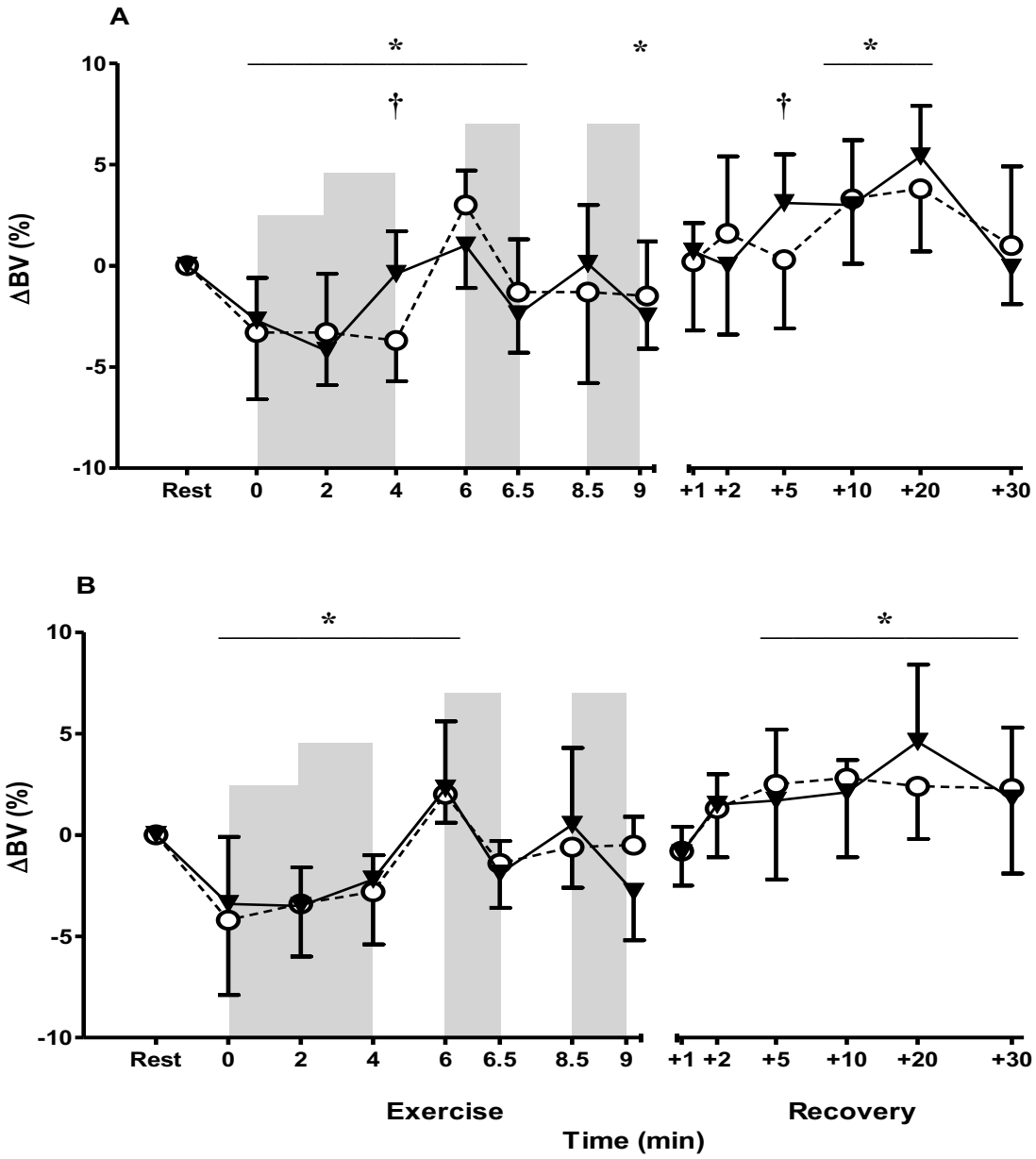

Figure 5.8 Changes in arterial BV (ΔBV_a) from rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$, and 80% $\dot{V}O_{2peak}$ immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Different to rest (time main effect, $P < 0.05$). † Post > than Pre (trial x time interaction, $P < 0.05$).

5.4.14 Plasma [Na^+]

Plasma $[Na^+]_a$ and $[Na^+]_v$ values at rest did not differ significantly between HIIT or CON at Pre, or Post compared to Pre in both groups. For HIIT, $[Na^+]_a$ and $[Na^+]_v$ increased above rest during EB1, during EB2 and recovery from 1 - 5 min (time main effect, $P < 0.05$; Figure 5.9, Figure 5.10). For HIIT, there was a significant trial x time interaction ($P < 0.05$) for $[Na^+]_a$, being less Post compared to Pre during exercise at 80% $\dot{V}O_{2peak}$. For CON, $[Na^+]_a$ increased above rest during exercise at 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$ and both sprint EB and remained greater during recovery from 1- 5 min; changes were similar for $[Na^+]_v$ except for 60% $\dot{V}O_{2peak}$ ($P < 0.05$; Figures 5.9 and 5.10).

5.4.15 Plasma [Ca^{2+}]

Plasma $[Ca^{2+}]_a$ and $[Ca^{2+}]_v$ values at rest did not differ significantly between HIIT or CON at Pre, or Post compared to Pre in both groups. For both HIIT and CON, plasma $[Ca^{2+}]_a$ increased from rest during exercise at 60% $\dot{V}O_{2peak}$ and remained greater for each subsequent EB, including recovery at 1, 2, 5 and 10 min (time main effect, $P < 0.05$).

For HIIT and CON, plasma $[Ca^{2+}]_v$ increased from rest during EB1 and EB2, and during recovery at 1- 10 min ($P < 0.05$, time main effect, Figure 5.12). For CON there was a trial x time interaction ($P < 0.05$,) with $[Ca^{2+}]_v$ greater Post than Pre at 1 min post-exercise ($P < 0.05$, Figure 5.12).

5.4.16 Plasma [Cl^-]

Plasma $[Cl^-]_a$ and $[Cl^-]_v$ values at rest did not differ significantly between HIIT or CON at Pre, or Post compared to Pre in both groups. For both HIIT and CON, $[Cl^-]_a$ increased during exercise at 60% $\dot{V}O_{2peak}$ and throughout exercise, then returned to rest at 10 min post exercise ($P < 0.05$, time main effect). For HIIT there was a trial x time interaction ($P < 0.05$) with

$[Cl^-]_a$ greater Pre than Post during recovery at 2 and 30 min ($P < 0.05$, Figure 5.13).

For both HIIT and CON, $[Cl^-]_v$ increased during exercise at 60% $\dot{V}O_{2peak}$ and remained above rest during sprint exercise, and during recovery at 1-5 min post exercise ($P < 0.05$, time main effect, Figure 5.14).

5.4.17 Plasma [Lac$^-$]

Plasma $[Lac^-]_a$ and $[Lac^-]_v$ values at rest did not differ significantly between Pre or Post for HIIT or CON. For both HIIT and CON, $[Lac^-]_a$ increased during exercise at 60% $\dot{V}O_{2peak}$ exercise and remained elevated during exercise and throughout 30 min recovery ($P < 0.05$, time main effect, Figure 5.15).

For both HIIT and CON, $[Lac^-]_v$ increased during exercise at 80% $\dot{V}O_{2peak}$ exercise and remained elevated during exercise and recovery ($P < 0.05$, time main effect, Figure 5.16). For HIIT, there was a trial x time interaction ($P < 0.05$), , with $[Lac^-]_v$ greater Pre than Post at 20 min recovery (Figure 5.16).

5.4.18 Plasma pH

Plasma pH_a and pH_v values at rest were not significantly different between Pre or Post for HIIT or CON. For both HIIT and CON, pH_a and pH_v decreased from 60% $\dot{V}O_{2peak}$ and remained lower for each subsequent EB and throughout 30 min recovery ($P < 0.05$, time main effect, Figures 5.17 and 5.18).

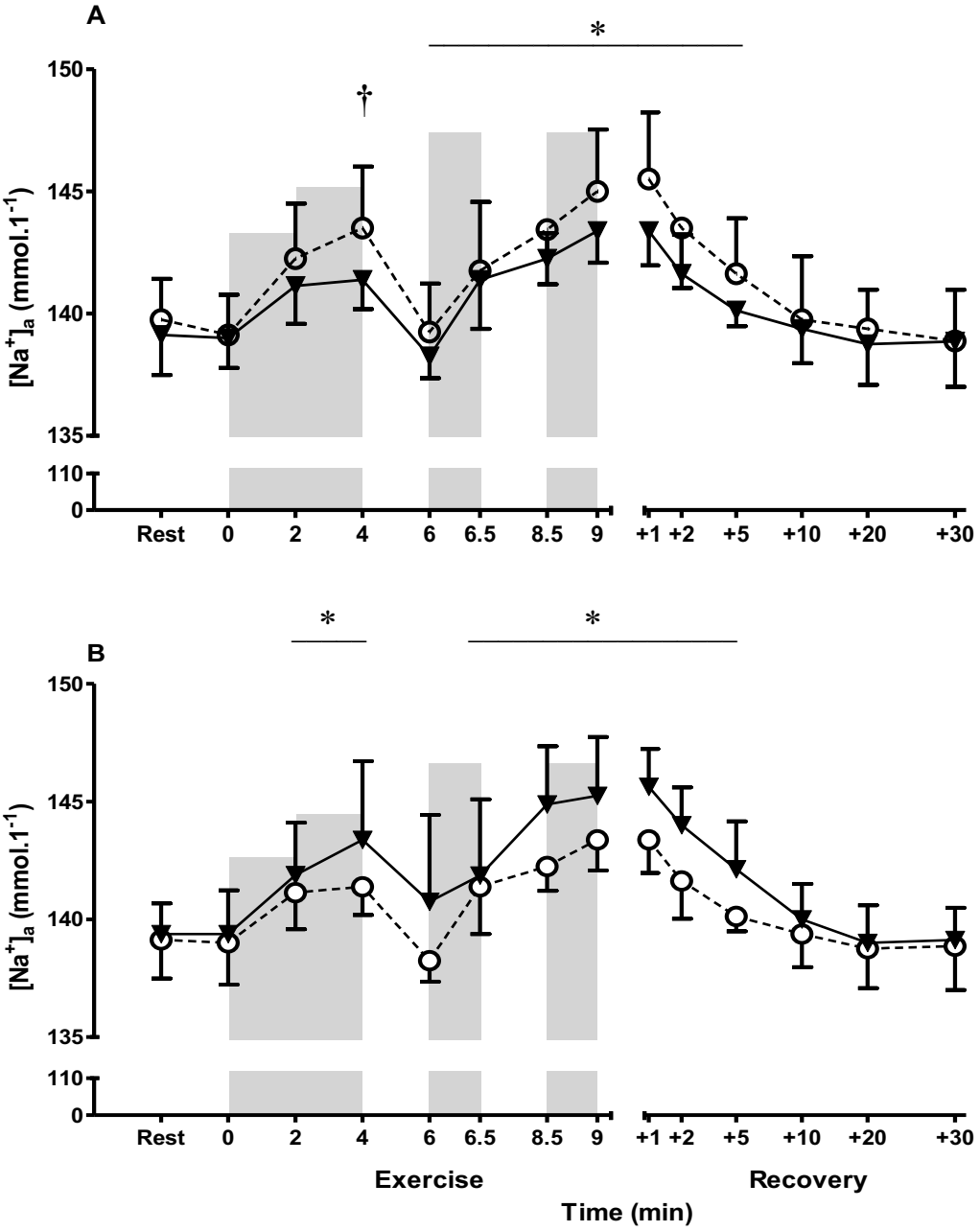

Figure 5.9 Plasma $[Na^+]_a$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼).* Greater than rest (time main effect, $P < 0.05$). † Post greater than pre (trial x time interaction, $P < 0.05$).

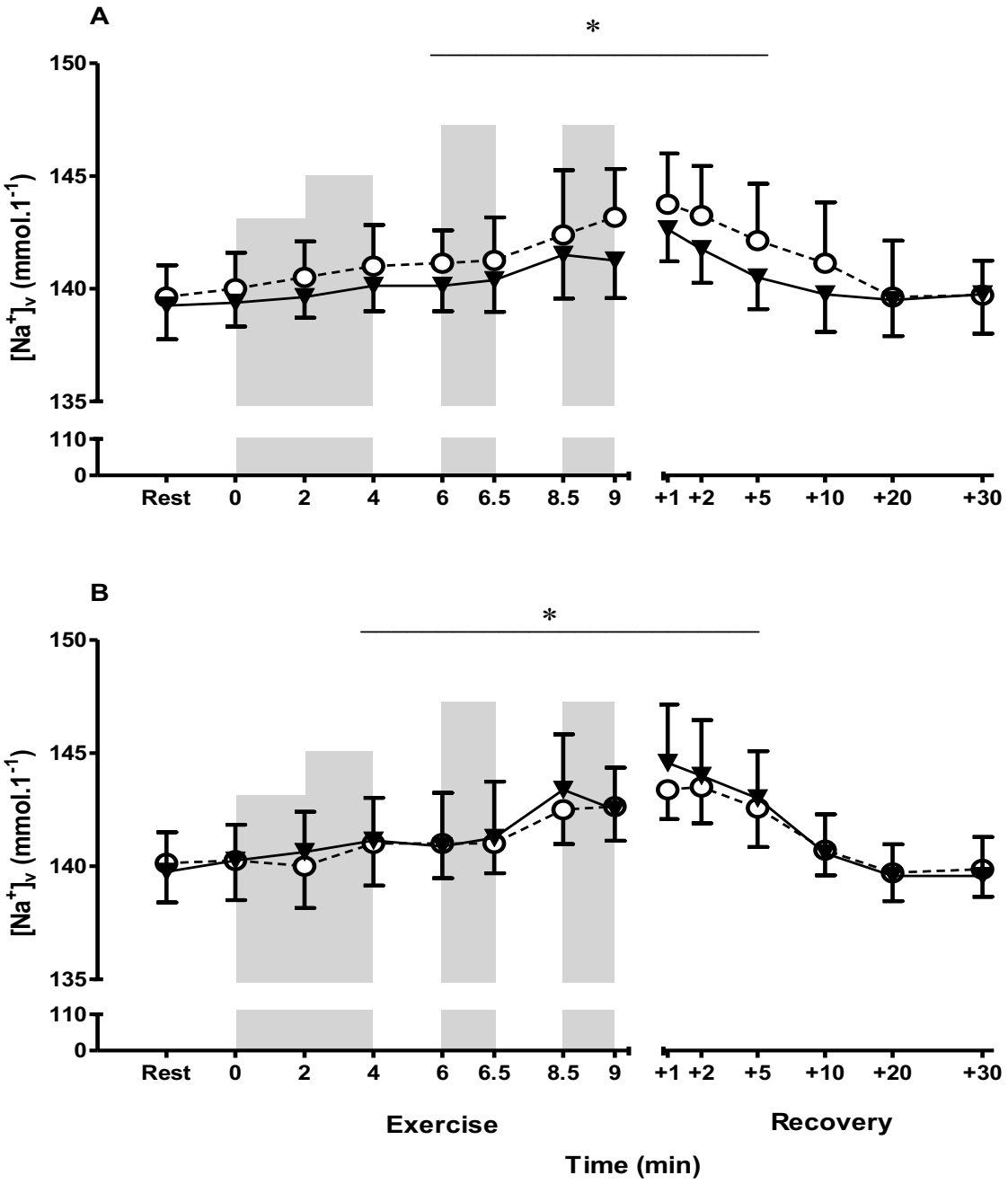

Figure 5.10 Plasma $[Na^+]_v$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (*n* = 8) and (B) CON (*n* = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$).

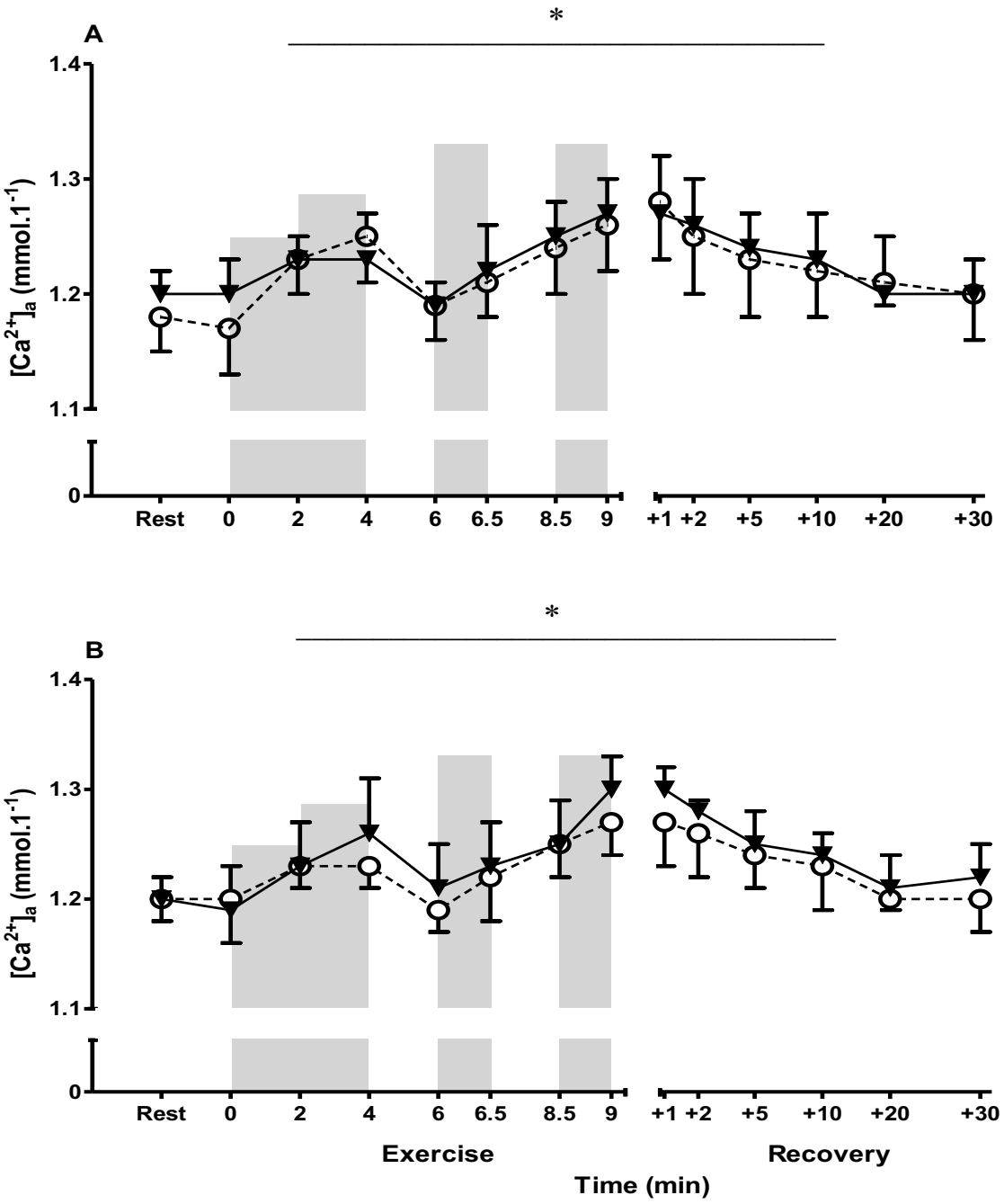

Figure 5.11 Plasma $[Ca^{2+}]_a$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$).

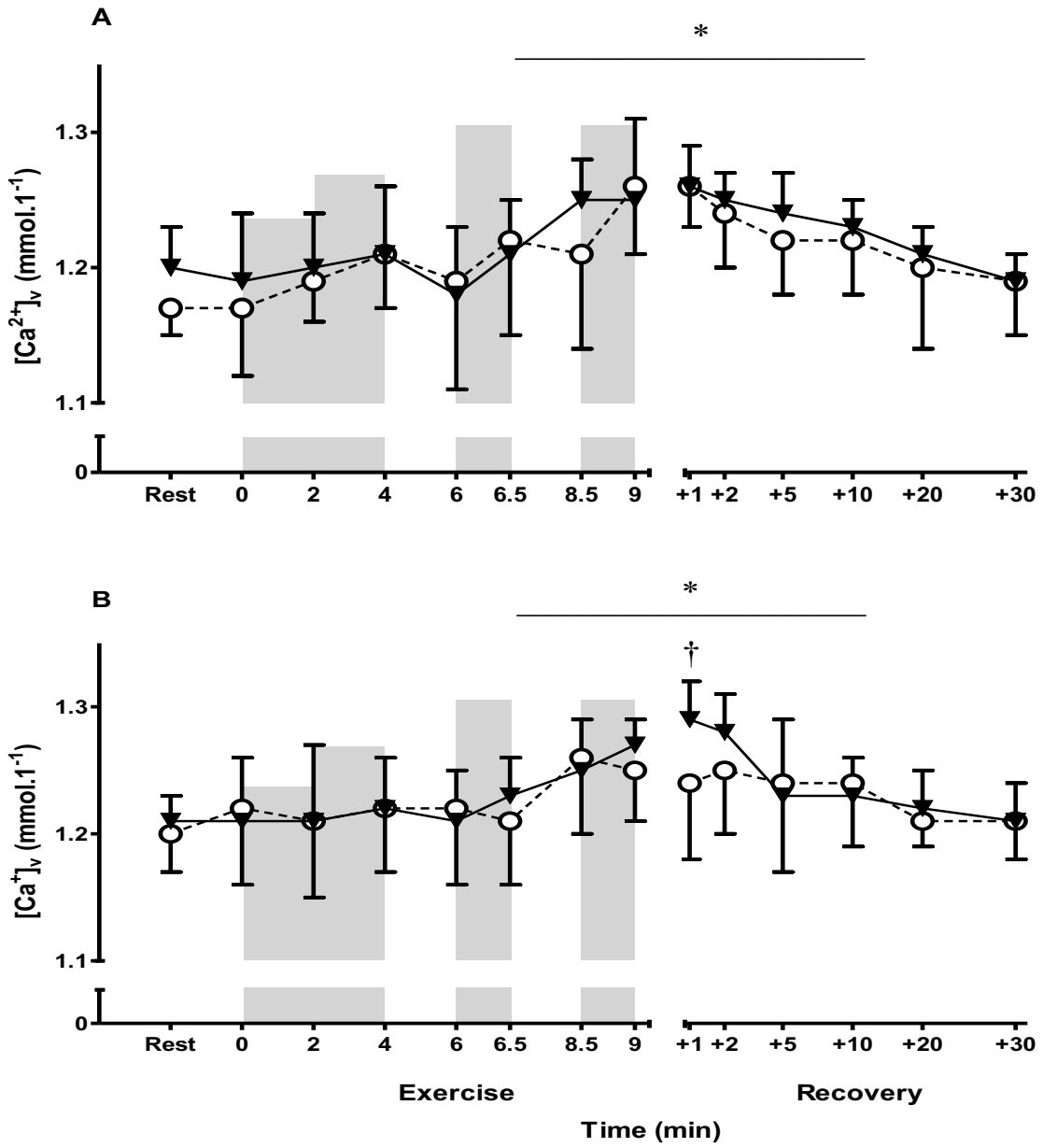

Figure 5.12 Plasma $[Ca^{2+}]_v$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$). † Post greater than pre (trial x time interaction, $P < 0.05$).

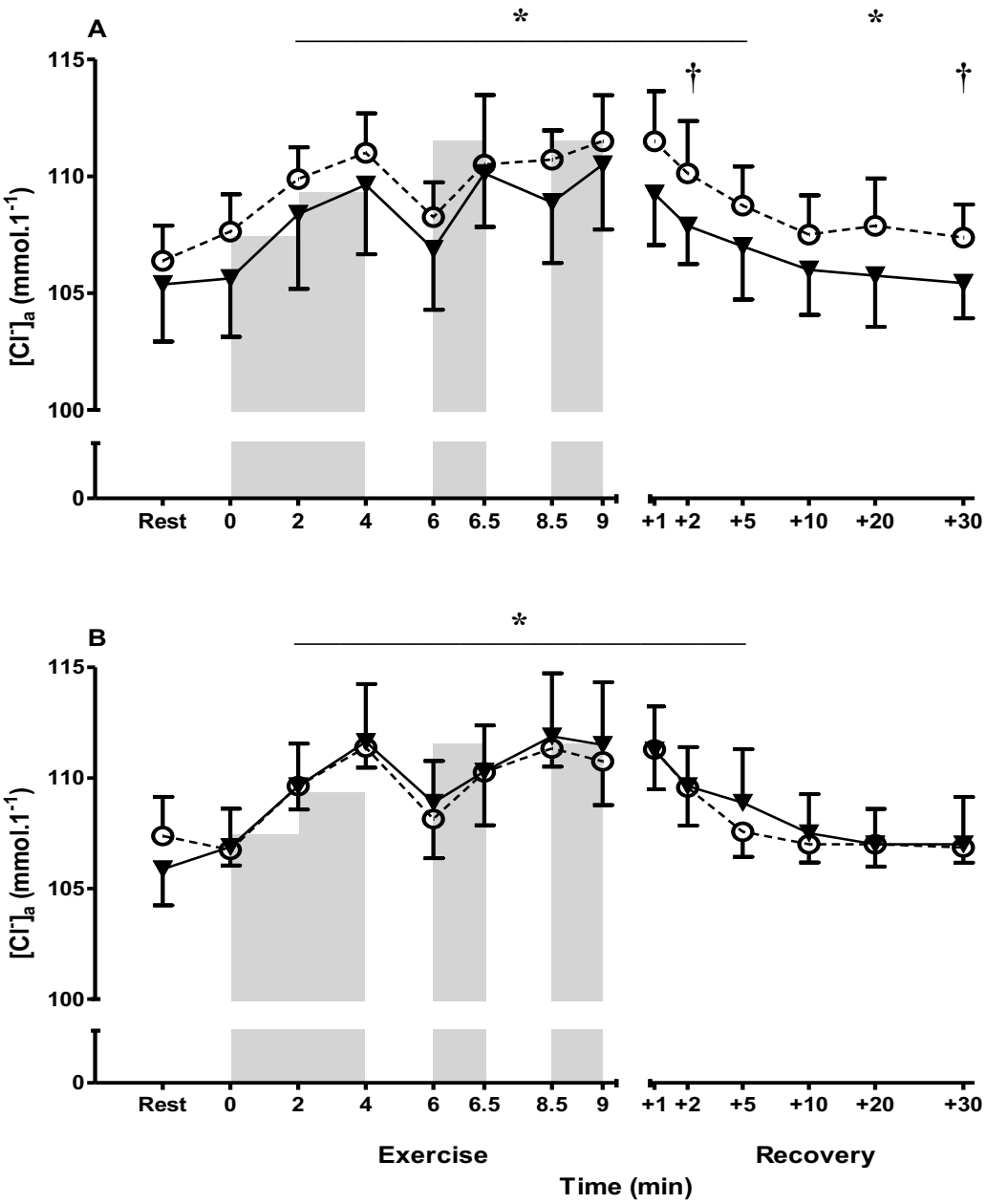

Figure 5.13 Plasma $[Cl^-]_a$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$). † Post greater than pre (trial x time interaction, $P < 0.05$).

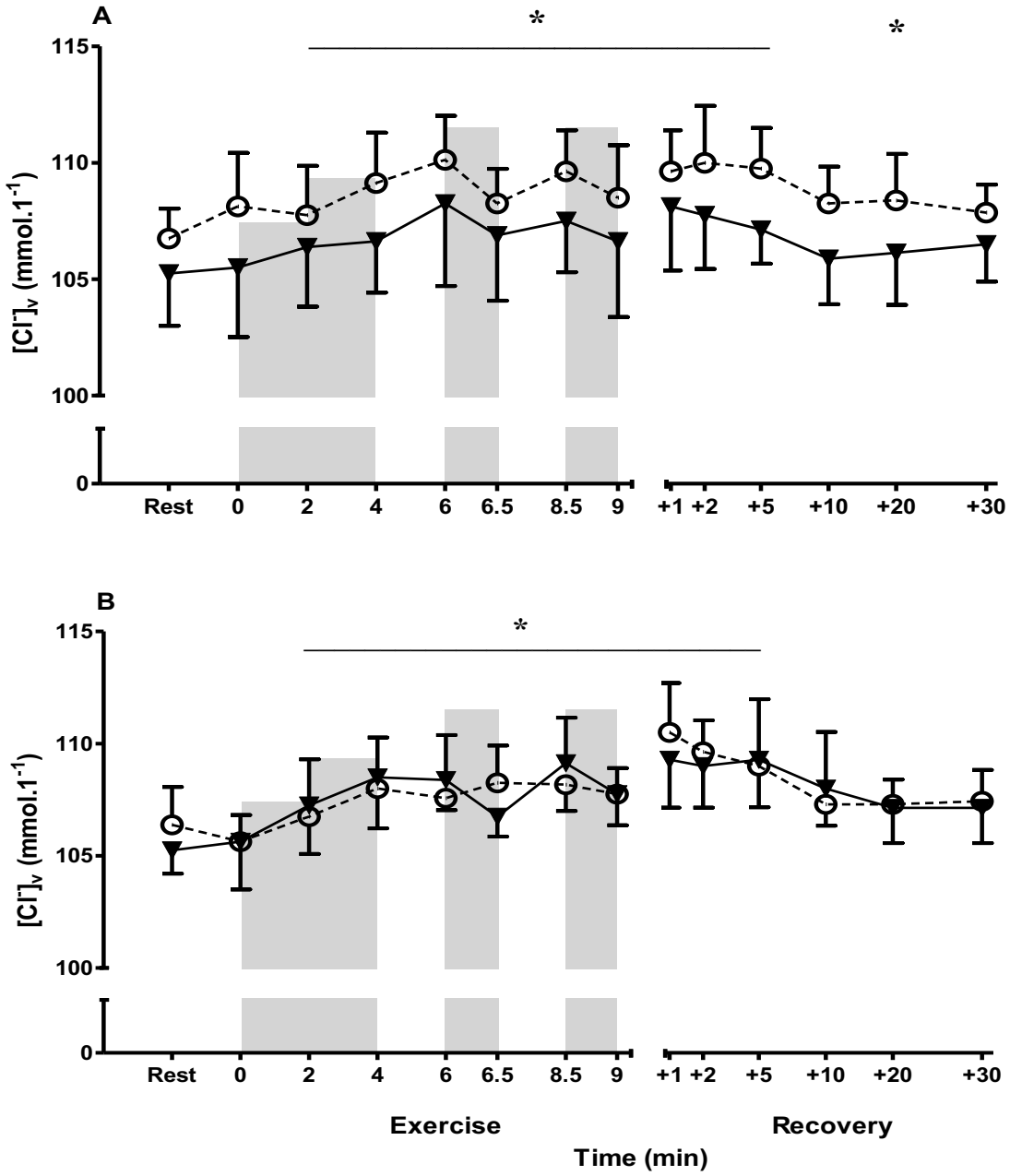

Figure 5.14 Plasma $[Cl^-]_v$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$). † Post greater than pre (trial x time interaction, $P < 0.05$).

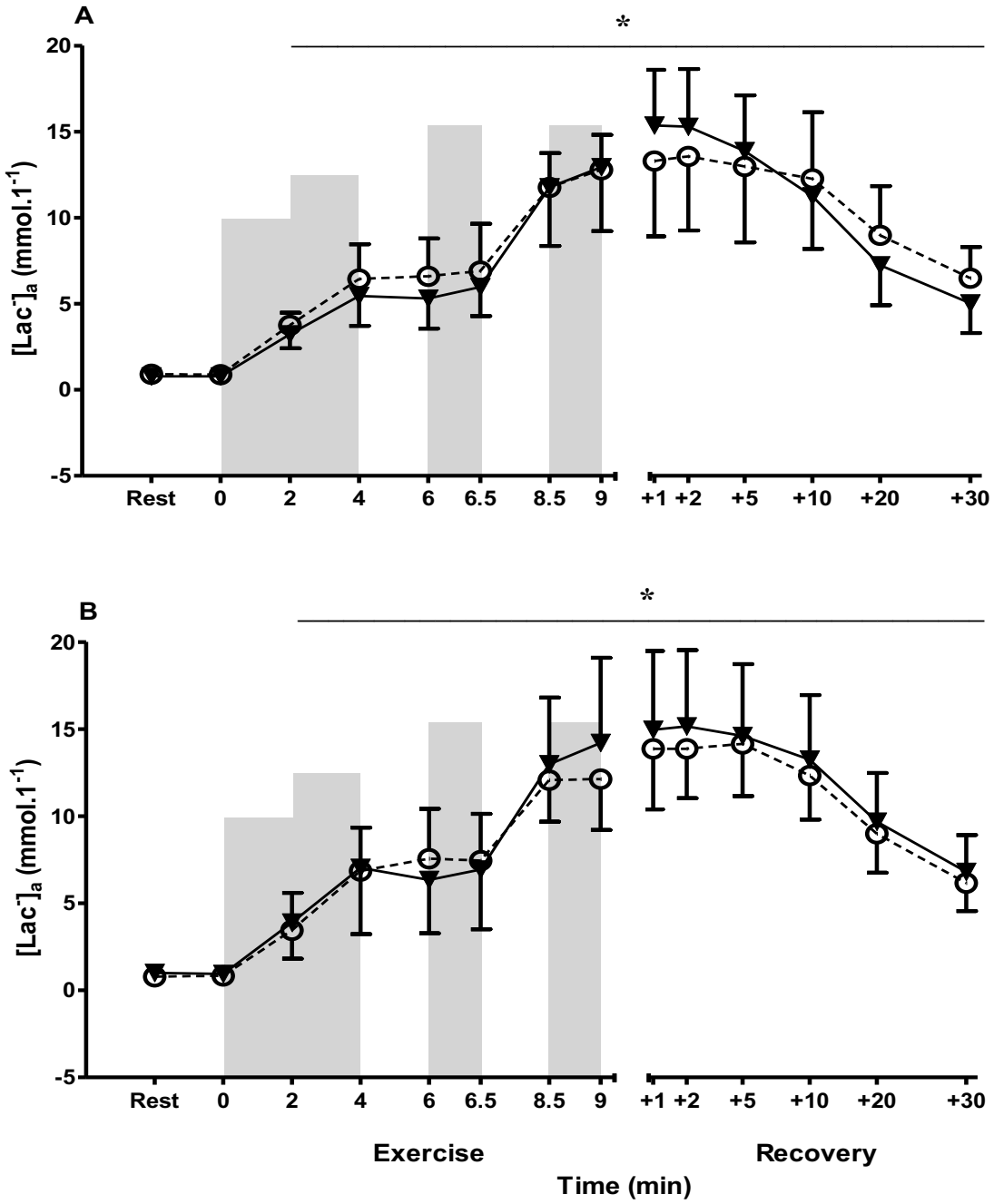

Figure 5.15 Plasma $[Lac^-]_a$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$).

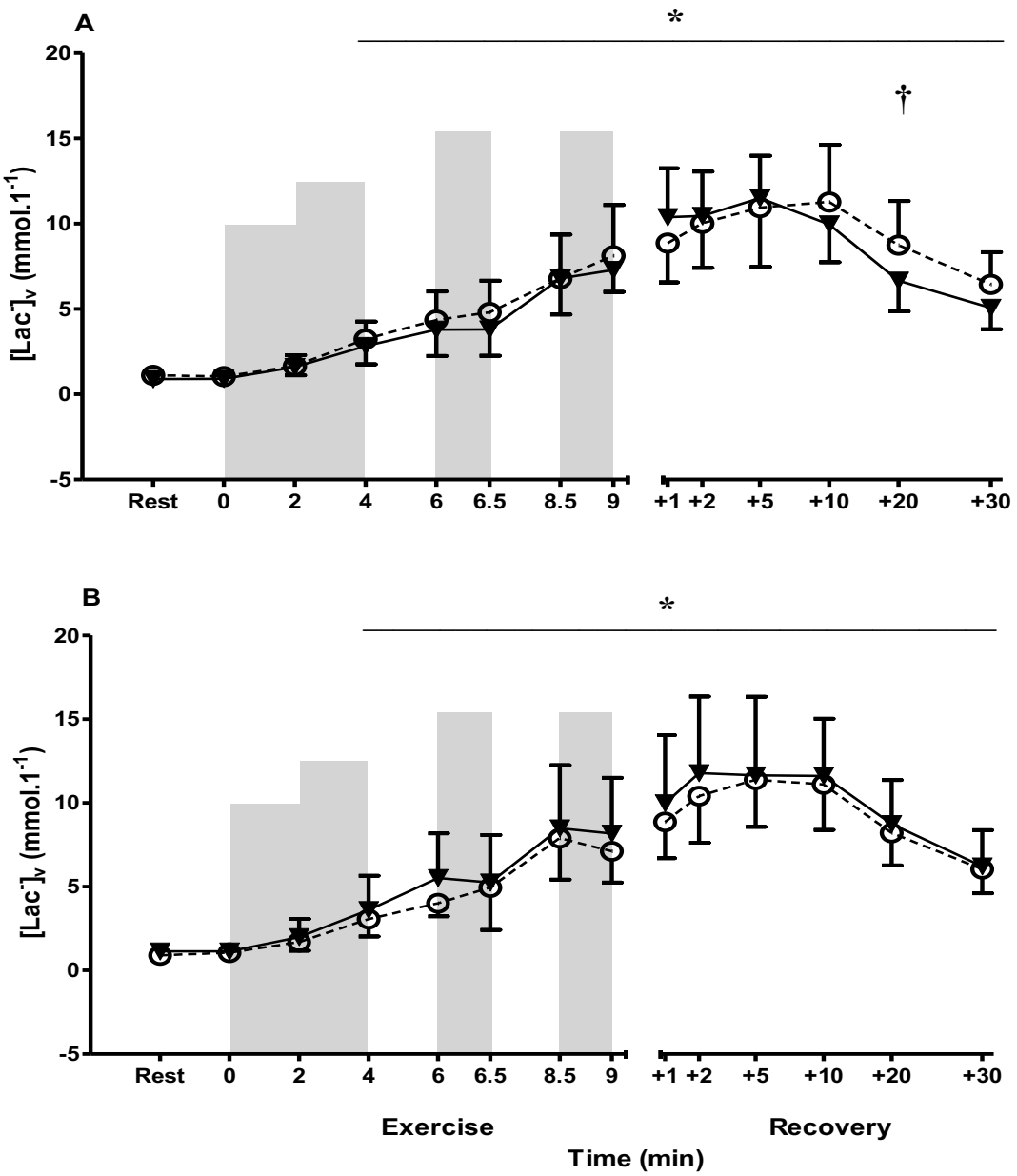

Figure 5.16 Plasma $[Lac^-]_v$ at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$). † Pre greater than Post (trial x time interaction, $P < 0.05$).

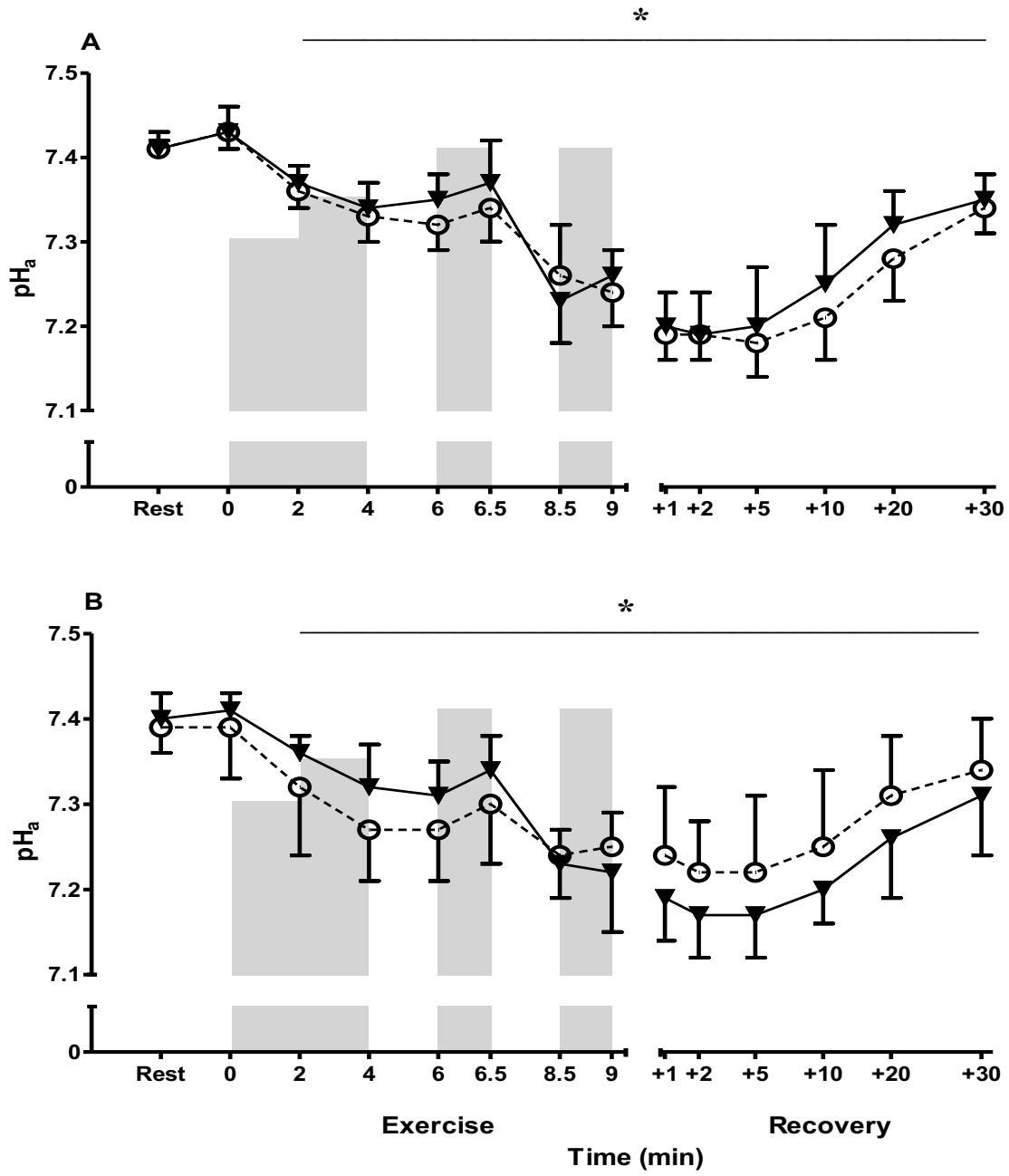

Figure 5.17 Plasma pH_a at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$).

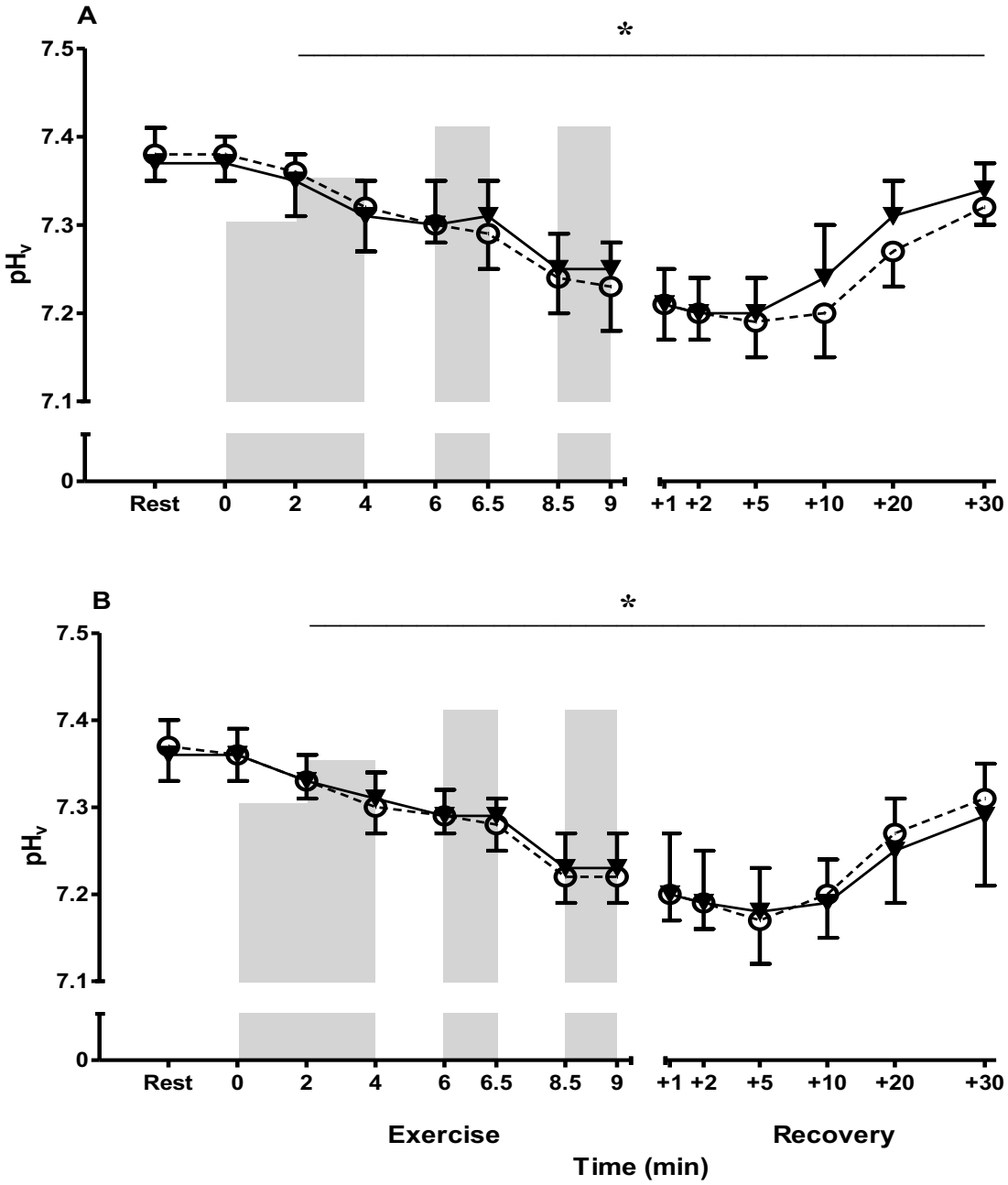

Figure 5.18 Plasma pH_v at rest, during cycling exercise for 2 min at each of 60% $\dot{V}O_{2peak}$ and 80% $\dot{V}O_{2peak}$, immediately prior to and in the final seconds of each of the two maximal 30 s sprint bouts and during 30 min recovery, conducted before and after 7 weeks (A) HIIT (n = 8) and (B) CON (n = 8). Values expressed as mean ± S.D. Shaded bars represent exercise bouts. Pre (**O**) and Post (▼). * Greater than rest (time main effect, $P < 0.05$).

5.5 Muscle contractile responses

5.5.1 Maximal voluntary contractions (MVC)

MVC at rest did not differ significantly between Pre or Post, for HIIT or CON. The MVC, expressed as a percentage of pre-exercise, decreased after each EB, and remained depressed at 10- and 30-min recovery, for both HIIT and CON ($P < 0.05$, time main effect; Table 5.4).

5.5.2 Potentiated quadriceps twitch (Q_{twpot})

The Q_{twpot} torque at rest did not differ significantly between Pre or Post, for HIIT or CON. The Q_{twpot}, expressed as a percentage of pre-exercise values, decreased after each EB, and remained depressed at 10- and 30-min recovery, for both HIIT and CON ($P < 0.05$, time main effect; Table 5.4).

5.5.3 Potentiated quadriceps paired twitch (Doublet)

The doublet torque at rest did not differ significantly between Pre or Post for HIIT. For HIIT, the doublet torque expressed as a percentage of pre-exercise, decreased after each EB, and remained depressed at 10 min recovery ($P < 0.05$, time main effect). For HIIT, there was a trial by time interaction ($P < 0.05$) with Post- greater than Pre at 10 min recovery (Table 5.4).

For CON doublet torque at rest did not differ significantly between Pre or Post. Torque decreased after each EB and remained depressed at 10- and 30-min recovery ($P < 0.05$, time main effect).

5.5.4 Potentiated quadriceps 20 Hz tetani

The 20 Hz tetani torque at rest did not differ significantly between Pre or Post for HIIT. For HIIT, 20 Hz tetani torque expressed as a percentage of pre-exercise, decreased after each EB, and remained depressed at 10- and 30-min recovery ($P < 0.05$, time main effect; Table 5.5).

For CON the 20 Hz tetani torque at rest did not differ significantly between Pre or Post. For CON, 20 Hz tetani expressed as a percentage of pre-exercise, decreased after each EB, and remained depressed at 10- and 30-min recovery ($P < 0.05$, time main effect; Table 5.5).

Table 5.5 Pre and Post-training MVC, twitch, doublet and 20 Hz tetani expressed as a percentage of rest for HIIT and CON.

				Percentage of pre-exercise				
				Exercise			Recovery	
Measure	Group	Trial	Rest	80% $\dot{V}O_{2peak}$	EB1	EB2	+10 min	+30 min
MVC	HIIT	Pre	100	89.2 ± 17.9 *	87.9 ± 18.3 *	85.5 ± 18.1 *	85.0 ± 27.0 *	83.3 ± 20.6 *
		Post	100	89.1 ± 22.2 *	90.2 ± 9.0 *	87.7 ± 8.6 *	83.7 ± 15.0 *	81.9 ± 17.5 *
	CON	Pre	100	90.4 ± 15.6 *	71.3 ± 16.9 *	71.0 ± 16.6 *	73.7 ± 15.7 *	79.3 ± 10.2 *
		Post	100	88.6 ± 15.2 *	76.4 ± 17.3 *	64.8 ± 13.7 *	73.6 ± 14.7 *	85.9 ± 16.0 *
Twitch	HIIT	Pre	100	63.3 ± 13.7 *	59.4 ± 11.4 *	50.7 ± 14.0 *	72.0 ± 17.2 *	78.6 ± 15.0 *
		Post	100	77.0 ± 17.4 *	62.4 ± 17.4 *	63.2 ± 29.9 *	66.3 ± 22.4 *	72.8 ± 27.8 *
	CON	Pre	100	65.9 ± 18.8 *	38.5 ± 12.3 *	46.1 ± 12.1 *	63.3 ± 12.1 *	81.1 ± 22.4 *
		Post	100	68.8 ± 11.5 *	52.7 ± 17.4 *	37.0 ± 10.1 *	70.0 ± 19.3 *	84.6 ± 17.6 *
Doublet	HIIT	Pre	100	66.9 ± 21.2 *	57.6 ± 16.4 *	53.1 ± 13.1 *	64.2 ± 15.4 *	77.6 ± 12.9
		Post	100	81.2 ± 19.4 *	72.8 ± 12.6 *	66.1 ± 15.7 *	100.4 ± 30.0 ¥	101.8 ± 32.4
	CON	Pre	100	92.7 ± 18.9 *	50.6 ± 10.2 *	47.5 ± 20.1 *	71.2 ± 24.7 *	91.4 ± 28.0 *
		Post	100	72.2 ± 17.8 *†	54.4 ± 10.8 *	43.0 ± 10.9 *	63.1 ± 27.7 *	86.8 ± 19.4 *
Tetani	HIIT	Pre	100	84.8 ± 30.9 *	90.3 ± 33.7 *	86.4 ± 25.2 *	89.8 ± 34.6	95.9 ± 45.0
		Post	100	75.8 ± 12.8 *	73.2 ± 11.8 *	70.1 ± 18.8 *	93.1 ± 33.1	98.2 ± 10.4
	CON	Pre	100	88.4 ± 22.4 *	68.0 ± 10.2 *	62.0 ± 17.7 *	77.0 ± 19.6 *	78.7 ± 15.0 *
		Post	100	83.3 ± 13.2 *	70.5 ± 11.5 *	63.5 ± 17.3 *	78.3 ± 10.9 *	89.2 ± 13.6 *

* less than rest, $p < 0.05$, time main effect

¥ Post greater than Pre, $p < 0.05$, trial x time interaction

† Post less than Pre, $p < 0.05$, trial x time interaction

5.6 Compound muscle activity (M-wave) evoked by quadriceps twitch

5.6.1 M-wave amplitude

The M-wave amplitude at rest did not differ significantly between Pre or Post for the VM or VL muscles for HIIT or CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, amplitude decreased after EB1 and EB2 for Pre and Post ($P < 0.05$ time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at 80% $\dot{V}O_{2peak}$ and at 10 min recovery (Table 5.6).

For HIIT, in VL, amplitude decreased after EB1 and EB2 for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at 80% $\dot{V}O_{2peak}$, EB1 and EB2 (Table 5.6).

For CON, in VM, amplitude decreased after EB1 for Pre and Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude being greater during Post than Pre at 80% $\dot{V}O_{2peak}$ (Table 5.6).

For CON, in VL, amplitude decreased after EB2 for Pre and Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude being less during Post than Pre at 30 min recovery (Table 5.6).

5.6.2 M-wave duration

The M-wave duration at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, duration increased after exercise at 80% $\dot{V}O_{2peak}$ and at EB1 and EB2 for Pre and Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$),

with duration being less during Post than Pre at 80% $\dot{V}O_{2peak}$ and at 30 min recovery (Table 5.5).

For HIIT, in VL, duration increased after exercise at 80% $\dot{V}O_{2peak}$ and at EB1 and EB2 for Pre and at EB1 and EB2 for Post ($P < 0.05$, time main effect; Table 5.5).

For CON, in VM, duration increased at 80% $\dot{V}O_{2peak}$ and at EB2 for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with duration being less during Post than Pre at 30 min recovery.

For CON, in VL, duration increased at 80% $\dot{V}O_{2peak}$, and at EB1 and EB2 for Pre and Post ($P < 0.05$, time main effect; Table 5.5).

5.6.3 M-wave area

The M-wave area at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, area there was a trial main effect ($P < 0.05$). For HIIT, in VM, area decreased at 80% $\dot{V}O_{2peak}$, and at EB1 and EB2 for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with area being greater during Post than Pre at EB2 (Table 5.6).

For HIIT, in VL, area there was a trial main effect ($P < 0.05$).

For CON, in VM, area increased after exercise at EB2 for Pre and Post ($P < 0.05$, time main effect; Table 5.6).

For CON, in VL, area decreased during recovery at 30 min for Pre and Post ($P < 0.05$, time main effect; Table 5.6).

Table 5.6 Twitch Pre and Post-training M-wave measures expressed as a percentage of rest for HIIT and CON

HIIT twitch percentage of pre-exercise								
				Exercise			Recovery	
Measure	Group	Trial	Rest	80% $\dot{V}o_{2peak}$	EB1	EB2	+10 min	+30 min
Amplitude	VM **	Pre	100	63.3 ± 18.4	55.3 ± 25.0 *	52.3 ± 20.8 *	76.2 ± 28.0	77.3 ± 34.1
		Post	100	91.5 ± 26.7 †	66.7 ± 35.4 *	80.9 ± 33.4 *	140.3 ± 53.9 †	99.3 ± 30.7
	VL	Pre	100	73.4 ± 24.4	55.5 ± 15.4 *	57.3 ± 18.7 *	93.5 ± 16.7	98.2 ± 14.5
		Post	100	101.8 ± 24.3 †	99.6 ± 33.3 †	100.5 ± 13.8 †	115.9 ± 41.8	120.7 ± 42.8
Duration	VM	Pre	100	151.8 ± 25.0 *	131.7 ± 32.4 *	133.6 ± 39.0 *	116.7 ± 24.0	118.3 ± 22.2
		Post	100	117.7 ± 23.0 * †	114.1 ± 18.3 *	119.8 ± 14.3 *	95.3 ± 10.2	93.5 ± 16.7 †
	VL	Pre	100	111.5 ± 18.4 *	122.5 ± 25.5 *	113.9 ± 30.5 *	90.9 ± 18.6	92.5 ± 15.2
		Post	100	105.6 ± 14.8	112.5 ± 35.9 *	115.3 ± 47.7 *	93.4 ± 15.6	87.5 ± 14.5
Area	VM **	Pre	100	53.2 ± 33.4 *	56.7 ± 40.1 *	54.5 ± 42.9 *	99.0 ± 39.3	93.3 ± 36.0
		Post	100	87.8 ± 44.1	72.3 ± 38.1	129.3 ± 71.9 †	133.0 ± 58.3	107.3 ± 38.5
	VL **	Pre	100	91.9 ± 13.4	82.2 ± 30.0	91.3 ± 18.2	84.0 ± 19.5	90.8 ± 15.6
		Post	100	104.3 ± 20.1	95.5 ± 33.2	102.7 ± 17.0	99.6 ± 21.0	101.0 ± 25.0
CON twitch percentage of pre-exercise								
Amplitude	VM	Pre	100	74.3 ± 26.0	68.3 ± 34.8 *	82.0 ± 53.0	105.1 ± 53.0	96.0 ± 37.4
		Post	100	111.9 ± 37.7 †	87.0 ± 46.2 *	97.0 ± 45.2	120.2 ± 57.1	87.5 ± 57.7
	VL	Pre	100	85.8 ± 27.0	92.0 ± 35.9	83.2 ± 32.5 *	98.9 ± 17.2	107.3 ± 26.4
		Post	100	97.0 ± 9.0	83.0 ± 16.7	82.4 ± 14.6 *	84.8 ± 14.3	83.5 ± 20.1 †
Duration	VM	Pre	100	122.3 ± 26.5 *	114.4 ± 16.4	140.7 ± 27.3 *	107.6 ± 33.5	96.4 ± 14.6
		Post	100	114.0 ± 19.2	118.0 ± 29.2	112.3 ± 32.6	92.6 ± 15.5	74.8 ± 16.8 †
	VL	Pre	100	117.0 ± 27.1 *	126.2 ± 33.4 *	144.5 ± 54.1 *	108.2 ± 30.5	111.4 ± 42.5
		Post	100	122.1 ± 40.0 *	133.8 ± 59.2 *	127.4 ± 27.6 *	93.4 ± 22.4	80.3 ± 14.7
Area	VM	Pre	100	126.8 ± 54.3	92.8 ± 25.9	120.5 ± 66.9 *	144.7 ± 67.1	105.6 ± 58.0
		Post	100	99.3 ± 53.7	108.2 ± 50.4	119.4 ± 61.3 *	125.1 ± 61.3	98.9 ± 53.0
	VL	Pre	100	112.3 ± 31.7	100.0 ± 38.7	100.8 ± 16.3	87.4 ± 29.0	83.9 ± 30.4 *
		Post	100	109.2 ± 33.9	97.8 ± 39.8	94.0 ± 10.9	83.3 ± 31.1	68.2 ± 42.8 *

* $p < 0.05$, time main effect; ** $p < 0.05$, trial main effect; † $p < 0.05$, trial x time interaction

5.7 Compound muscle activity (M-wave) evoked by quadriceps doublet

5.7.1 M-wave amplitude

The M-wave amplitude at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, amplitude decreased at 80% $\dot{V}O_{2peak}$, EB1 and EB2 and remained depressed at 10 and 30 min recovery for Pre ($P < 0.05$, time main effect; Table 5.7) but increased after exercise at 80% $\dot{V}O_{2peak}$, EB1 and EB2 and during recovery at 10 and 30 min for Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at EB1 and EB2 and during recovery at 10 and 30 min (Table 5.7)

For HIIT, in VL, amplitude decreased after EB1 and during recovery at 10 min for Pre and Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre during recovery at 30 min (Table 5.7).

For CON, in VM, amplitude decreased at 80% $\dot{V}O_{2peak}$, EB1 and EB2 for Pre and Post ($P < 0.05$, time main effect) and during recovery at 30 min for Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at EB1 and EB2 (Table 5.7).

For CON, in VL, amplitude decreased after EB1 for Pre and Post ($P < 0.05$, time main effect; Table 5.7).

5.7.2 M-wave duration

The M-wave duration at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, duration increased after EB1 and EB2 for Pre and Post ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with duration less during Post than Pre at EB1.

For HIIT VL duration, increased after EB1 and EB2 for Pre ($P < 0.05$, time main effect) and decreased after EB2 for Post ($P < 0.05$, time main effect); there was a trial x time interaction ($P < 0.05$), with duration less during Post than Pre at 80% $\dot{V}O_{2peak}$, after EB1 and EB2 and at 10 min recovery (Table 5.7).

For CON, in VL, duration increased after EB1 for Pre ($P < 0.05$, time main effect); there was a trial x time interaction ($P < 0.05$), with duration less during Post than Pre after EB2 and during recovery at 10 min (Table 5.7).

5.7.3 M-wave area

The M-wave area at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, area there was a trial main effect ($P < 0.05$). For HIIT, in VM, area decreased after EB1 and EB2 for Pre ($P < 0.05$, time main effect) and increased at 80% $\dot{V}O_{2peak}$, after EB1 and EB2 for Post ($P < 0.05$, time main effect); there was a time x trial interaction ($P < 0.05$), with area greater during Post than Pre at 80% $\dot{V}O_{2peak}$, EB1 and EB2 and during recovery at 10 and 30 min (Table 5.7)

For HIIT, in VL, area decreased after EB1 and during recovery at 10 min for Pre and Post ($P < 0.05$, time main effect; Table 5.7).

For CON VM and VL there was no trial main effect, time main effect or a trial x time interaction (Table 5.7).

Table 5.7 Doublet Pre and Post-training M-wave measures expressed as a percentage of rest for HIIT and CON

HIIT doublet percentage of pre-exercise								
				Exercise			Recovery	
Measure	Group	Trial	Rest	80% $\dot{V}o_{2peak}$	EB1	EB2	+10 min	+30 min
Amplitude	VM **	Pre	100	77.9 ± 36.3 *	55.8 ± 36.1 *	53.0 ± 34.8 *	73.8 ± 29.0 *	75.3 ± 24.5 *
		Post	100	105.5 ± 65.2 *	114.9 ± 55.4 *†	159.3 ± 75.5 *†	145.3 ± 95.3 *†	135.6 ± 78.1 *†
	VL	Pre	100	102.3 ± 43.9	82.2 ± 29.8 *	76.2 ± 36.8	75.8 ± 18.9 *	77.7 ± 15.9
		Post	100	90.2 ± 25.4	79.7 ± 27.5 *	93.8 ± 30.2	83.2 ± 35.2 *	115.9 ± 45.4 †
Duration	VM	Pre	100	106.1 ± 3.9	111.4 ± 12.7 *	111.6 ± 14.4 *	97.3 ± 8.7	98.5 ± 4.2
		Post	100	105.9 ± 17.4	104.9 ± 16.6 *†	107.5 ± 16.2 *	105.7 ± 8.7	100.6 ± 10.6
	VL	Pre	100	110.3 ± 11.2	118.7 ± 16.7 *	122.5 ± 17.4 *	101.8 ± 4.8	99.3 ± 5.5
		Post	100	97.4 ± 7.6 ¥	100.7 ± 12.6 ¥	95.7 ± 4.4 *¥	92.4 ± 9.0 ¥	95.1 ± 12.2
Area	VM **	Pre	100	77.9 ± 17.9	52.7 ± 18.4 *	54.1 ± 14.3 *	74.8 ± 36.7	77.1 ± 29.5
		Post	100	125.3 ± 63.1 †*	106.2 ± 66.4 *†	128.4 ± 51.5 *†	101.3 ± 40.5 †	110.2 ± 52.5 †
	VL	Pre	100	95.0 ± 28.5	84.4 ± 28.8 *	87.0 ± 47.0	80.5 ± 20.4 *	81.7 ± 14.5
		Post	100	93.8 ± 17.9	77.9 ± 33.2 *	93.9 ± 28.6	74.1 ± 29.0 *	92.4 ± 19.7
CON doublet percentage of pre-exercise								
Amplitude	VM	Pre	100	70.1 ± 21.0 *	59.4 ± 21.6 *	64.4 ± 33.0 *	87.0 ± 33.6	88.6 ± 17.8
		Post	100	90.9 ± 28.9 *	88.9 ± 24.7 *†	92.9 ± 37.5 *†	100.8 ± 43.5	87.7 ± 25.9 *
	VL	Pre	100	90.3 ± 37.9	82.0 ± 38.9 *	94.0 ± 37.5	88.9 ± 28.5	92.4 ± 16.3
		Post	100	97.3 ± 33.2	84.4 ± 38.0 *	75.2 ± 45.5	96.7 ± 32.9	74.9 ± 54.0
Duration	VM	Pre	100	111.4 ± 9.1	106.6 ± 8.2	106.0 ± 7.6	101.7 ± 7.6	100.1 ± 9.4
		Post	100	106.0 ± 17.4	104.9 ± 16.6	107.5 ± 16.2	105.7 ± 8.7	100.6 ± 10.6
	VL	Pre	100	110.3 ± 10.4	109.8 ± 7.3 *	113.8 ± 6.7	102.5 ± 6.7	104.5 ± 5.9
		Post	100	100.9 ± 4.3	106.6 ± 10.2	89.4 ± 37.9 †	97.0 ± 13.6 †	76.4 ± 48.2
Area	VM	Pre	100	95.0 ± 28.5	83.0 ± 29.1	94.8 ± 51.8	86.9 ± 45.9	91.3 ± 43.0
		Post	100	110.3 ± 57.7	104.6 ± 33.8	146.4 ± 56.0	131.2 ± 54.0	71.7 ± 43.4
	VL	Pre	100	105.8 ± 24.9	96.9 ± 18.4	94.5 ± 34.8	82.7 ± 20.3	103.9 ± 17.3
		Post	100	111.4 ± 17.9	99.0 ± 21.9	75.2 ± 41.0	98.5 ± 14.7	69.9 ± 44.1

* $p < 0.05$, time main effect; ** $p < 0.05$, trial main effect; † $p < 0.05$, trial x time interaction

5.8 Compound muscle activity (M-wave) evoked by quadriceps 20 Hz tetani

5.8.1 M-wave amplitude

The M-wave amplitude at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, there was a trial main effect ($P < 0.05$).

The HIIT, in VM, amplitude decreased at 80% $\dot{V}O_{2peak}$, EB1, EB2 and remained depressed at 10 min recovery for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at EB1 and EB2 and during recovery at 10 min (Table 5.8).

For HIIT, in VL, there was a trial main effect ($P < 0.05$); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at EB1 and EB2 and during recovery at 10 min (Table 5.8).

For CON, in VM, amplitude decreased at 80% $\dot{V}O_{2peak}$, EB1 and EB2 and remained depressed at 30 min recovery for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with amplitude greater during Post than Pre at EB1 and EB2 and during recovery at 10 min (Table 5.8).

5.8.2 M-wave duration

The M-wave duration at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, duration increased after EB1 and EB2 for Pre ($P < 0.05$, time main effect,); there was a significant trial x time interaction ($P < 0.05$), with duration less for Post than Pre at EB2 (Table 5.8).

For HIIT, in VL, duration increased after exercise at EB1 and EB2 for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with duration less during Post than Pre at EB2 (Table 5.8).

For CON, in VM, duration increased after EB1 and EB2 for Pre ($P < 0.05$, time main effect).

For CON, VL, duration increased after EB1 and EB2 for Pre ($P < 0.05$, time main effect), there was a significant trial x time interaction ($P < 0.05$), with duration during Post less than Pre at EB2 (Table 5.8).

5.8.3 M-wave area

The M-wave duration at rest did not differ significantly between Pre or Post for VM or VL muscles for HIIT and CON. Changes in all M-wave variables with exercise and recovery were expressed as a percentage of Pre-exercise values.

For HIIT, in VM, area decreased at 80% $\dot{V}O_{2peak}$, EB1, EB2 and remained depressed during recovery at 10 min for Pre ($P < 0.05$, time main effect). For HIIT VM area, there was a trial main effect ($P < 0.05$), with area during Post greater than Pre (Table 5.8). There was a significant time x trial interaction ($P < 0.05$), with area during Post greater than Pre at 80% $\dot{V}O_{2peak}$, EB1, EB2 and during recovery at 10 min (Table 5.8).

For HIIT VL, there was a trial main effect ($P < 0.05$). For HIIT, in VL, area decreased at 80% $\dot{V}O_{2peak}$, and EB2 for Pre ($P < 0.05$, time main effect); there was a significant trial x time interaction ($P < 0.05$), with area during Post greater than Pre at 80% $\dot{V}O_{2peak}$, after EB1 and EB2 and during recovery at 10 min.

For CON, in VM, area decreased after EB1 and EB2 for Pre ($P < 0.05$, time main effect); there was a significant time x trial interaction ($P < 0.05$), with area during Post greater than Pre at 80% $\dot{V}O_{2peak}$, after EB1 and EB2 and during recovery at 10 and 30 min (Table 5.8).

For CON, in VL, area decreased after EB1 and EB2 for Pre ($P < 0.05$, time main effect).

Table 5.8 20Hz tetani Pre and Post-training M-wave measures expressed as a percentage of rest for HIIT and CON

HIIT tetani percentage of pre-exercise								
				Exercise			Recovery	
Measure	Group	Trial	Rest	80% $\dot{V}o_{2peak}$	EB1	EB2	+10 min	+30 min
Amplitude	VM **	Pre	100	50.3 ± 22.8 *	39.6 ± 19.7 *	32.1 ± 18.2 *	64.6 ± 17.4 *	73.6 ± 26.3
		Post	100	94.9 ± 37.3 †	122.1 ± 39.3 †	95.9 ± 44.3 †	169.5 ± 45.6 †	124.8 ± 91.4
	VL**	Pre	100	70.9 ± 13.8	56.1 ± 14.1	49.8 ± 19.6	65.8 ± 23.7	79.2 ± 8.9
		Post	100	87.1 ± 27.6	112.9 ± 43.9 †	87.3 ± 27.4 †	103.9 ± 12.7 †	101.2 ± 54.5
Duration	VM	Pre	100	109.5 ± 5.8	114.1 ± 6.0 *	114.5 ± 8.7 *	97.8 ± 10.2	94.1 ± 9.5
		Post	100	98.0 ± 17.9	104.3 ± 20.5	72.1 ± 45.8 †	69.6 ± 43.2	80.7 ± 34.4
	VL	Pre	100	112.2 ± 7.7	115.2 ± 12.2 *	115.8 ± 13.4 *	99.6 ± 8.0	96.8 ± 11.2
		Post	100	104.9 ± 18.0	105.5 ± 18.7	100.5 ± 11.5 †	99.2 ± 7.5	81.0 ± 33.9
Area	VM **	Pre	100	47.9 ± 21.8 *	39.6 ± 18.1 *	35.4 ± 20.1 *	70.0 ± 41.2 *	95.0 ± 62.6
		Post	100	106.0 ± 45.3 †	165.9 ± 81.6 †	243.3 ± 155.7 †	131.9 ± 69.4 †	116.9 ± 88.1 †
	VL **	Pre	100	64.6 ± 19.2 *	54.8 ± 15.8	51.3 ± 17.8 *	68.5 ± 23.2	77.0 ± 15.6
		Post	100	95.7 ± 32.2 †	126.9 ± 72.8 †	94.1 ± 32.0 †	95.9 ± 11.2 †	105.9 ± 34.3
CON tetani percentage of pre-exercise								
Amplitude	VM	Pre	100	71.3 ± 20.9 *	46.0 ± 19.3 *	42.9 ± 21.3 *	63.3 ± 25.3	74.7 ± 16.2 *
		Post	100	73.8 ± 35.5	74.1 ± 37.5 †	68.3 ± 16.0 †	104.0 ± 38.6 †	75.2 ± 78.6
	VL	Pre	100	81.6 ± 4.7	68.1 ± 15.1	52.2 ± 12.5	72.1 ± 9.2	98.3 ± 35.5
		Post	100	79.4 ± 27.4	78.1 ± 37.0	74.8 ± 25.6	78.8 ± 41.1	46.2 ± 40.5
Duration	VM	Pre	100	109.2 ± 10.1	114.3 ± 15.6 *	112.8 ± 13.4 *	104.0 ± 12.4	102.6 ± 8.3
		Post	100	100.3 ± 1.5	102.8 ± 12.2	104.1 ± 8.4	99.3 ± 9.1	99.6 ± 9.5
	VL	Pre	100	102.9 ± 13.0	102.9 ± 13.3 *	107.0 ± 17.0 *	101.1 ± 12.3	93.6 ± 7.1
		Post	100	103.4 ± 18.7	102.1 ± 12.3	104.7 ± 7.6 †	100.7 ± 10.9	81.0 ± 41.4
Area	VM	Pre	100	78.4 ± 39.8	59.2 ± 40.7 *	51.0 ± 35.0 *	62.6 ± 30.8	79.6 ± 31.0
		Post	100	102.4 ± 53.4 †	100.5 ± 54.5 †	111.0 ± 92.0 †	115.2 ± 35.9 †	128.9 ± 88.4 †
	VL	Pre	100	94.5 ± 22.1	86.6 ± 34.3 *	78.5 ± 28.1 *	94.5 ± 23.7	91.6 ± 19.8
		Post	100	82.5 ± 36.1	83.6 ± 30.5	92.5 ± 16.9	87.5 ± 31.3	70.5 ± 33.6

* $p < 0.05$, time main effect; ** $p < 0.05$, trial main effect; † $p < 0.05$, trial x time interaction

5.9 DISCUSSION

This study explored whether HIIT would enhance K^+ regulation during matched, submaximal exercise, as well as during repeated 30 s sprints and whether this occurred along with enhanced sprint performance and reduced fatigue effects on quadriceps muscle voluntary and evoked contractions and accompanying M-waves. The main findings regarding K^+ regulation were that HIIT reduced arterial $[K^+]$ and $\Delta[K^+]_a$ during 80% $\dot{V}O_{2peak}$ cycling exercise, when power output was matched before and after training; also that $[K^+]_a$ was less at 1 min in recovery after the second 30 s sprint bout. Interestingly, the $[K^+]_a$ and $\Delta[K^+]_a$ during the two 30s sprints did not differ after training. A surprising finding was that HIIT did not increase sprint performance, with no significant increases after HIIT in Peak Power (9%, NS) or Total Work (4%, NS); thus the $\Delta[K^+]$ $work^{-1}$ ratio was also unchanged after HIIT. This improved K^+ regulation during submaximal exercise and at1 min after sprint exercise after HIIT, is possibly mediated through a greater Na^+, K^+-ATPase activity in the active muscles. A larger re-uptake of K^+ by inactive muscle seems unlikely since HIIT did not affect the arterio-venous $[K^+]$ difference across the inactive forearm muscle. The intense exercise did produce clear fatigue effects, with depressed muscle torque after each exercise bout for voluntary (MVC) and evoked contractions (twitch, doublet, 20Hz). These changes were, however, unchanged by HIIT. Following fatiguing high intensity interval sprint exercise, M-wave amplitude and area declined, whereas duration increased. The lack of effect of HIIT on measures of muscle function and excitability probably reflects the limited effects of training on sprint exercise performance and circulating $[K^+]$; these data are also consistent with $[K^+]$ being tightly regulated during exercise, before as well as after training.

5.9.1 Decreased circulating K^+ after HIIT

An important finding was that $[K^+]_a$ decreased by ~0.46 mmol.1^{-1} during exercise at 80% $\dot{V}O_{2peak}$ after HIIT, with no differences found between Pre and Post measures in CON. This finding that HIIT improves K^+ regulation is consistent with conclusions from previous sprint training studies in humans (McKenna, Schmidt et al. 1993, McKenna, Heigenhauser et al. 1997, Harmer, McKenna et al. 2000, Nielsen, Mohr et al. 2004). In contrast to this submaximal exercise finding, HIIT did not affect the $[K^+]$ responses during the two 30 s maximal sprint efforts. Similarly, the $\Delta[K^+]$/work ratio didn't differ after training. The underlying mechanisms for the small reduction in $[K^+]_a$ at 80% $\dot{V}O_{2peak}$ and at 1 min after sprint exercise after HIIT are likely due to reduced release of K^+ from contracting and previously contracted skeletal muscles . Hence, it may be speculated that HIIT might also have reduced the interstitial $[K^+]$ in contracting skeletal muscle at these times during cycling exercise and recovery. If so, this would most likely occur through a larger cellular K^+ re-uptake due to increased muscle Na^+,K^+-ATPase activity. This would be consistent with the finding that intense intermittent training reduced the interstitial potassium ($[K^+]_I$) during knee extensor exercise (Nielsen, Mohr et al. 2004). It is unlikely that these findings were due to increased K^+ removal by inactive skeletal muscle, since there were no clear effects of training on the arterio-venous $[K^+]$ difference across the inactive forearm muscles. A possible explanation for the lesser increase in $[K^+]$ following HIIT is an increase in Na^+,K^+-ATPase as reported earlier with this training regime (McKenna, Schmidt et al. 1993, Harmer, McKenna et al. 2000). However, in the participants in this HIIT study, neither the Na^+,K^+-ATPase content ($[^3H]$ouabain binding site content), nor the Na^+,K^+-ATPase α_1, α_2, β_1 and β_2 isoform protein abundances were elevated after HIIT (Altarawneh *et al*., Unpublished findings). The reason for this lack of adaptation in muscle Na^+,K^+-ATPase is unclear, but is consistent with the non-significant changes in power output and total work performed during intense cycling bouts in the present study. It remains possible that an

increased Na^+,K^+-ATPase activity in-vivo might underlie the lower plasma $[K^+]_a$ at 1 min post-exercise following HIIT.

Although there was a rapid rise in plasma $[K^+]$ during exercise, indicating the loss of K^+ from the contracting muscle (Sjøgaard, Adams et al. 1985, Medbo and Sejersted 1990), and a rapid decline in plasma $[K^+]$ during recovery, indicating K^+ removal by tissues, including active and inactive muscle, there were very few differences after HIIT (or within CON between Pre and Post measures). Muscle contractions increase $[K^+]_I$ which have been shown to impair muscle force development in isolated muscles (Nielsen, Mohr et al. 2004, Nielsen and de Paoli 2007, Cairns and Lindinger 2008), although this effect is primarily countered by an increase in the muscle Na^+,K^+-ATPase activity (Sejersted and Sjøgaard 2000). Nielsen, Mohr et al (2004b) found that one-legged knee extensor HIIT for 7 weeks reduced $[K^+]_I$ during exercise; this was associated with a delayed fatigue during intense exercise and suggested interstitial K^+ is involved in the development of fatigue (Nielsen, Mohr et al. 2004). Furthermore, interstitial $[K^+]$ was considerably higher than arterial and venous plasma $[K^+]$ at similar work intensities (Juel, Pilegaard et al. 2000) However, possible training effects on $[K^+]_I$, where K^+ may exert its detrimental effects, cannot be determined from this study .

5.9.2 No Effect of HIIT on power or work output

A surprising finding was that measures of peak power, work and fatigue index during 30 s all-out exercise bouts all showed no significant improvements after HIIT. The lack of change in peak power output after HIIT is contrary to other studies where mean and peak power and work output typically increased and fatigability reduced, in sprint interval training group (Sjøgaard 1991, McKenna 1992, McKenna, Schmidt et al. 1993, Burgomaster, Howarth et al. 2008), although is consistent with one earlier finding (Nalcakan 2014). The lack of upregulation of

muscle Na^+,K^+-ATPase content in these participants may be an important factor in explaining the lack of increase in peak and mean power outputs after HIIT.

Furthermore, K^+ handling is likely to be of importance for maintaining sarcolemmal excitability during muscle contractions and any system that counteracts accumulation of extracellular K^+ may enhance muscle performance and delay the onset of fatigue during intense exercise. The accumulation of metabolites and ions in muscle interstitium stimulates sensory feedback from group III/IV muscle afferents to the central nervous system, thus causing muscle discomfort (Pollak, Swenson et al. 2014) and provide a regulatory input for motor command centres (Amann, Blain et al. 2011). Maintenance of ion homeostasis is thus essential to sustain force production and power output during intense exercise.

Although the intense exercise of the present study caused marked metabolic or ionic perturbations (Ca^{2+}, Cl^-, H^+, K^+, $lactate^-$, Na^+ and P_i), the combined effects of any changes in these after training on excitation–contraction coupling of skeletal muscle, or mechanical efficiency may not have been sufficient to significantly impair muscle performance and muscle fatigue.

A limitation of the present study may have been that the small sample size for both HIIT and CON contributed to the failed detection of differences due to a low statistical power. However, beneficial performance effects were reported in previous studies using this training regime with similar sample size (McKenna, Schmidt et al. 1993, Harmer, McKenna et al. 2000). It is difficult to explain this lack of adaptation as participants were all highly motivated and were strongly encouraged in an effort to maximise performance. Compliance rates were high with all participants completing, 100% (21 ± 0), all HIIT sessions.

5.9.3 Effects of Intense exercise and HIIT on MVC and evoked muscle torque

Previous studies have demonstrated that an extracellular [K^+] up to 8 mM was associated with small reductions of 10–20% in force, whilst 10 and 12.5 mM K^+ resulted in force decrements of up to 25–75% and 60–100%, respectively (Nielsen, Hilsted et al. 1998). The findings of interstitial [K^+] greater than 10 mM during intense contractions (Juel, Pilegaard et al. 2000), suggest that similar depressive effects of elevated K^+ may have impaired torque development (Juel, Pilegaard et al. 2000). Consistent with this, fatiguing exercise decreased torque during an MVC as well as for Q_{twpot}, doublet and 20 Hz contractions. An expected finding was that the MVC was depressed at the end of the intense exercise bouts (HIIT, -12% and CON, -35%), following HIIT. Further, the reduction in twitch torque after exercise was considerably greater (HIIT, -49% and CON, -36%), similar to previous chapters.

An interesting finding was that HIIT did not affect the post-exercise MVC, potentiated $Q_{tw,}$ Doublet and 20 Hz tetani values, expressed as a percentage of pre-exercise values. This occurred despite the lower $[K^+]_a$ during exercise for Post compared to Pre-train in HIIT. One possible explanation is that HIIT failed to enhance work output during the sprint bouts and thus the response to the acute fatigue stimulus was unchanged with training. Alternately, the variability in the measurements, coupled with the low sample size meant that possible effects may have been missed. Whilst positive adaptations in performance in earlier sprint training studies (McKenna, Schmidt et al. 1993, Harmer, McKenna et al. 2000, Harmer, Ruell et al. 2006) it is reasonable to suggest HIIT may have contributed to the lower decline in muscle performance, however this was not the case here, as there was no training effect on fatigue.

Whilst peripheral fatigue may be the main factor determining exercise performance during brief very intense exercise where disturbances of muscle ionic and metabolic homeostasis are prominent (McKenna, Bangsbo et al. 2008), many factors might be responsible for training-induced improvements in exercise performances. As described (Gibala, Little et al. 2006), these

are particularly "*complex and determined by numerous physiological (e.g. cardiovascular, muscle metabolic, neural, respiratory, thermoregulatory) and psychological attributes (e.g. mood, motivation, perception of effort)*". Hence, as there was no improvement in performance, it is not possible from this study to draw conclusions on the potential importance of a link between K^+, fatigue and muscle torque generation in humans.

5.9.4 Muscle excitability (M-wave) following HIIT

Interestingly, the M-wave duration and area characteristics were perturbed with fatigue, and consistent with previous chapters and other findings (Bigland-Ritchie, Furbush et al. 1986, Garland and McComas 1990, Behm and St-Pierre 1997, Enoka and Duchateau 2008, Allen, Lamb et al. 2008a). During Pre, the M-wave associated with twitch in VM showed depressed amplitude, elongated duration and depressed area following sprint bouts; in VL amplitude was also depressed and duration elongated. These changes are consistent with possibility that skeletal muscle (i.e., sarcolemmal or t-tubular) excitability may be impaired, leading to the development of fatigue. It was anticipated that after fatiguing exercise there would be a decrease in M-wave amplitude and area, with an increase in duration reflecting slowing conduction rates that would also counteract the decrease in area. The increases in $[K^+]$ and changes in M-wave amplitude here, together with the acute decline in power output during intermittent sprint exercise, demonstrates that peripheral mechanisms may be the predominant cause of fatigue, consistent with previous observations (Clausen 2011, Bishop 2012). A possible explanation is that a depolarisation is likely to occur during exercise (Nielsen, Hilsted et al. 1998), with activation of the Na^+,K^+-ATPase to counteract the depolarisation as a result of high interstitial K^+ (Nielsen, Hilsted et al. 1998). The depolarisation probably causes a combined effect of a reduced Ca^{2+} release due to action potential depression and a complete loss of excitability in some fibres (Cairns, Hing et al. 1997). Large $[K^+]_a$ during intense

exercise, probably is associated also with large increases in interstitial [K^+], suggests elevated K^+ is likely to have an impact on Ca^{2+} release and torque development. These findings of depressive effects of exercise on M-wave characteristics differs from findings in a previous study which reported, that after voluntary isometric exercise, with plasma [K^+] increased, there was no loss of muscle excitability or torque, whilst the M-waves were potentiated early in the recovery phase (West 1996, Fowles, Green et al. 2002). This may reflect different effects between isometric and dynamic contractions possibly due to the differential effects on mechanical and physiological properties of skeletal muscle.

Findings from the present study for each of the Q_{twpot}, doublet and 20 Hz tetani were that M-wave amplitude and area for VM declined less and duration increased less for HIIT, Post compared to Pre. Similarly, M-wave area decreased less for Post to Pre during recovery for HIIT in VM and VL. These findings point to the possibility of better preservation of M-waves after training. However, results were variable and with some inconsistencies across times and between the two muscles studied. It is likely that these peripheral mechanisms are responsible with tendency for improved maintenance of muscle M-waves after HIIT. These could reflect increased activity of Na^+,K^+-ATPase, attenuating disturbances of Na^+,K^+ gradients in active skeletal muscle cells, and thereby contributing to the maintenance of excitability during intense exercise.

5.9.5 Conclusions

Following HIIT, consisting of repeated 30 s all out cycling efforts, $[K^+]_a$ regulation was increased, evidenced by lower $[K^+]_a$ during submaximal exercise and early post-sprint recovery. However, after HIIT there were no significant improvements in sprint exercise performance, during either two maximal sprint bouts, or during the training itself. Furthermore, whilst acute exercise depressed quadriceps muscle voluntary and evoked contractions, these

changes were not attenuated after HIIT. The results did show a greater recovery of torque after HIIT for the doublet, but this was not consistent with the other evoked torque measures. These measures of MVC and evoked muscle torque were, however variable. Following fatiguing intermittent sprint exercise, there were declines in M-wave amplitude and area and an elongation of duration. After HIIT, findings of lesser effects of fatigue on M-wave characteristics in VM suggest a possible preservation of excitability and a greater recovery of M-wave amplitude, which may indicate some improvements with training. However, these findings also varied across contraction times and muscles. A possible greater recovery of excitability would be a useful adaptive strategy for repeated contractions. Further studies are required to investigate this possibility. However, this would not seem to have major implications for performance during cycling and isometric quadriceps contractions, as this was not improved in these participants after HIIT.

CHAPTER 6
GENERAL DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

This thesis investigated K^+ regulation during and following high-intensity cycling and the effects of contracting skeletal muscle mass, acute oral digoxin treatment and high-intensity interval training (HIIT) on K^+ regulation and fatigue. The effects of elevated K^+ on skeletal muscle excitability and contractile function during and after high-intensity cycling are of considerable interest, as the impaired propagation of action potentials along the sarcolemma and throughout the t-tubular network may exacerbate fatigue and contribute to reduced exercise performance.

6.1 General discussion

6.1.1 Regulation of $[K^+]$ during and following exercise

6.1.1.1 Arterial $[K^+]$ during and following exercise

Arterial plasma $[K^+]$ increased markedly during exercise in all three studies (Chapters 3, 4 and 5), reaching ~6 mM during intense exercise; although this peak was moderate when compared to the extremely high $[K^+]$ of ~9-14 mM achieved in muscle interstitial spaces during intense contractions (Juel, Pilegaard et al. 2000, Nordsborg, Mohr et al. 2003). This plasma $[K^+]_a$ was therefore consistent with expectations that this would typically be 3-6 mM lower than in muscle interstitium during intense contractions (Green S, Langberg H et al. 2000, Nielsen, Mohr et al. 2004). Hence, with a $[K^+]_a$ of ~ 6 mM, muscle interstitial $[K^+]$ was probably substantially increased, similarly to as much as 9-14 mM; whilst the exact $[K^+]_I$ is unknown, it was probably close to a level considered potentially important in the development of fatigue (Cairns, Leader et al. 2011), for all three studies.

Overall, exercising with a large contracting muscle mass (2L), acute digoxin administration and HIIT each modulated systemic $[K^+]_a$, compared to their control or alternate group. The $[K^+]_a$ results are fully detailed in previous chapters and the exercise main effects are summarised here. Plasma $[K^+]_a$ increased throughout exercise from ~3.9 mM at rest reaching ~6.1 and ~5.6 mM at fatigue, for 2L and 1L, respectively ($P < 0.05$). For digoxin and Placebo, $[K^+]_a$ increased during exercise from ~3.9 mM rest to ~6.5 and ~6.6 mM at fatigue, respectively ($P < 0.05$). Pre- and post-HIIT, plasma $[K^+]_a$ increased from ~3.9 mM at rest to ~5.1 and ~5.2 mM at fatigue, respectively ($P < 0.05$). Thus plasma $[K^+]$ was substantially increased during exercise, with elevations in plasma $[K^+]$ during 2L compared to 1L cycling, and in digoxin compared to placebo ($P < 0.05$, treatment main effect), with lower $[K^+]_a$ in post- compared to pre-HIIT ($P < 0.05$, trial x time interaction).

A simple plot of the peak rise in $[K^+]_a$ during exercise ($\Delta[K^+]_a$) shows the absolute rise and the effects of these interventions during exercise (Figure 6.1); there were no differences in $\Delta[K^+]_a$ between interventions. The source of this rapid increase in plasma $[K^+]_a$ is K^+ released from the intracellular to extracellular space of contracting skeletal muscle, then diffusing into the venous effluent and eventually being mixed centrally before being recirculated via arterial blood pumped to the peripheral arteries. The increase in $[K^+]_a$ also corresponds to increased exercise intensity (Hallen 1996), but is modulated by cellular K^+ reuptake due to increased skeletal muscle Na^+,K^+-ATPase activity (Medbo and Sejersted 1990, Verburg, Hallén et al. 1999). Therefore, it is likely that intense-exercise leads to a greater uptake of K^+, caused by an increase in Na^+,K^+-ATPase activity, both in previously active and inactive muscles, as well as in other tissues (McKenna, Heigenhauser et al. 1997, Sejersted and Sjøgaard 2000, Nielsen, Mohr et al. 2004, Cairns, Inman et al. 2017).

During early recovery, there was a rapid fall in plasma [K^+] from peak exercise values in each study. The exercise main effects are summarised here. Plasma $[K^+]_a$ decreased from peak exercise to early recovery; with the peak values at the end of exercise versus the lowest measure during recovery for each of the trials, being from ~6.1 to ~3.9 mM for 2L and from ~5.6 to ~4.1 mM for 1L ($P < 0.05$, time main effect). For digoxin and Placebo, the decrease from peak exercise to early recovery was ~6.6 to ~3.6 mM and from ~6.6 to ~3.5 mM, respectively ($P < 0.05$, time main effect). For Pre- and Post-HIIT, plasma $[K^+]_a$ decreased from peak exercise to early recovery was from ~5.6 to ~3.9 mM and ~5.3 to ~3.8 mM, respectively ($P < 0.05$, time main effect).

Plotting the post-exercise decline in $[K^+]_a$ during exercise ($\Delta[K^+]_a$) shows declines ranging between ~1.5 - 3 mM (Figure 6.2) and shows the effects of these interventions. For 2L and post-HIIT, the decline in $[K^+]_a$ was greater whereas for digoxin this was less compared to their alternate groups ($P<0.05$), which is consistent with the post-exercise decline rate likely being proportional to both the magnitude of the active muscle mass and the exercise intensity (Nielsen and de Paoli 2007). This post-exercise decline rate is likely influenced by the adrenergic system, which becomes increasingly active during high-intensity exercise, and is augmented with a larger muscle mass than with a smaller muscle mass (Hallen, Saltin et al. 1996). Catecholamines are known to regulate K^+ distribution, with α-adrenergic receptors impairing and β-adrenergic receptors stimulating cellular entry of K^+, whilst β_2-Receptor–induces stimulation of K^+ uptake is mediated by activation of the Na^+,K^+-ATPase. Hence these effects are important in regulating the muscle cell release of K^+ during exercise (Williams, Gervino et al. 1985), therefore enhancing net K^+ clearance during recovery (Figure 6.2). Decreasing the net loss of K^+ from the muscle cells and/or increasing the removal of K^+ from the interstitium might be anticipated to delay the onset of fatigue, as proposed to occur after HIIT. Conversely, worsening these might be anticipated to exacerbate fatigue during exercise

as proposed with a large muscle mass or acute digoxin intervention.

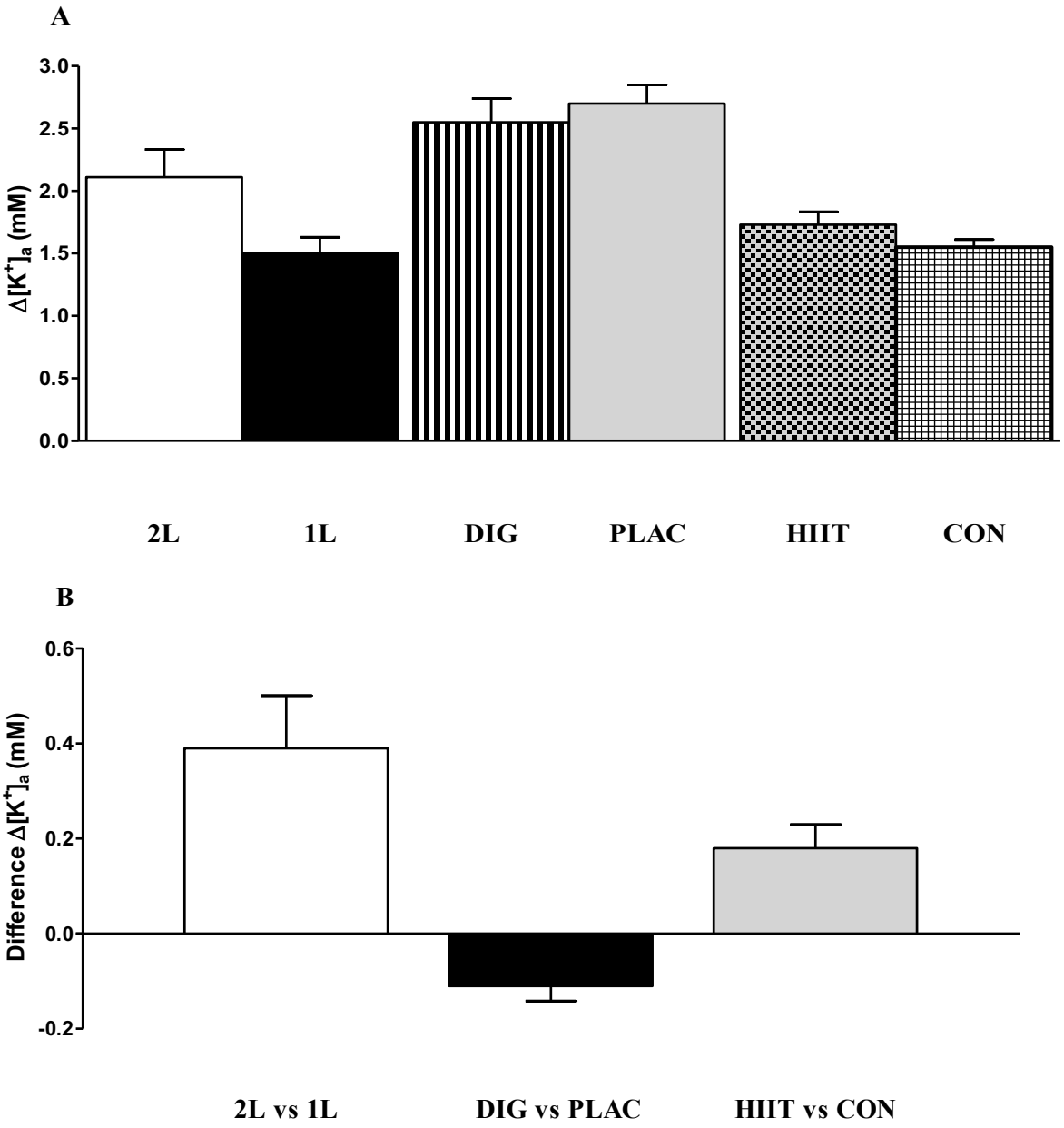

Figure 6.1 The rise in $[K^+]_a$ during exercise ($\Delta[K^+]_a$)(A) defined as the peak $[K^+]_a$ during exercise minus the baseline measure during each of the trials and (B) the difference in $\Delta[K^+]_a$ between trials within an intervention (2L minus 1L, n=10, Chapter 3; DIG minus PLAC, n=10, Chapter 4; and HIIT minus CON, n=8, Chapter 5). Data presented as $\pm$ SD.

Abbreviations: 2L, two leg; 1L, single leg; DIG, digoxin; PLAC, placebo; HIIT, High-Intensity Interval Training; CON, Control

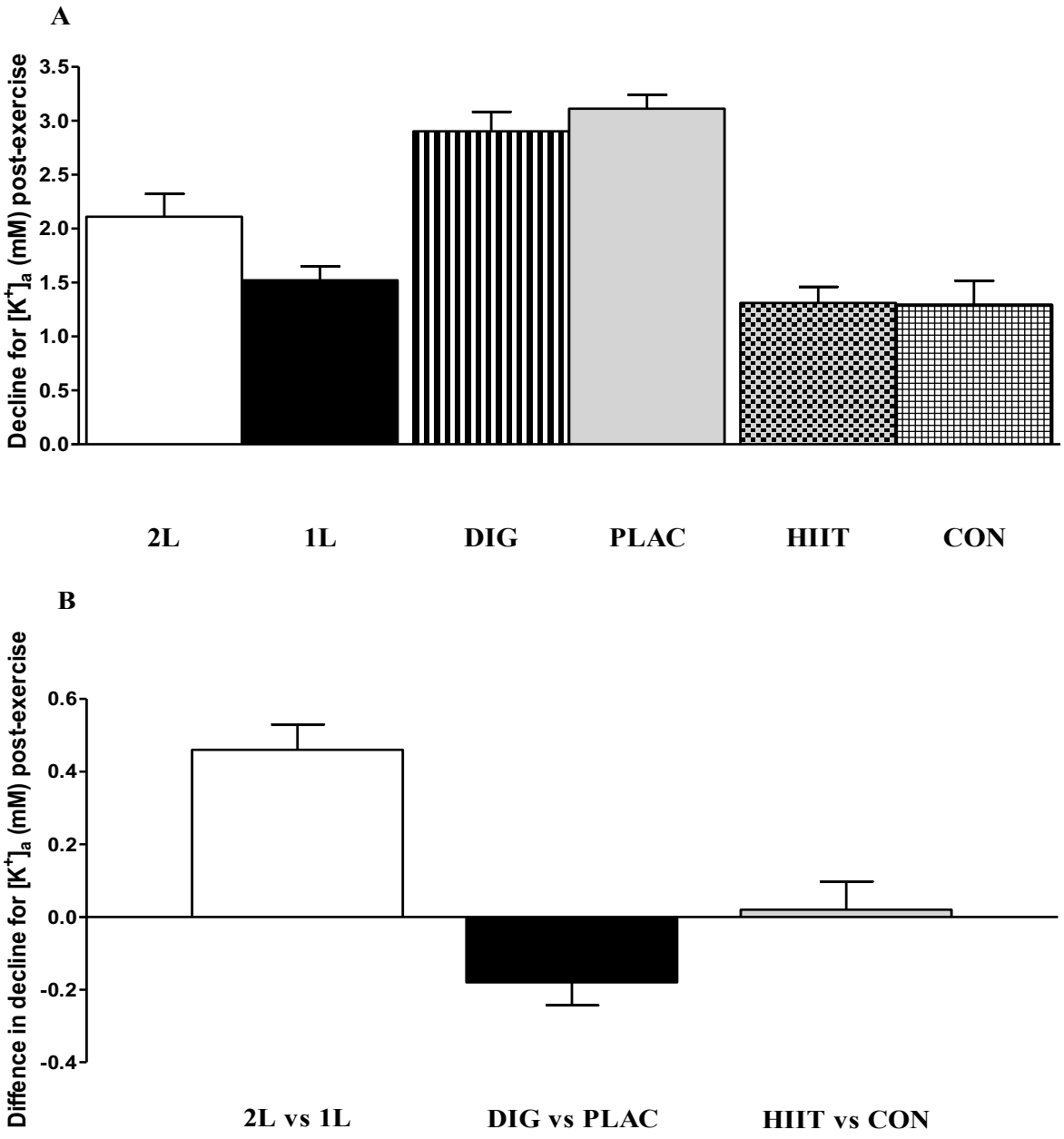

Figure 6.2 The decline in $[K^+]_a$ post-exercise (A) defined as the $[K^+]_a$ measure at the end of exercise minus the lowest measure during recovery for each of the trials and (B) the difference in decline for $[K^+]_a$ between interventions (2L minus 1L, n=10, Chapter 3; DIG minus PLAC, n=10, Chapter 4; and HIIT minus CON, n=8, Chapter 5). Data presented as $\pm$ SD.

6.2.2 Venous [K^+] and the arterio-venous [K^+] difference during and following exercise

During leg cycling exercise, the $[K^+]_{a-v}$ difference across the inactive forearm was higher than rest throughout exercise to fatigue ($P < 0.05$, time main effect, Study 1), suggesting increased K^+ uptake by inactive muscle, probably via activation of muscle Na^+,K^+-ATPase. The $[K^+]_{a-v}$ difference across the forearm was also greater in 2L than 1L ($P < 0.05$, treatment main effect). This also suggests greater K^+ uptake by inactive muscle when exercising with a larger muscle mass as in 2L cycling. For both HIIT and CON (Study 3), the $[K^+]_{a-v}$ difference across the forearm increased with submaximal and sprint exercise ($P < 0.05$, time main effect), although $[K^+]_{a-v}$ did not differ between trials.

The antecubital venous plasma [K^+] ($[K^+]_v$) and the arterio-venous [K^+] difference ($[K^+]_{a-v}$) increased during exercise and decreased during recovery, indicated by plots of the delta values from rest to peak exercise, or from peak exercise to lowest point in recovery (Figures 6.3-6.5). It can be seen that the $\Delta[K^+]_v$ was substantially less than the $\Delta[K^+]_a$, being only ~ ¼ to ~½, with the positive $[K^+]_{a-v}$ indicating net uptake into the inactive forearm muscles. This involvement of inactive muscle in K^+ regulation, together with the known K^+ release from contracting muscles (Nielsen and de Paoli 2007, McKenna, Bangsbo et al. 2008), suggests that the amount of active muscle mass may directly affect both muscle K^+ release and inactive muscle K^+ clearance during exercise. It is likely the net reuptake of K^+ into the forearm muscles was due to an increase in Na^+,K^+-ATPase activity, thus ablating increases in circulating [K^+] due to K^+ loss from exercising muscles (Lindinger 1995a). It is also likely that circulating catecholamines induced by intense exercise stimulated the Na^+,K^+-ATPase in skeletal muscle, thus attenuating the accumulation in the muscle interstitial [K^+] and the resulting detrimental effects of elevated K^+ membrane excitability. However, the $[K^+]_{a-v}$ alone does not determine K^+ release or uptake, which is the product of blood flow and the $[K^+]_{a-v}$ difference. Therefore,

any differences in flow will also influence the interpretation. Forearm blood flow was not measured in this thesis and so no conclusions can be drawn on this.

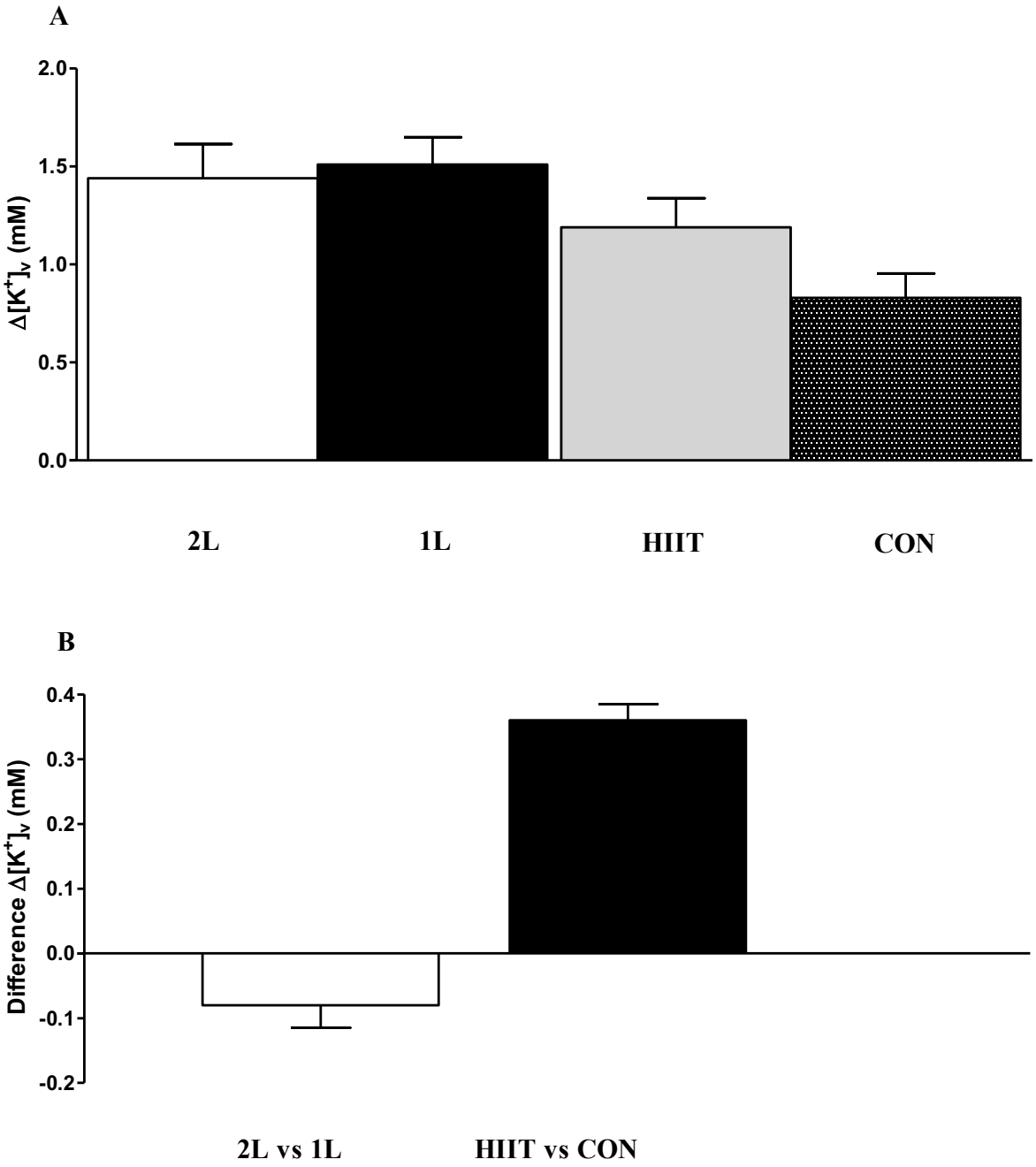

Figure 6.3 The rise in $[K^+]_v$ during exercise ($\Delta[K^+]_v$)(A) defined as the peak $[K^+]_v$ during exercise minus the baseline measure during each of the trials and (B) the difference in $\Delta[K^+]_v$ between interventions (2L minus 1L, n=10, Chapter 3; and HIIT minus CON, n=8, Chapter 5). Data presented as $\pm$ SD.

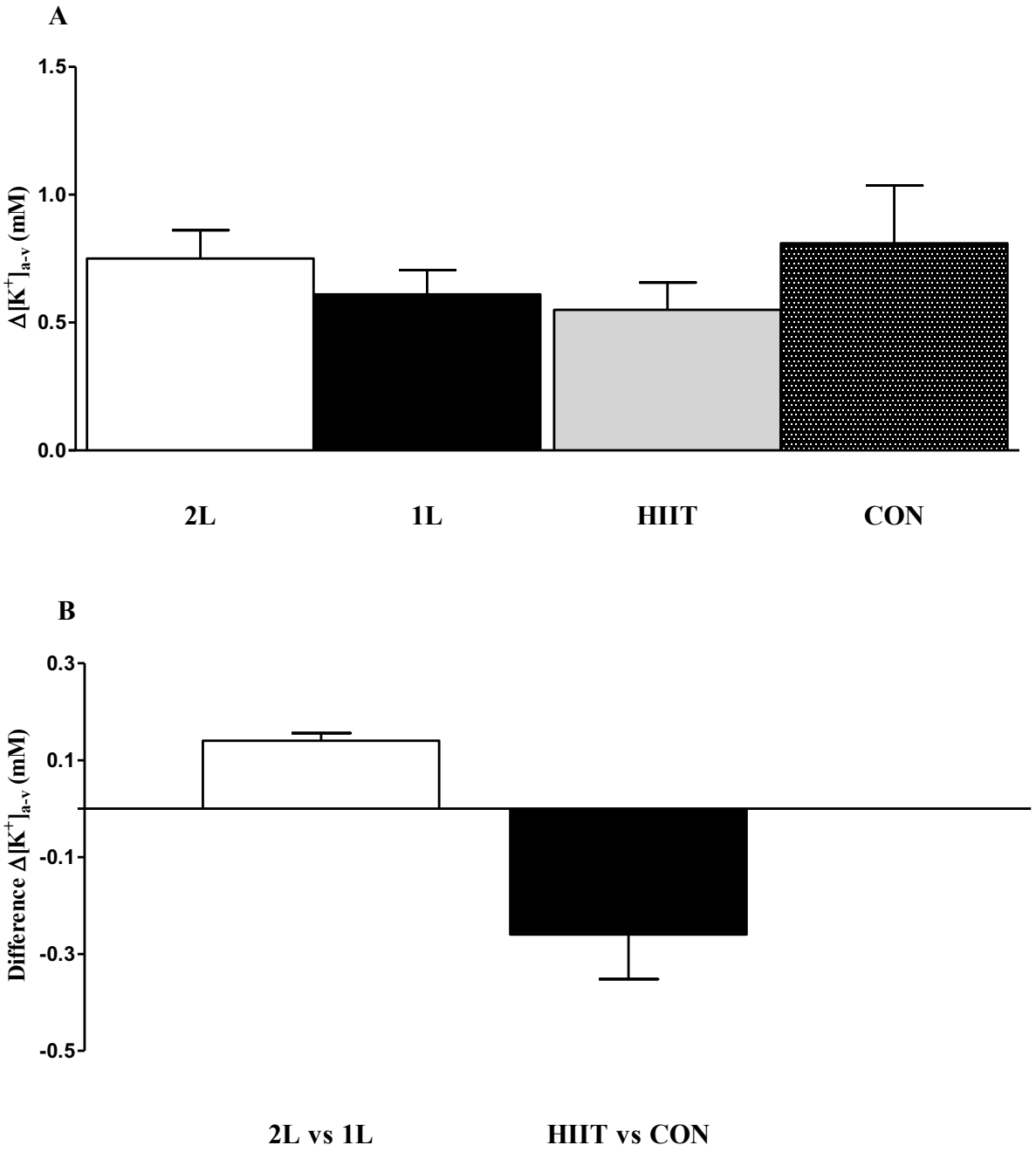

Figure 6.4 The rise in $[K^+]_{a-v}$ during exercise ($\Delta[K^+]_v$)(A) defined as the peak $[K^+]_v$ during exercise minus the baseline measure during each of the trials and (B) the difference in $\Delta[K^+]_{a-v}$ between interventions (2L minus 1L, n=10, Chapter 3; and HIIT minus CON, n=8, Chapter 5). Data presented as ± SD.

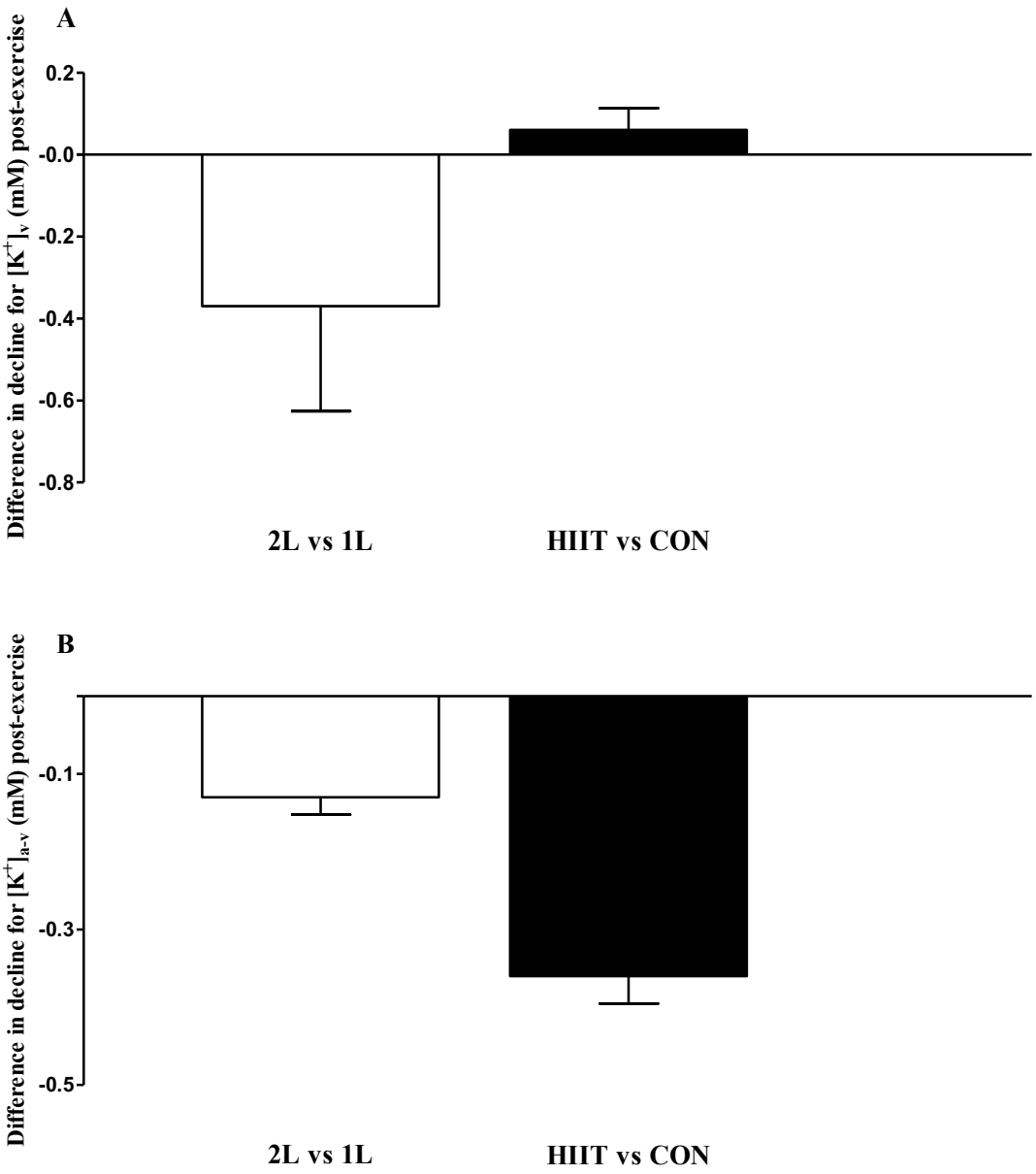

Figure 6.5 The difference in decline for $[K^+]_v$ post-exercise (A) defined as the $[K^+]_v$ end of exercise measure minus the lowest measure during recovery for each of the trials and (B) the difference in decline for $[K^+]_{a-v}$ between interventions (2L minus 1L, n=10, Chapter 3; and HIIT minus CON, n=8, Chapter 5). Data presented as $\pm$ SD.

6.3 Impacts of muscle mass, digoxin and HIIT on K^+ regulation and fatigue during exercise and recovery

6.3.1 Impacts of muscle mass

The higher plasma $[K^+]_a$ and a lower $[K^+]_v$ during high-intensity cycling exercise most likely reflect both increased K^+ release from contracting skeletal muscles and clearance from inactive muscles during exercise. Both K^+ release and reuptake and or/clearance are likely greater during large muscle mass exercise.

During exercise, plasma $[K^+]_a$ was higher in 2L than 1L by ~ 0.49 mM ($P < 0.05$, trial main effect). There was also a greater $\Delta[K^+]_a$ observed in 2L than 1L during the final EB at 23 min and at fatigue ($P < 0.05$, trial x time interaction). The $[K^+]_v$ was less in the 2L than 1L during EB1 by ~ 0.21 mM ($P < 0.05$, trial x time interaction). There was also a higher $[K^+]_{a-v}$ during 2L than 1L ($P < 0.05$, trial main effect).

Fatigue occurred during dynamic exercise as the participants cycled to exhaustion. Plotting the decline in MVC post-exercise (Figure 6.6) shows declines ranging between 15% and 29% at fatigue for 2L and 1L, respectively The declines in evoked torque shows declines at fatigue for each of the $Q_{tw,pot}$ (44% and 54%; Figure 6.2), doublet (26% and 40%) and 20 Hz torque (34% and 34%), for 2L and 1L respectively. Thus, there was clear evidence of fatigue as demonstrated by impaired voluntary and evoked quadriceps muscle torque generation. There was some impaired excitability evidenced through twitch M-wave amplitude decline throughout exercise which remained lower during recovery, whilst duration was extended after fatiguing exercise, in both VM and VL muscles ($P < 0.05$, time main effect). Furthermore, VM twitch M-wave area was also reduced after fatigue ($P < 0.05$). There were, however, no differences in the percentage decline in muscle torque between 1L and 2L.

Despite the higher $[K^+]_a$ and greater $\Delta[K^+]_a$ at fatigue with the larger muscle mass (Figures 3.5-3.7), 2L exercise was not associated with greater changes in the post-exercise evoked torques

for Qtw_{pot}, doublet or 20 Hz contractions (Figures 3.19-21). A possible explanation is recovery of skeletal muscle interstitial K^+ with diffusion and blood flow during rest periods (Cairns and Lindinger 2008), between the intermittent exercise bouts and before the 1 min post-exercise measures, which may allow membrane excitability and muscle force/torque to recover or be sustained, thus delaying the development of fatigue and maintaining muscle contractile and cycling performance. Muscle contractions acutely increase Na^+,K^+-ATPase activity which acts to stabilise transmembrane [K^+] gradients and membrane excitability, protecting against fatigue (Clausen 2008). However, during intense exercise some Na^+,K^+-ATPase may become inactivated and precipitate further ionic disturbances and muscle fatigue (McKenna, Bangsbo et al. 2008).

Hence, the higher $[K^+]_a$ in 2L was not associated with either delayed time to fatigue during cycling exercise to exhaustion and attenuated declines in MVC, evoked torque percentage and M-wave (amplitude and area) declines compared with 1L. In summary, the effects of the large muscle mass intervention undertaken on subsequent K^+ regulation and evoked torque, in healthy humans performing intense cycling exercise, demonstrate that the relative amounts of active and inactive muscle are likely to play a critical role in the regulation of systemic K^+ but not fatigue, at least as measured by time to exhaustion during intense dynamic exercise, and both voluntary and evoked quadriceps muscle torque generation post-exercise.

6.3.2 Impacts of digoxin on K^+ regulation and muscle fatigue during exercise and recovery

During digoxin, plasma $[K^+]_a$ was slightly greater than placebo (4.93 ± 0.2 vs. 4.88 ± 0.2, respectively) and the post-exercise $[K^+]_a$ decline was less for digoxin (both $P < 0.05$, treatment main effect). The higher [K^+] during exercise to fatigue and during early recovery with digoxin

is consistent with the 7.8% earlier onset of fatigue found. Given that digoxin binds to and inhibits a small fraction of the Na^+,K^+-ATPase in skeletal muscle (Schmidt, Bundgaard et al. 1995), it is likely that the higher $[K^+]$ during exercise and smaller post-exercise decline in plasma $[K^+]$ with digoxin was associated with an increased K^+ loss from contracting muscle during exercise and also by lower K^+ re-uptake post-exercise, due to a partial-blockade of the Na^+,K^+-ATPase in skeletal muscle. A partial blockade of Na^+,K^+-ATPase by digoxin demonstrates that healthy human skeletal muscle is adaptable and resilient to acute Na^+,K^+-ATPase inhibitory challenges that would be expected to perturb Na^+/K^+ fluxes in healthy muscle. Interestingly, the plasma $\Delta[K^+]_a$ during exercise was similar for digoxin and placebo (Figure 6.1), indicating the small effects of digoxin during cycling exercise.

It was hypothesised that digoxin would impair muscle torque development and excitability - exacerbating the decline in M-wave amplitude following cycling to fatigue. However, digoxin administration did not alter the exercise-induced reductions in MVC or in the evoked torque during a twitch, doublet or 20 Hz contractions. The MVC for digoxin and placebo decreased during exercise and remained low in recovery ($P < 0.05$, time main effect, Figure 4.5), declining for digoxin at fatigue to ~67% and for placebo to ~66% of baseline values. The Q_{twpot} torque for digoxin and placebo decreased during exercise and recovery ($P < 0.05$, time main effect, Figure 4.6), for digoxin at fatigue to ~50% and for placebo to ~46% of baseline values. The doublet torque for digoxin and placebo decreased during exercise and recovery ($P < 0.05$, time main effect, Figure 4.7), for digoxin at fatigue to ~57% and for placebo to ~56% of baseline values. The tetani torque for digoxin and placebo decreased during exercise and recovery ($P < 0.05$, time main effect, Figure 4.7), for digoxin at fatigue to 81% and for placebo to 76%.

Thus, despite the shorter cycling time to fatigue and the slightly higher $[K^+]_a$ during digoxin compared to placebo, the post-exercise percentage reductions in MVC or the evoked torque during a twitch, doublet or 20 Hz contractions did not differ between trials. Inhibiting a large fraction of Na^+,K^+-ATPase in muscle would block AP propagation along the sarcolemmal and t-tubular membranes and cause muscle fatigue (Clausen 2015). Any inhibitory effect of digoxin would also be coincident with the large overall activation of Na^+,K^+-ATPase in contracting muscle, which would produce a very large inward, hyperpolarising current for K^+ (Clausen 2011). Therefore it is possible that the digoxin intervention used resulted in too small a fractional inhibition of muscle Na^+,K^+-ATPase to sufficiently exacerbate K^+ fluxes to the extent necessary to impair muscle fibre membrane excitability properties and contribute to the early onset of fatigue. However, since contractile measures were made at 1 min post-exercise, it is also quite possible that a rapid detrimental effect during the actual exercise bout may have been missed.

6.3.3 Impacts of HIIT on K^+ regulation and muscle fatigue during exercise and recovery

After HIIT, $[K^+]_a$ was less than pre-training during exercise at 80% $\dot{V}O_{2peak}$ by ~0.46 mM and also at 1 min recovery , whereas the $[K^+]_v$ was greater at EB4 than pre-training (Chapter 5, Figures 5.3-5.4). The decreased $[K^+]_a$ during exercise at 80% $\dot{V}O_{2peak}$ suggests HIIT improves K^+ regulation, which is consistent with general findings of improved K^+ regulation with previous sprint training studies (McKenna, Schmidt et al. 1993, McKenna, Heigenhauser et al. 1997, Harmer, McKenna et al. 2000, Nielsen, Mohr et al. 2004). The underlying mechanisms for the reduction in $[K^+]_a$ at 80% $\dot{V}O_{2peak}$ and after HIIT are likely due to reduced release of K^+ from contracting skeletal muscles, consistent with the lower $[K^+]_a$ evident at 1 min after sprint exercise. From this it may be speculated that HIIT also reduced the interstitial $[K^+]$ in

contracting skeletal muscle during cycling exercise; if so, this would most likely occur through a larger K^+ re-uptake due to increased Na^+,K^+-ATPase activity. However, across the inactive forearm musculature, there was no difference between trials for $[K^+]_{a-v}$ (Chapter 5, Figure 5.6). Although differences in forearm blood flow could modify K^+ uptake; this seems unlikely with intense training of the leg knee extensor and hip extensor muscles. In earlier studies, a reduced resting and recovery plasma $[K^+]$ and greater muscle K^+ uptake during exercise after intense training were consistent with findings of increased Na^+,K^+-ATPase content in skeletal muscle (McKenna, Schmidt et al. 1993, McKenna, Heigenhauser et al. 1997). Whilst measures of Na^+,K^+-ATPase content were not undertaken in this thesis, these were analysed separately and surprisingly did not increase significantly following HIIT in these participants. There were no correlations between muscle Na^+,K^+-ATPase content and Na^+,K^+-ATPase isoforms abundances α_1, ($r = 0.46$, $p = 0.457$ or α_2 $r = 0.021$, $p = 0.480$), or significant differences after ST in Na^+,K^+-ATPase α_1 ($p = 0.268$, $d = 0.34$), or α_2 ($p = 0.341$, $d = 0.21$) isoform protein abundances. There were also no significant differences found after ST in NKA β_1 ($p = 0.375$, $d = 0.17$) or β_2 ($p = 0.424$, isoform protein abundances (Altarawneh et al. unpublished data). This lack of muscle Na^+,K^+-ATPase upregulation therefore likely explains the very small impacts of HIIT in this study on K^+ homeostasis. The reasons for this lack of adaptation is not clear, but are also consistent with the lack of performance improvement after HIIT, despite participants being capable of performing more than double the work outputs during training sessions (i.e 4 bouts in Week 1, 10 bouts in Weeks 4-7) after HIIT.

Consistent with the lack of difference in $[K^+]$ during intense exercise after HIIT, the declines in MVC and evoked torque for Q_{twpot}, doublet and 20 Hz tetani contractions following each exercise bout, including recovery at 30 min, were not significantly different between pre- and post-training for HIIT. The lack of difference between trials might be explained by the muscle interstitial $[K^+]$ not being high enough to have impaired membrane excitability (Fitts 1994). It

is also possible that any K^+-impaired membrane excitability might also be countered by acutely increased muscle Na^+,K^+-ATPase activity, which promotes re-uptake of K^+ into the intracellular space. The M-wave findings post-HIIT show amplitude and area declined less and duration increased less compared to pre-HIIT. A reduction in M-waves has been shown in fatigued muscles during sustained MVC; most likely due to a decline in excitability at the muscle fibre membrane (Bigland-Ritchie, Jones et al. 1979, Bigland-Ritchie, Johansson et al. 1983). It is therefore possible that HIIT was effective in maintaining the motor-discharge which possibly contributes to the restoration of voluntary force, indicating maintenance of muscle excitability. However, similar reductions were found at 1 min post-exercise after HIIT. Any decline in muscle force-generating capacity is possibly related to a reduction in muscle excitability due to the propagation of action potentials along the sarcolemma being inhibited by elevated interstitial [K^+]. The small decline in M-wave amplitude and a lack of change in power output for HIIT suggests the increases in [K^+] were likely to contribute to fatigue during intermittent sprint exercise. During sprint bouts the fatigue index was high (EB2 61.9 ± 16.8 vs 62.5 ± 21.2 %, Pre vs. Post, respectively), indicating fatigue.

A weakness of these studies was that measures of quadriceps muscle MVC and evoked torque and excitability were all conducted post-exercise, after a standard delay of 1 min. Thus, undertaking measurements during the non-contracting phase of leg cycling, rather than at 1 min post-exercise would increase the probability of detecting any changes more relevant to muscle contractions rather than recovery. Increased sensitivity of M-wave measures would also be beneficial. It was difficult to detect excitability accurately with these measures used, possibly due to factors highlighted in a recent review (Rodriguez-Falces and Place 2018). These authors indicated that the first and second phase of the M-wave behaved differently

during fatiguing exercise and argued on this basis that specifically analysing the first phase of M-waves separately would most likely improve the identification and interpretation of changes in muscle fibre membrane excitability with fatiguing exercise (Rodriguez-Falces and Place 2018). Unfortunately, due to the way signals were recorded and processed, it wasn't possible to review the data to calculate first phase of M-wave data collected in this thesis to recalculate the two suggested phases.

Finally, there is the potential that not all motor units were recruited during the evoked contractions. Although the stimulation protocols/methods were consistent, and the ramp protocols employed showed no significant further increase in torque, there is always the possibility that muscle motor units were not fully recruited. Use of electrical stimulation procedures where a far higher supramaximal stimulus could be employed than was possible with magnetic stimulation would be useful to more fully demonstrate full activation. It should be recognised however, that such procedures are painful for participants.

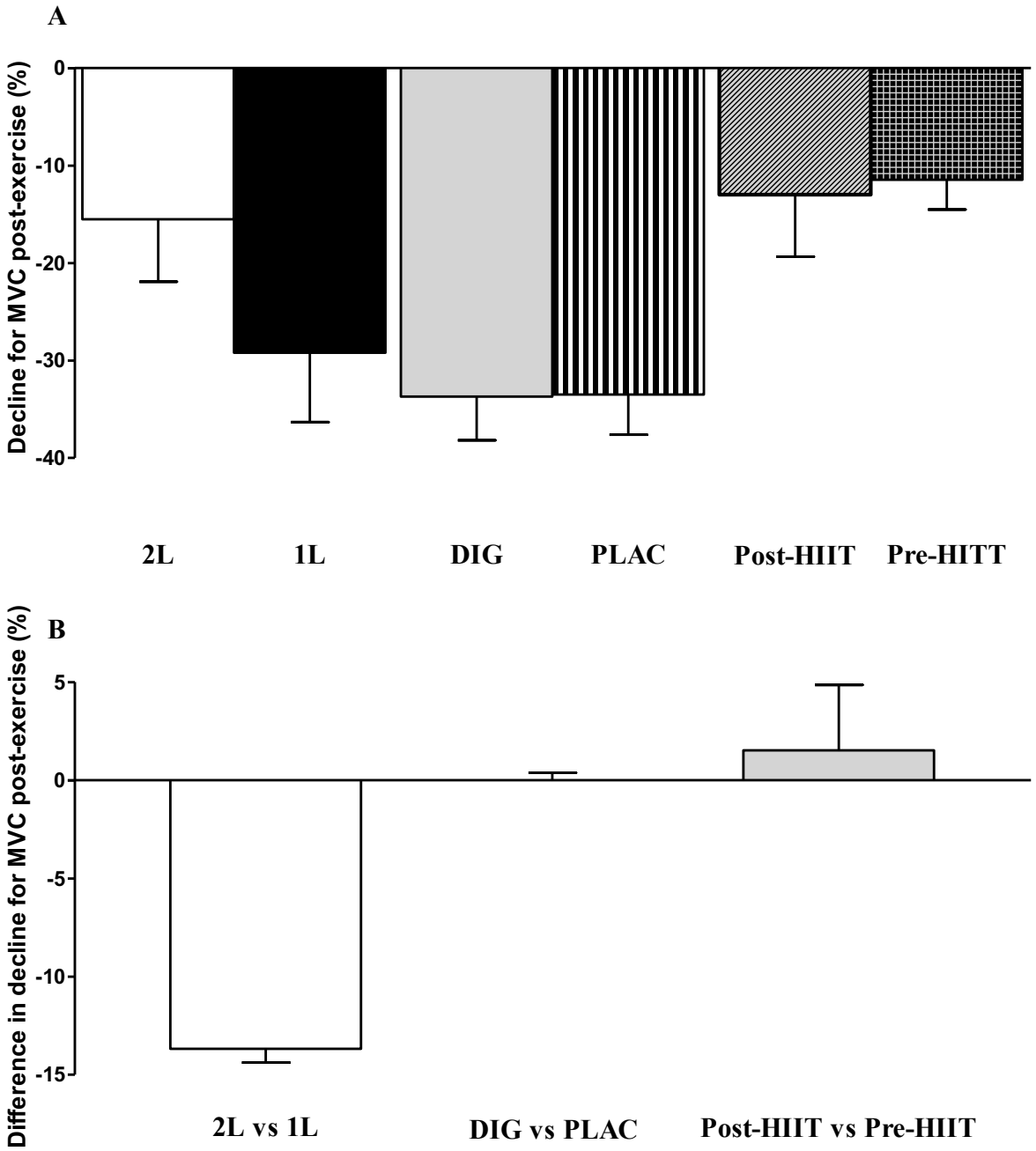

Figure 6.6 The decline in MVC post-exercise expressed as a percentage (%) (A) defined as the MVC % at the end of exercise minus the baseline % for each of the trials and (B) the % difference in decline for MVC between interventions (2L minus 1L, n=10, Chapter 3; DIG minus PLAC, n=10, Chapter 4; and HIIT minus CON, n=8, Chapter 5). Data presented as ± SD.

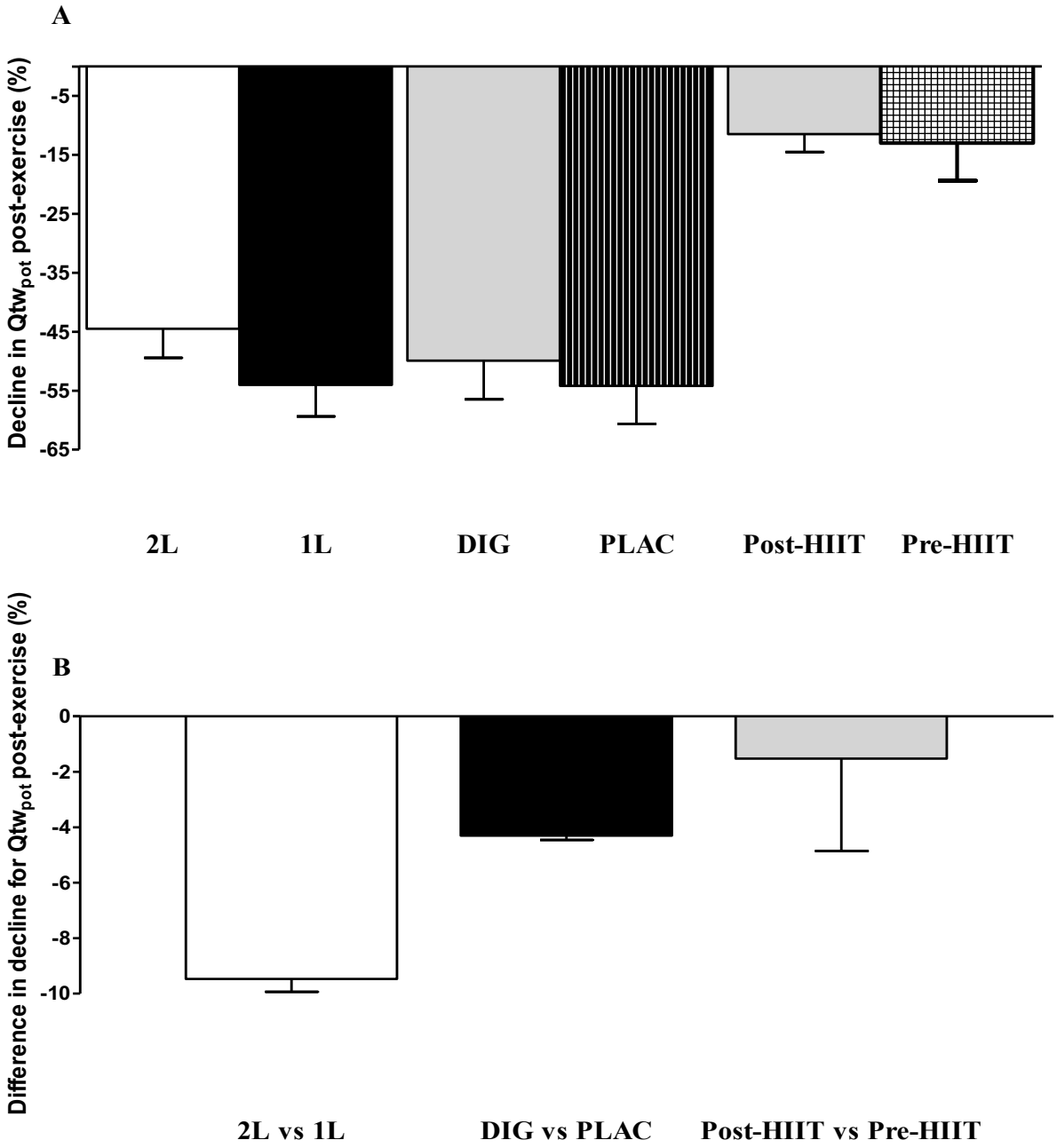

Figure 6.7 The decline for Qtw_{pot} post-exercise expressed as a percentage (%) (A) defined as the Qtw_{pot} end of exercise measure minus the baseline measure for each of the trials and (B) the difference in decline for Qtw_{pot} between interventions (2L minus 1L, n=10, Chapter 3; DIG minus PLAC, n=10, Chapter 4; and HIIT minus CON, n=8, Chapter 5). Data presented as ±SD.

6.4 Conclusions

In conclusion, the three interventions were effective in modulating $[K^+]_a$ compared to their alternate groups, with elevations during 2L versus 1L cycling, small increases during digoxin across all times versus placebo, whilst HIIT lowered plasma $[K^+]_a$ at the end of 80% $\dot{V}O_{2peak}$ exercise and at 1 min recovery Post- compared to Pre-train. As each of the MVC and the evoked $Q_{tw,pot}$, doublet and 20 Hz torque declined after fatiguing exercise and remained depressed at the end of recovery it is probable that a reduction in contractile function contributes to fatigue during exercise. However, altered muscle mass and HIIT were not effective in modulating dynamic exercise performance, whilst for digoxin the exercise time to fatigue was shorter, indicating greater fatigability. Further, reductions in MVC or evoked torque post-exercise do not seem to be substantially altered by either digoxin or HIIT, although any decline in twitch torque is most likely less after large muscle mass than small muscle mass exercise. The M-wave characteristics are likely to be altered with exercise, with reductions in both amplitude and area and lengthening of duration contributing to the onset of fatigue. Apart from minor differences, there is some evidence of intervention effects on M-wave characteristics with fatigue. Although the M-waves did not differ between 2L vs. 1L or digoxin vs. placebo; however, the differences after HIIT suggest intense exercise is a major factor in the development of fatigue.

The major conclusions from this thesis are:

Chapter 3 - Effects of contracting muscle mass on arterial and venous $[K^+]$ and fatigue during intense intermittent cycling.

i) A higher plasma $[K^+]_a$ and a greater rise in plasma $[K^+]_a$ were observed for 2L than 1L during the EB to fatigue, during high-intensity intermittent cycling.

ii) There was also a wider $[K^+]_{a-v}$ across the inactive forearm during 2L than 1L

high-intensity intermittent cycling.

iii) Fatigue-induced cessation of exercise time did not differ between 2L and 1L.

iv) The quadriceps MVC decreased following each EB, but with no differences in the percentage declines between 2L and 1L; the evoked Q_{twpot} torque also declined with fatigue and decreased less for 2L than 1L.

v) The M-wave characteristics of amplitude, area and duration were all modified following high-intensity intermittent cycling consistent with fatigue, but these did not differ between 2L and 1L.

Chapter 4 - The effects of an acute oral dose of digoxin on plasma K^+ regulation, muscle performance and muscle excitability during and following high-intensity cycling in healthy adults.

i) Plasma $[K^+]_a$ was greater in digoxin than placebo, during and following high-intensity exercise and recovery.

ii) During recovery from exercise, the $-\Delta[K^+]_a$ was less negative for digoxin than for placebo.

iii) Exercise time to fatigue was 7.8% shorter with digoxin compared to placebo, indicating greater fatigability.

iv) Digoxin did not alter the exercise-induced reductions in torque generated during MVC, or evoked contractions measured during Q_{twpot}, doublet or 20Hz tetani, or in the M-wave characteristics with evoked contractions.

Chapter 5 – Effects of sprint training on arterial and venous $[K^+]$ during and following high-intensity interval cycling, as well as muscle excitability and fatigue.

i) Plasma $[K^+]_a$ for HIIT Post was less than Pre-train at 80% $\dot{V}O_{2peak}$ and at 1 min

recovery after intense sprint bouts.

ii) Plasma $[K^+]_v$ at the end of the sprint exercise bouts was greater Post than Pre-train.

iii) HIIT did not change peak power, work or fatigue-index during the two 30 s maximal sprints.

iv) HIIT did not reduce the post-exercise percentage decreases in quadriceps MVC or evoked Q_{twpot}, doublet or 20Hz torque.

v) The M-wave characteristics for post-HIIT show amplitude and area declined less and duration increased less compared to pre-HIIT.

6.5 Limitations

An important limitation of the present thesis was that K^+ regulation was measured only in arterial and antecubital venous plasma, but not in femoral venous plasma. Such measurement, together with blood flow measures would have allowed determination of femoral venous plasma $[K^+]$, and K^+ release from contracting leg muscles (Nielsen, Mohr et al. 2004, McKenna, Bangsbo et al. 2008), reflecting changes in muscle interstitial $[K^+]$ (Green S, Langberg H et al. 2000), and in skeletal muscle Na^+,K^+-ATPase activity (McKenna, Bangsbo et al. 2008). Therefore, the measure of interstitial K^+ would have most likely been higher during exercise than arterial plasma and enhancing understanding of the changes in the muscle. The measure of catecholamine concentrations and blood flow across active and inactive muscles may have provided a more precise calculation of actual K^+ fluxes and enhanced understanding of the effects of Na^+,K^+-ATPase on K^+ regulation during and after fatiguing exercise.

Another limitation was that different cycling protocols were utilised in the three studies. Each investigation may have benefited through the linking of results from the same

protocols to better understand the effect of [K^+] on fatigue.

Reducing the variability of the evoked torque and M-wave measures would assist in the precise interpretation of the effect of an intervention such as exercise and digoxin on muscle excitability. Peripheral fatigue development, as studied here, presents as one of many potential mechanisms able to influence central motor output and performance. Therefore, a limitation that the relative contributions of the central fatigue-causing mechanisms and its effects on [K^+] during exercise were not quantified.

An additional limitation is that an underestimation of the magnitude of peripheral fatigue of quadriceps muscle MVC and evoked torque and excitability may have been caused by the fixed 1 min delay between end-exercise and post-exercise neuromuscular measurements. This represented the time needed to physically position the subjects and probe. Thus, undertaking measurements during exercise, rather than at 1 min post-exercise would increase the probability of detecting any changes more relevant to muscle contractions rather than recovery. It is also possible that M-wave measures lacked sensitivity, and that analysing the first phase of M-waves separately would most likely improve the identification and interpretation of changes in muscle fibre membrane excitability with fatiguing exercise (Rodriguez-Falces and Place 2018).

6.6 Recommendations for future research

Further research is required to enhance understanding of the effects of K^+ on muscle performance and fatigue. It would be of interest to further investigate the effects of these interventions by measuring simultaneously K^+ release from contracting muscles and K^+ uptake by inactive muscles, with an arterio-venous difference across the contracting leg and across the inactive forearm. It would be useful to apply a more rapid sampling technique to

measure muscle K^+ fluxes across muscle during exercise and early recovery, such as using indwelling K^+ microelectrodes (Hallen and Sejersted 1993) to detect rapid changes. Combining these measures with the microdialysis technique to sample interstitial [K^+] in contracting muscle would be highly advantageous (Green, Bülow et al. 1999). Evaluating in-vivo skeletal muscle Na^+,K^+-ATPase activity and E_m would also allow for a more detailed analysis of the potential impacts of K^+ regulation in skeletal muscle. Development of new methods are however required for these latter measures. Furthermore, future research should quantify the exact contracting and inactive muscle mass, to allow precise calculations of K^+ release from active skeletal muscle and reuptake by inactive muscle. In addition, measuring catecholamine concentrations and the blood flow across active and inactive muscles would enable precise calculation of actual K^+ fluxes and enhance understanding of the effects of Na^+,K^+-ATPase on K^+ regulation during and after fatiguing exercise.

Implementing a different stimulation technique to allow measures of muscle torque and excitability during the non-contracting phase of leg cycling, rather than at 1 min post-exercise would enhance the sensitivity and validity of these measures. Increased sensitivity of M-wave measures would also be beneficial. For future studies, it is recommended that analysing the first phase of M-waves separately would most likely improve the identification and interpretation of changes in muscle fibre membrane excitability with fatiguing exercise (Rodriguez-Falces and Place 2018).

Finally, the exercise models chosen in this thesis meant that it was also difficult to induce major increases in circulating [K^+], which would also likely mean that lesser increases occurred in muscle interstitial [K^+]. Thus future studies should consider more intense exercise models to more substantially elevate extracellular [K^+], such as treadmill sprinting (Medbø and Sejersted 1990) or rowing (Atanasovska, Petersen et al. 2014, Atanasovska, Smith et al. 2018). These should be in addition to more comprehensive measures of [K^+] as indicated above, together with evoked twitches and M-waves measured during rather than post-exercise. These

approaches would enable firmer conclusions on the possible importance of K^+ disturbances during intense exercise for muscle fatigue and performance in humans.

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APPENDICES

VICTORIA UNIVERSITY
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Appendix A
CARDIOVASCULAR AND OTHER RISK FACTORS QUESTIONNAIRE
Chapters 3, 4 & 5

In order to be eligible to participate in the experiment investigating: **"The effects of manipulating potassium on muscle excitability and fatigue during intense exercise"** you are required to complete the following questionnaire which is designed to assess the risk of you having a cardiovascular event occurring during an exhaustive exercise bout.

Name: _____ **Date:** _____

Age: _____ **years** **Weight:** _____ **kg** **Height:** _____ **cm** **Gender: M F**

Give a brief description of your average activity pattern in the past 2 months:

_____

_____

_____

Circle the appropriate response to the following questions.

1.	Are you overweight?	Yes	No	Don't know
2.	Do you smoke?	Yes	No	Social
3.	Are you an asthmatic?	Yes	No	Don't Know
4.	Are you a diabetic?	Yes	No	Don't Know
5.	Does your family have a history of diabetes?	Yes	No	Don't Know
6.	Do you have a thyroid disorder?	Yes	No	Don't Know
7.	Does your family have a history of thyroid disorders?	Yes	No	Don't Know
8.	Do you have a pituitary disorder?	Yes	No	Don't Know
9.	Does your family have a history of pituitary disorders?	Yes	No	Don't Know
10.	Do you have a heart rhythm disturbance?	Yes	No	Don't Know
11.	Do you have a high blood cholesterol level?	Yes	No	Don't Know
12.	Do you have elevated blood pressure?	Yes	No	Don't Know
13.	Are you being treated with diuretics?	Yes	No	

14. Are you on any other medications? Yes No

List all medications? (including oral contraceptives) _____

15. Do you think you have any medical complaint or any other reason which you know of which you think may prevent you from participating in strenuous exercise? Yes No

If Yes, please elaborate

_____

16. Have you had any musculoskeletal problems that have required medical treatment (eg, broken bones, Joint reconstruction etc)? Yes No

If Yes, please provide details (including dates)

_____

17. Are you currently pregnant or expect to become pregnant during the time in which this experiment is conducted? Yes No

18. Does your family have a history of premature cardiovascular problems

(e.g. heart attack, stroke)? Yes No Don't Know

I, _____, believe that the answers to these questions are true and correct.

Signed: _____ Date: _____

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Appendix B

ARTERIAL & VENOUS CATHETERISATION QUESTIONNAIRE

Chapters 3, 4 & 5

NAME:

_____

ADDRESS:

_____

DATE: _____ AGE: _____ years

1. Have you or your family suffered from any tendency to bleed excessively? (eg. Haemophilia) or bruise very easily? Yes No

   If yes, please elaborate

   _____

2. Are you allergic to local anaesthetic? Yes No

   If yes, please elaborate

   _____

3. Do you have any skin allergies? Yes No

   If yes, please elaborate

   _____

4. Have you any other allergies? Yes No

   If yes, please elaborate

   _____

5. Are you currently on any medication? Yes No

   If yes, what is the medication?

   _____

6. Do you have any other medical problems? Yes No

If yes, please elaborate

_____

7. Have you ever fainted when you had an injection or blood sample taken? Yes No

If yes, please elaborate

_____

8. Have you previously had heparin infused or injected? Yes No

If yes, please elaborate

_____

9. Do you or other members of your family have Raynauds disease, or suffer from very poor circulation in the fingers, leading to painful fingers that turn white/blue?

Yes No

If yes, please elaborate

_____

To the best of my knowledge, the above questionnaire has been completed accurately and truthfully.

Signature: _____ Date:_____

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Appendix C

MAGNETIC STIMULATION QUESTIONNAIRE

Chapters 3, 4 & 5

NAME:

_____

ADDRESS:

_____

DATE: _____ AGE: _____ years

2. Have you any electrical devices fitted? (eg. Pace maker)

Yes No

If yes, please elaborate

_____

2. Do you have any adverse reactions to exercise? Yes No

If yes, please elaborate

_____

3. Have you ever fainted when performing strenuous exercise? Yes No

If yes, please elaborate

_____

4. Have you previously experienced magnetic stimulation? Yes No

If yes, please elaborate

_____

5. Do you have any skin allergies? Yes No

If yes, please elaborate

_____

6. Have you any other allergies? Yes No

If yes, please elaborate

_____

7. Are you currently on any medication? Yes No

If yes, what is the medication?

_____

8. Do you have any other medical problems? Yes No

If yes, please elaborate

_____

9. Do you or other members of your family have Raynauds disease, or suffer from very poor circulation in the legs/fingers, leading to painful legs/fingers that turn white/blue? Yes No

If yes, please elaborate

_____

To the best of my knowledge, the above questionnaire has been completed accurately and truthfully.

Signature: _____ Date:_____

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Appendix D
INFORMATION TO PARTICIPANTS INVOLVED IN RESEARCH
Chapter 3

You are invited to participate

You are invited to participate in a research project entitled: **The effects of muscle mass on arterial and venous [K+], muscle excitability and fatigue during intense exercise**.

This project is being conducted by a student researcher Trevor Farr ***as part of a PhD study*** at Victoria University, under the supervision of Professor Michael McKenna from Institute of Sport, Exercise and Active Living (ISEAL).

Project explanation

The aim of this project is to examine the effects of:

1. muscle mass, and exercise intensity on arterial and venous [K^+], muscle excitability and fatigue

This project aims to investigate the effects of large muscle mass, and high intensity exercise on arterial and venous potassium concentration ([K^+]), muscle excitability and fatigue.
Exhaustive exercise is well known to impair muscle excitability and alter muscle properties as a result of muscle electrical activity (action potential), in particular changes in ions and metabolites. Short term high intensity exercise is typical of many team sports, which are played worldwide. Furthermore, little is known about the effect muscle mass has on potassium concentration, muscle excitability and fatigue. Recent studies have investigated short term high intensity exercise and shown large increases in the arterial blood plasma potassium concentration and an accumulation of potassium inside and outside the contracting muscles. This has been linked with muscle fatigue during intense exercise in humans, via muscle activity. Here we will focus on the effects of the regulation of potassium concentrations, which are integral in sustaining muscle contractions. Muscle contractile properties and excitability will also be accessed via muscle force and relaxation and the muscle activity (M-wave) characteristics, respectively as they are perturbed with fatigue. Understanding the effects of this type of activity on skeletal muscle will make an important contribution to knowledge. This knowledge is especially relevant to understanding processes of muscle excitability and muscle fatigue.

The following inclusion/exclusion criteria provide guidelines to your means of participating in this research project.

Inclusion criteria-:
ages 18-35
free from injury, skin or anaesthetic allergies
free from bleeding disorders
no known neuromuscular or cardiovascular diseases

Exclusion criteria-:
ages under 18 or over 35
suffering skeletal muscle injury, or
skin or anaesthetic allergies
bleeding disorder
neuromuscular or cardiovascular diseases

What will I be asked to do?

You will be required to complete a total of 5 **visits in the laboratory**
Perform the following:
Graded exercise test ($\dot{V}O_{2peak}$): Two graded exercise tests (two & one leg) will be performed with 48Hr separating each test. These tests will determine the maximal work rate which you can complete for a sustained period, and determine oxygen uptake via measurement of expired gases. The cycle ergometer will be set up according to your individual physical characteristics. You will be fitted with a Polar heart rate strap (which is not restrictive to movement, and is commonly used by athletes) and with an adult-size mouthpiece to breathe through to collect expired gas. You will then be requested to undertake the test, which consists of an increasing incremental exercise on an electronically-braked cycle ergometer. At the conclusion of the test, you will be given a drink and perform a self-paced cool down. All testing will be performed under the Exercise Physiology Laboratory's (School of Sport and Exercise Science, VU) guidelines for maximal exercise testing.

Single Leg Cycle Exercise

You will be requested to perform Single Leg (single leg = dominant leg) Cycle Exercise comprising 6 x 2 min bouts, followed by a time to fatigue bout with 90 s between bouts for peripheral fatigue assessment (PFA). This test is
performed at 80% of the 1-leg graded exercise test. Following the sixth bout, you will cycle at 90% of the 1-leg graded exercise test until fatigue.
Exercise will be initiated with the dominant leg, with the crank arm positioned 45° forward to the vertical axis. You will be asked to remain seated during the cycle exercise and during the recovery periods. The cycle ergometer will be equipped with toe-clips to prevent your feet from slipping. The high intensity efforts, each lasting only a few minutes, and with short recovery, are designed to reduce muscle excitability and produce fatigue.
Blood (venous & arterial) samples will be drawn from antecubital vein and radial artery respectively, before and after each exercise bout.

Two Leg Cycle Exercise

You will be requested to perform a Two Leg Cycle Exercise, comprising 6 x 2 min bouts, followed by a time to fatigue bout with 90 s between bouts for peripheral fatigue assessment (PFA). This test is performed aa the single leg cycle exercise.

Electromyography (EMG) recording

During the Cycling Exercises, EMG signals of the quadriceps muscles (*vastus lateralis and*, *vastus medialis,)*, will be recorded via skin surface electrodes to estimate muscle activation. Recording electrodes will be fixed (attached to the skin) longitudinally over the area of greatest muscle bulk. The reference electrode will be fixed over an electrically-neutral site (epicondyle of femur). Electrode site preparation will be thoroughly performed before the beginning of every test by careful preparation of the skin (shaving, light abrasion and cleaning with alcohol swab). The position of the EMG electrodes will be marked with indelible ink to ensure that they are placed in the same location at subsequent visits. To ensure low levels of movement artefact, electrode cables will be fastened to the subjects' body with medical adhesive tape and wrapped in net. There is no discomfort associated with the application, wearing, or removal of the EMG electrodes.

Peripheral Magnetic Stimulation

While sitting in the chair to assess your maximal strength, a series of electrical stimulations of the quadriceps will be used at rest and during the contractions to measure muscle function properties. Magnetic stimulation is painless, however you may experience a slight discomfort during stimulation. A thorough preliminary session to get accustomed to the stimulation will be performed.

Maximal voluntary contraction (MVC) test

This test will determine the maximal isometric strength of your quadriceps muscle. You will be seated in a chair, with the knee flexed at 90° (0° = knee fully extended). The upper body, hips and thigh will be strapped into the chair to reduce body movement. You will be asked to perform a couple of short maximal knee extensions of 4 s before and immediately after the sprint exercise.

Venous Catheterisation

Blood samples will be taken during rest, exercise and recovery via a catheter placed in the arm. The catheter consists of a needle and teflon tubing. The tubing is fed over the top of the needle on entering the vein. The needle is then withdrawn, leaving only the teflon tubing in your vein for the remainder of the experiment. A tap (stopcock) is placed into the tubing so the flow of blood along the tubing can be altered at will. This procedure allows the taking of multiple blood samples without the need for multiple venepuncture (puncturing of the vein). Each time a blood sample is taken, a small volume of fluid will be injected to keep the catheter from clotting. Catheterisation is slightly uncomfortable, with minimal possibility of bruising and infection. The use of sterile, disposable catheters, syringes, single dose vials and aseptic techniques will markedly reduce the possibility of infection. Only staff qualified and experienced in venepuncture will be used in order to prevent complications. Although the possibility of infection, bleeding, local blood clots, local swelling and redness, and bruising are remote, should any one of these conditions eventuate, please inform us immediately and then consult your doctor.

Arterial Catheterisation

A similar catheter will be used as above and inserted into the radial artery (wrist). Pain is minimised by use of a local anaesthetic. Infection is unlikely as an experienced medical practitioner will perform all arterial catheterisations.

What will I gain from participating?

Potential benefits to you include the opportunity to be involved in human research and gaining valuable research experience, furthering your knowledge, networking and exploring opportunities for the future. Furthermore, you will have the opportunity to improve your fitness levels and discuss fitness and lifestyle strategies with researchers.

How will the information I give be used?

No persons other than the investigators will be privy to any information that may identify you.
Professor Mike McKenna, Dr Francois Billaut, Dr Aaron Petersen, Mr Trevor Farr.
The purpose of these persons having access is to review and discuss information provided.

What are the potential risks of participating in this project?

The **physical risks** associated with the performance testing will not be greater than that experienced by you during one of your standard training sessions. However, the cycle exercise involves a highly unlikely risk of sudden death due to heart failure or fainting episode. Fainting **episode** risks or precipitating factors include; high intensity exercise on a cycle ergometer, particularly if followed immediately by passive recovery on the ergometer, high intensity exercise if you suffer with low exercise tolerance; previous fainting or light-headedness during procedures or associated with exercise. Signs and symptoms may include; precipitous drop in heart rate during recovery (common) or exercise (rare); drop in blood pressure; facial pallor; fixed facial expression; pupils constricted; you become uncommunicative or slurring of words; restless and irritability; sweating; fatigue (if exercising). While fainting episodes are not uncommon, they are reversed quickly when employing first aid management plan, and long-term risks are minimal. Furthermore, the cycle exercises and the knee extensor exercise carry the risk of muscle soreness, stiffness and the potential for soft tissue injury.

If you have any concerns regarding your participation Dr. Harriet Speed (registered psychologist) is available for counselling. Her contact details are: (03) 99195412 or at harriet.speed@vu.edu.au.

How will this project be conducted?

Methodology

Research design:

You will be required to complete a total of 5 **visits in the laboratory**.

Please note you will be asked to provide personal health information.

Visit 1: **Preliminary Screening and Pre-Test Procedures**

Preliminary screening, you will be requested to complete the Cardiovascular Risk Questionnaire. To proceed with the study, you must be healthy, free from injury and known neuromuscular or cardiovascular diseases (as assessed via questionnaires). You will be given the opportunity to ask any questions about the study. The principal investigator will then assess your suitability for participation in the study.

Following clearance, you will be thoroughly ***familiarised***; Single and Two Leg Cycle Exercise that will be used in the main experimental trials magnetic stimulation, electromyography (EMG), maximal voluntary contraction (MVC), two and single leg cycling and Borge scale**.**

Visit 2: **Pre-Test Procedures**

You will be requested to perform a two leg graded exercise test (GXT) on a cycle ergometer to determine aerobic fitness and to allow workload determination for the following two leg cycle exercise sessions. The following familiarisation procedures are exactly the same as Visit 1.

Visit 3: **Familiarisation**

You will be requested to perform a single leg graded exercise test on a cycle ergometer to determine aerobic fitness and to allow workload determination for the following single leg cycle exercise sessions. This session is exactly the same as Visit 1 & 2 familiarisation procedures.

Visit 4: **Experimental Exercise Performance and Muscle Function Assessment**

Upon arriving to the lab, you will be asked to lie down on a bench where venous access will be achieved via the cannulation of an antecubital vein and radial artery, resting blood samples will then be taken. After this you will be prepared for the positioning of skin surface electrodes of the right lower limb. **Electromyography (EMG) recording of** the quadriceps muscles (*vastus lateralis and vastus medialis)*

will be recorded continuously via electrodes to estimate muscle activation. The EMG signals will also be used to analyse M-wave. To determine whether quadriceps stimulation is supramaximal, we will obtain three single twitches every 30 s at 50, 60, 70, 80, 85, 90, 95, and 100% of maximal power output of the stimulator. A maximal voluntary contraction (MVC) followed by three single twitches at 1 Hz followed by another MVC and three paired twitches at 20Hz and finally another MVC and three 20Hz trains will then be performed to asses potentiated twitch force. A 5 min warm-up at 70 W will be performed, then rest for another 1 min. The Single Leg Cycle Exercise will then be initiated on an electrically-braked cycle-ergometer (Excalibur sport, Lode®, Netherlands). During the Single Leg Exercise, immediately after each two minute exercise bout blood samples (venous & arterial) will be drawn from antecubital vein and radial artery respectively, after each exercise bout, and at 0, 1, 2, 5, 10, 20 & 30 min post exercise. Three single stimulations at 1Hz and three paired stimulations at 20Hz will be performed pre, post immediately and post 10 & 30min exercise to asses muscle force and EMG signals. Blood samples and twitch & doublet stimulations are performed following exercise bouts 1, 3 & 6 to measure fatigue and recovery. Following the experimental exercise, all instrumentation will be removed and a self-paced cool down will be performed. During the recovery period, you will be monitored, and allowed to leave following recovery.

Visit 5: **Experimental Exercise Performance and Muscle Function Assessment**
All procedures are the same as Visit 4 except that a Two Leg Cycle Exercise will be performed

Who is conducting the study?
Victoria University, School of Sport and Exercise Science, Institute of Sport, Exercise and Active Living

Professor Michael McKenna: (w) 9919 4499 (email) Michael.mckenna@vu.edu.au
Dr Aaron Petersen: (w) 9919 9452 (email) aaron.petersen@vu.edu.au
Trevor Farr: (w) 9919 4066 (email) trevor.farr@vu.edu.au

Any queries about your participation in this project may be directed to the Principal Researcher listed above.
If you have any queries or complaints about the way you have been treated, you may contact the Ethics and Biosafety Coordinator, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 phone (03) 9919 4148.

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Appendix E

CONSENT FORM FOR PARTICIPANTS INVOLVED IN RESEARCH
Chapter 3

INFORMATION TO PARTICIPANTS:
We would like to invite you to be a part of a **PhD project** into:
"**The effects of muscle mass on arterial and venous [K+], muscle excitability and fatigue during intense exercise**".

As part of the informed consent process, participants have been provided with ***'Information to Participants Involved in Research Letter'*** *prior to obtaining consent.*

CERTIFICATION BY SUBJECT

I, ... of .....(suburb)

certify that I am at least 18 years old* and that I am voluntarily giving my consent to participate in the study:
The effects of potassium on muscle excitability and fatigue during high intensity exercise being conducted at Victoria University by: Prof Mike McKenna and Trevor Farr.

I certify that the objectives of the study, together with any risks and safeguards associated with the procedures listed hereunder to be carried out in the research, have been fully explained to me by Trevor Farr and that I freely consent to participation involving the below mentioned procedures:

- **Graded exercise test ($\dot{V}O_{2peak}$) (*Single & Two Leg)***
- ***Single & Two Leg Cycle Test***
- ***Maximal Voluntary Contraction***
- **Electromyography (EMG) recording**
- **Peripheral Magnetic Stimulation**
- **Maximal Voluntary Contraction**
- **Blood Sampling**

I certify that I have had the opportunity to have any questions answered and that I understand that I can withdraw from this study at any time and that this withdrawal will not jeopardise me in any way. I also understand that I will be required to provide information regarding my personal health.

I have been informed that the information I provide will be kept confidential.

Signed: Date:

Any queries about your participation in this project may be directed to a researcher:
Professor Michael McKenna: (w) 9919 4499 (email) Michael.mckenna@vu.edu.au
Dr Aaron Petersen: (w) 9919 9452 (email) aaron.petersen@vu.edu.au

Trevor Farr: (w) 9919 4066 (email) trevor.farr@live.vu.edu.au

If you have any queries or complaints about the way you have been treated, you may contact the Ethics & Biosafety Coordinator, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 phone (03) 9919 4148

Appendix F
Individual Raw Data
Chapter 3

Table A 1.0 Plasma $[K^+]_a$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery						
		Time (min)																							
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	3.83	5.55	5.49	5.61	5.54	5.79	5.39	4.67	5.92	5.46	5.62								5.92	4.84	4.44	3.92	4.09	4.05	4.09
2	3.74	5.02	5.46	5.59	5.20	5.32	5.39	4.48	5.17	5.46	5.75	5.74	5.89						5.89	4.48	4.11	4.03	4.27	4.21	4.17
3	4.06	4.85	4.80	4.77	4.88	4.86	4.82	4.69	4.84	4.92	4.97	4.66	4.91	5.16	5.36	5.59	5.63	5.69	5.69	5.10	5.53	4.35	4.50	4.42	4.55
4	4.12	5.20	4.68	4.84	4.90	5.03	4.96	4.30	4.95	5.32	5.64	5.79	5.80	5.93	6.08				6.08	4.56	4.16	4.02	4.06	4.08	4.15
5	3.90	4.79	4.58	4.69	4.77	4.60	4.61	4.28	4.70	4.93	5.12	5.20	5.41						5.41	4.38	4.05	3.73	4.14	3.98	4.09
6	3.58	5.45	5.15	5.09	5.28	5.13	5.26	4.43	5.12	6.14	5.45	7.12	7.28	7.32	7.42	7.53			7.53	5.03	4.67	3.68	3.91	3.80	3.82
7	3.85	4.58	4.49	4.57	4.90	4.91	4.98	4.61	4.98	5.20	6.43	5.61	5.72	5.99	6.14				6.14	4.80	4.39	4.12	4.16	4.27	4.35
8	4.21	5.42	5.59	5.57	5.36	5.75	5.62	4.53	5.76	6.14	5.42	5.74	5.89						5.89	4.51	3.80	3.56	3.81	3.88	3.87
9	3.93	4.84	4.78	4.89	4.75	4.84	4.89	4.07	4.95	5.29	6.05	5.52	5.72	5.76	5.85				5.85	4.23	3.94	3.72	3.85	3.83	3.85
10	3.99	5.60	5.47	5.37	5.51	5.61	5.46	4.64	5.20	5.76	5.76	6.29	6.40	6.36	6.17				6.17	4.49	4.34	4.05	4.15	3.98	3.93
n	10	10	10	10	10	10	10	10	10	10	10	10							10	10	10	10	10	10	10
Mean	3.92	5.13	5.05	5.10	5.11	5.18	5.14	4.47	5.16	5.46	5.62								6.06	4.64	4.34	3.92	4.09	4.05	4.09
SD	0.19	0.36	0.43	0.40	0.30	0.42	0.33	0.20	0.39	0.44	0.42								0.56	0.29	0.49	0.24	0.21	0.20	0.23
delta		1.21	1.13	1.18	1.19	1.26	1.22	0.55	1.24	1.54	1.70								2.14	0.72	0.42	0.00	0.17	0.13	0.17

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	4.24	5.63	5.45	5.19	4.70	4.80	4.75	4.47	4.78	5.19	5.12								5.12	4.78	4.34	4.10	4.25	4.37	4.17
2	3.98	4.85	4.95	4.88	4.91	4.96	5.00	4.53	4.98	5.24	5.57	5.76	5.81						5.81	4.30	3.97	3.82	4.37	3.97	4.14
3	3.44	4.94	4.75	4.86	4.81	4.78	4.85	4.44	4.89	4.72	5.06	5.12	5.25	5.39					5.39	4.48	4.23	4.09	4.27	4.21	3.80
4	4.06	4.87	4.88	4.82	4.88	5.03	5.02	4.53	4.81	5.14	5.46	5.61	5.86						5.86	5.24	4.34	4.09	4.50	4.30	4.20
5	4.02	5.08	4.72	4.91	4.38	4.52	4.48	4.28	4.61	4.68	4.85								4.85	4.39	4.25	4.00	4.01	4.28	4.31
6	3.85	4.99	4.86	4.78	4.76	4.75	4.72	4.92	5.16	5.37	5.30	5.39	5.57	5.41					5.41	4.73	4.17	4.03	4.07	3.93	4.00
7	3.84	4.86	4.80	4.83	4.85	5.11	4.87	4.94	5.01	5.16	5.65	5.44	5.54	5.71	5.77				5.77	4.83	4.52	4.05	4.23	4.31	4.23
8	4.32	5.12	5.15	5.14	4.75	5.17	5.10	4.44	5.76	5.56	5.23	5.85	5.88						5.88	5.04	4.17	3.74	4.03	3.96	3.98
9	3.91	4.95	4.95	4.90	4.96	4.92	4.94	4.74	4.92	5.07	5.84	5.24	5.37	5.45	5.68	5.60	5.77	5.92	5.92	4.91	4.62	4.47	4.59	4.61	4.59
10	3.48	5.61	5.59	5.68	5.54	5.61	5.60	4.81	5.27	5.59	5.65								5.65	4.56	4.29	4.23	4.19	3.96	3.94
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	10
Mean	3.91	5.09	5.01	5.00	4.85	4.97	4.93	4.61	5.02	5.17	5.37								5.57	4.73	4.29	4.06	4.25	4.19	4.14
SD	0.28	0.29	0.30	0.27	0.29	0.30	0.29	0.23	0.32	0.30	0.31								0.36	0.30	0.18	0.20	0.19	0.23	0.22
delta		1.18	1.10	1.09	0.94	1.05	1.02	0.70	1.11	1.26	1.46								1.65	0.81	0.38	0.15	0.34	0.28	0.22

Table A 1.1 Plasma $[K^+]_v$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery					
		Time (min)																						
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	3.76	4.31	4.46	4.80	4.68	5.15	5.15	4.21	4.57										4.57	4.66	4.50	3.59	3.74	3.89	3.91
2	3.91	4.63	4.54	4.55	4.61	4.92	4.84	4.19	4.63										4.63	4.94	4.38	4.10	4.32	4.19	4.25
3	3.90	4.40	4.45	4.26	4.43	4.42	4.62	4.44	4.70	4.83	4.82	4.60	4.92	4.99	5.09	5.06	5.31	5.53	5.53	4.91	4.32	4.39	4.52	4.52	4.54
4	4.04	4.97	4.71	4.65	4.63	4.69	4.54	4.40	4.45	4.68	4.87	4.98	5.07	5.37	5.37				5.37	4.67	4.36	4.04	4.07	4.02	3.94
5	4.14	4.44	4.73	4.77	4.77	4.78	4.45	4.49	4.54	4.66	5.47	5.65							5.65	4.65	4.44	4.21	4.22	4.21	4.06
6	3.70	5.07	4.44	4.51	4.63	4.70	4.75	4.56	4.37	4.64	5.06	4.98	5.28	5.30	5.49	5.14			5.14	4.16	4.04	3.68	3.76	3.79	3.78
7	3.87	4.45	4.27	4.58	4.71	4.54	4.68	4.43	4.67	4.85	4.87	4.92	5.03	5.12	5.20				5.20	4.98	4.48	4.17	4.22	4.23	4.21
8	4.11	4.21	4.15	4.42															4.42						
9	3.95	4.04	4.35	4.26	4.42	4.66	4.58	4.23	4.49	4.75	5.04	5.23	5.36	5.38	5.53				5.53	4.34	4.06	4.04	3.87	4.06	4.07
10	3.54	4.73	4.86	4.65	4.38	4.23	4.18	4.12	4.63	5.10	5.59	5.90	5.99	6.01					6.01	4.45	4.28	4.07	4.09	4.04	3.78
n	10	10	10	10	10	9	9	9	9	9	7	7							10	9	9	9	9	9	9
Mean	3.89	4.53	4.50	4.55	4.58	4.68	4.64	4.34	4.56	4.79	5.10								5.21	4.64	4.32	4.03	4.09	4.11	4.06
SD	0.19	0.33	0.22	0.19	0.14	0.27	0.27	0.16	0.11	0.16	0.31								0.52	0.28	0.17	0.25	0.26	0.21	0.25
delta		0.63	0.60	0.65	0.69	0.78	0.75	0.45	0.67	0.90	1.21								1.31	0.75	0.43	0.14	0.20	0.21	0.17

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	3.92	4.55	4.53	4.87	4.68	4.80	4.83	4.38	4.54	4.56	4.95	5.05	5.16						5.16	4.88	4.27	3.63	3.63	3.84	3.81
2	3.95	4.66	4.48	4.58	4.54	4.76	4.77	4.45	4.64	4.75	5.01	5.28	5.38						5.38	4.49	4.02	3.81	4.21	3.97	4.05
3	3.71	4.64	4.34	4.06	4.03	4.16	4.25	4.63	4.28	4.50	4.63	4.70	4.87	5.05					5.05	4.52	4.23	3.91	4.00	4.07	3.65
4	4.00	4.46	4.59	4.68	4.63	4.83	4.84	4.50	4.77	5.14	5.31	5.45	5.59						5.59	4.98	4.54	4.30	4.44	4.23	4.24
5	4.16	4.74	4.87	5.00	4.58	4.53	4.60	4.60	4.55	4.62	4.76								4.76	4.45	4.22	4.08	4.22	4.32	4.36
6	3.53	5.15	4.47	4.25	4.28	4.36	4.44	4.70	4.96	5.31	5.09	5.10	5.22	5.12					5.12	4.96	4.55	4.18	4.11	3.98	3.98
7	3.79	4.15	5.10	4.42	4.58	4.72	4.57	4.64	4.77	4.96	4.95	5.06	5.04	5.21	5.34				5.34	4.90	4.52	4.14	4.21	4.26	4.17
8	4.02	4.61	4.48	4.01	4.38	4.50	4.28	4.34	4.46	4.64	4.68	4.96	5.08						5.08	5.15	4.54	3.88	4.11	4.09	4.06
9	3.86	4.93	4.61	4.98	4.68	4.71	4.78	4.67	4.93	4.91	5.00	5.15	5.26	5.54	5.69	5.52	5.78	5.84	5.84	4.96	4.57	4.62	4.64	4.70	4.88
10	3.15	5.47	5.31	5.08	5.15	5.44	5.91	5.06	5.56	6.27	5.38								5.38	4.04	4.02	4.02	3.86	3.79	
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	9
Mean	3.81	4.74	4.68	4.59	4.55	4.68	4.73	4.60	4.75	4.97	4.98								5.27	4.73	4.35	4.06	4.14	4.13	4.13
SD	0.29	0.37	0.31	0.40	0.29	0.34	0.47	0.20	0.36	0.53	0.25								0.30	0.34	0.22	0.28	0.28	0.27	0.35
delta		0.93	0.87	0.78	0.74	0.87	0.92	0.79	0.94	1.16	1.17								1.46	0.92	0.54	0.25	0.33	0.32	0.32

Table A 1.2 Plasma $[K^+]_{a-v}$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery					
		Time (min)																						
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.07	1.24	1.03	0.81	0.86	0.64	0.24	0.46	1.35	5.46	5.62								1.35	0.18	-0.06	0.33	0.35	0.16	0.18
2	-0.17	0.39	0.92	1.04	0.59	0.40	0.55	0.29	0.54	5.46	5.75	5.74	5.89						2.57	-0.46	-0.27	-0.07	-0.05	0.02	-0.08
3	0.16	0.45	0.35	0.51	0.45	0.44	0.20	0.25	0.14	0.09	0.15	0.06	-0.01	0.17	0.27	0.53	0.32	0.16	-0.01	0.19	1.21	-0.04	-0.02	-0.10	0.01
4	0.08	0.23	-0.03	0.19	0.27	0.34	0.42	-0.10	0.50	0.64	0.77	0.81	0.73	0.56	0.71				0.73	-0.11	-0.20	-0.02	-0.01	0.06	0.21
5	-0.24	0.35	-0.15	-0.08	0.00	-0.18	0.16	-0.21	0.16	0.27	-0.35	-0.45							-0.45	-0.27	-0.39	-0.48	-0.08	-0.23	0.03
6	-0.12	0.38	0.71	0.58	0.65	0.43	0.51	-0.13	0.75	1.50	0.39	2.14	2.00	2.02	1.93	2.39			2.00	0.87	0.63	0.00	0.15	0.01	0.04
7	-0.02	0.13	0.22	-0.01	0.19	0.37	0.30	0.18	0.31	0.35	1.56	0.69	0.69	0.87	0.94				0.69	-0.18	-0.09	-0.05	-0.06	0.04	0.14
8	0.10	1.21	1.44	1.15															1.15						
9	-0.02	0.80	0.43	0.63	0.33	0.18	0.31	-0.16	0.46	0.54	1.01	0.29	0.36	0.38	0.32				0.36	-0.11	-0.12	-0.32	-0.02	-0.23	-0.22
10	0.45	0.87	0.61	0.72	1.13	1.38	1.28	0.52	0.57	0.66	0.17	0.39	0.41	0.35					0.41	0.04	0.06	-0.02	0.06	-0.06	0.15
n	10	10	10	10	9	9	9	9	9	9	9								10	9	9	9	9	9	9
Mean	0.03	0.61	0.55	0.55	0.50	0.44	0.44	0.12	0.53	1.66	1.67								0.88	0.02	0.09	-0.07	0.04	-0.04	0.05
SD	0.00	0.58	0.52	0.53	0.47	0.42	0.41	0.09	0.50	1.63	1.65								0.85	-0.01	0.06	-0.10	0.01	-0.07	0.02
delta		0.58	0.52	0.53	0.47	0.42	0.41	0.09	0.50	1.63	1.65								0.85	-0.01	0.06	-0.10	0.01	-0.07	0.02

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.32	1.08	0.92	0.32	0.02	0.00	-0.08	0.09	0.24	0.63	0.17								0.17	-0.10	0.07	0.47	0.62	0.53	0.36
2	0.04	0.19	0.47	0.30	0.37	0.20	0.23	0.08	0.34	0.49	0.56	0.48	0.43						0.43	-0.19	-0.05	0.01	0.16	0.00	0.09
3	-0.27	0.30	0.41	0.80	0.78	0.62	0.60	-0.19	0.61	0.22	0.43	0.42	0.38	0.34					0.38	-0.04	0.00	0.18	0.27	0.14	0.15
4	0.06	0.41	0.29	0.14	0.25	0.20	0.18	0.03	0.04	0.00	0.15	0.16	0.27						0.27	0.26	-0.20	-0.21	0.06	0.07	-0.04
5	-0.14	0.34	-0.15	-0.09	-0.20	-0.01	-0.12	-0.32	0.06	0.06	0.09								0.09	-0.06	0.03	-0.08	-0.21	-0.04	-0.05
6	0.32	-0.16	0.39	0.53	0.48	0.39	0.28	0.22	0.20	0.06	0.21	0.29	0.35	0.29					0.35	-0.23	-0.38	-0.15	-0.04	-0.05	0.02
7	0.05	0.71	-0.30	0.41	0.27	0.39	0.30	0.30	0.24	0.20	0.70	0.38	0.50	0.50	0.43				0.50	-0.07	0.00	-0.09	0.02	0.05	0.06
8	0.30	0.51	0.67	1.13	0.37	0.67	0.82	0.10	1.30	0.92	0.55	0.89	0.80						0.80	-0.11	-0.37	-0.14	-0.08	-0.13	-0.08
9	0.05	0.02	0.34	-0.08	0.28	0.21	0.16	0.07	-0.01	0.16	0.84	0.09	0.11	-0.09	-0.01	0.08	-0.01	0.08	0.11	-0.05	0.05	-0.15	-0.05	-0.09	-0.29
10	0.33	0.14	0.28	0.60	0.39	0.17	-0.31	-0.25	-0.29	-0.68	0.27								0.27	0.52	0.27	0.21	0.33	0.17	
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	9
Mean	0.11	0.35	0.33	0.41	0.30	0.28	0.21	0.01	0.27	0.21	0.40								0.34	-0.01	-0.06	0.01	0.11	0.06	0.02
SD	0.00	0.25	0.23	0.30	0.20	0.18	0.10	-0.09	0.17	0.10	0.29								0.23	-0.11	-0.16	-0.10	0.00	-0.04	-0.08
delta		0.25	0.23	0.30	0.20	0.18	0.10	-0.09	0.17	0.10	0.29								0.23	-0.11	-0.16	-0.10	0.00	-0.04	-0.08

Table A 1.3 Blood Hb_a ($g\text{-}dL^{-1}$) at rest, during and following high-intensity cycling exercise

2L

		Exercise																Recovery						
		Time (min)																						
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	13.80	15.50	15.65	15.75	15.65	16.00	15.65	15.80	16.15										16.15	15.70	15.65	15.35	15.30	14.50	14.45
2	13.35	15.40	15.45	15.75	15.75	15.70	15.85	14.85	15.35										15.35	14.20	14.75	13.95	14.75	14.40	14.35
3	14.80	15.90	15.90	16.00	16.00	16.10	16.00	15.85	16.00	15.90	16.05	15.95	16.15	16.10	16.10	16.20	16.30	16.30	16.35	15.90	15.70	15.95	15.65	15.50	15.20
4	13.60	14.65	14.90	15.00	14.95	15.10	14.95	14.80	15.00	15.30	15.25	15.30	15.65	15.45	15.90				15.90	15.00	15.10	14.65	14.40	13.55	14.00
5	14.55	15.10	15.25	15.40	15.20	15.20	15.35	15.10	15.20	15.30	15.40	15.35	15.50						15.50	15.30	15.15	14.85	14.65	14.80	14.60
6	15.10	16.90	17.10	17.15	17.25	17.00	17.15	16.90	17.10	17.15	17.25	17.30	17.40	17.32	17.29	17.35			17.35	17.10	16.85	16.70	16.20	15.40	14.90
7	13.35	14.70	14.80	14.70	14.85	15.05	15.15	15.10	15.20	15.30	15.40	15.35	15.50	15.50	15.60				15.60	15.30	15.25	15.00	14.60	14.35	14.00
8	14.60	15.60	16.00	16.40	16.30	16.20	16.40	16.20	16.50	16.50	16.60								16.60	16.50	16.10	16.00	15.60	15.20	14.80
9	14.80	15.30	15.60	15.70	15.50	15.40	15.80	15.50	15.80	15.80	15.80	15.80	16.00	16.10	16.40				16.40	15.70	15.60	15.00	14.80	14.30	14.00
10	12.90	14.10	14.30	14.40	14.30	14.10	14.30	14.10	14.30	14.40	14.30	14.40	14.50	14.50					14.50	14.20	14.00	13.10	13.00	12.30	12.50
n	10	10	10	10	10	10	10	10	10	8	8								10	10	10	10	10	10	10
Mean	14.09	15.32	15.50	15.63	15.58	15.59	15.66	15.42	15.66	15.71	15.76								15.97	15.49	15.42	15.06	14.90	14.43	14.28
SD	0.77	0.77	0.77	0.81	0.83	0.80	0.79	0.80	0.81	0.84	0.90								0.79	0.91	0.77	1.04	0.88	0.95	0.75
delta		1.23	1.41	1.54	1.49	1.50	1.58	1.34	1.58	1.62	1.67								1.89	1.41	1.33	0.97	0.81	0.35	0.20

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	13.80	15.10	15.20	15.30	15.20	15.20	15.20	15.10	15.30	15.30	15.40	15.60	15.50						15.50	15.50	15.10	14.90	14.80	14.20	14.10
2	13.60	15.60	15.80	15.80	15.80	15.80	15.90	15.70	15.80	13.70	16.00	16.10	16.00	16.10					16.10	15.40	15.50	15.50	14.90	14.60	14.25
3	13.70	14.60	14.80	15.10	15.00	15.20	15.20	15.30	15.40	15.40	15.70	15.60	15.75						15.75	15.60	15.30	15.40	14.60	14.55	13.30
4	13.90	15.00	15.00	15.60	15.10	15.10	15.40	15.20	15.40	15.60	15.40								15.40	15.10	15.00	14.70	14.50	14.40	13.70
5	15.00	16.30	16.50	16.40	16.40	16.30	16.40	16.50	16.70	16.80	17.00	17.20	17.10	16.70					16.70	16.60	16.40	16.00	15.40	14.90	14.60
6	12.90	14.20	14.40	14.60	14.55	14.70	14.55	14.45	14.70	14.85	14.80	14.90	15.00	15.00	14.70				14.70	14.85	14.40	14.15	13.70	13.20	13.10
7	14.30	14.90	15.20	15.10	14.00	15.60	15.60	14.50	15.60	15.50	12.90	16.10	15.90						15.90	15.80	15.70	15.10	15.00	14.60	14.30
8	13.80	15.00	15.00	15.00	15.00	15.20	15.20	15.20	15.20	15.20	15.30	15.30	15.40	15.30	15.50	15.30	15.30	15.20	15.20	15.10	14.90	14.80	15.60	13.90	13.90
9	12.40	13.50	13.70	13.80	14.00	13.90	13.90	13.70	13.80	13.90	13.90								13.90	13.70	13.40	13.10	12.80	12.40	12.20
10	15.60	16.30	16.60	16.70	16.50	16.90	16.50	16.40	16.40	16.60									16.60	16.50	16.20	16.10	15.80	16.00	15.20
n	10	10	10	10	10	10	10	10	10	10	9								10	10	10	10	10	10	10
Mean	13.90	15.05	15.22	15.34	15.16	15.39	15.39	15.21	15.43	15.29	15.16								15.58	15.42	15.19	14.98	14.71	14.28	13.87
SD	0.92	0.87	0.89	0.84	0.87	0.83	0.79	0.86	0.82	0.99	1.19								0.85	0.83	0.87	0.89	0.90	0.97	0.84
delta		1.15	1.32	1.44	1.26	1.49	1.49	1.31	1.53	1.39	1.26								1.68	1.52	1.29	1.08	0.81	0.38	-0.04

Table A 1.4 Blood Hb_V ($g\text{-}dL^{-1}$) at rest, during and following high-intensity cycling exercise

2L	Rest				Exercise														Recovery						
					Time (min)																				
Subject	0	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	13.85	14.65	15.30	15.50	15.45	16.35	15.55	15.55	15.60										15.60	16	16.00	14.90	15.05	14.70	13.95
2	13.95	14.70	15.05	15.35	15.45	15.50	15.55	15.15	15.10										15.10	15.35	15.20	14.70	14.45	14.10	14.20
3	14.10	15.80	15.85	15.90	16.05	15.95	16.00	15.80	15.95	15.85	15.60	15.60	15.90	16.15	16.30	15.75	16.25	16.30	16.50	16.00	15.45	15.60	15.50	15.35	15.00
4	13.45	14.45	14.85	15.05	14.80	14.80	14.75	14.75	14.70	14.65	14.95	14.90	14.80	15.25	15.60				15.60	14.95	15.00	14.40	13.30	13.85	13.00
5	14.30	15.35	15.15	15.75	15.40	15.45	15.55	15.32	15.15	15.15	15.40	15.70							15.70	15.45	15.40	15.00	14.70	14.55	14.50
6	14.35	16.70	16.50	16.95	17.05	17.05	17.25	16.95	16.60	16.90	17.30	16.70	17.20	17.15	17.40	17.45			17.45	16.70	16.95	16.55	15.95	15.55	14.90
7	13.35	14.50	14.75	14.75	14.75	15.00	15.10	15.00	15.15	15.00	15.35	15.40	15.35	15.40	15.40				15.40	15.30	15.25	14.80	14.65	14.45	14.00
8	14.00	14.30		15.30															15.30						
9	14.40	15.30	15.80	15.30	15.80	15.80	15.70	15.70	15.70	15.70	16.00	16.10	16.10	16.00	16.00				16.00	15.60	15.50	15.00	14.20	14.10	14.20
10	12.00	13.60	13.80	13.60	13.50	13.70	13.80	13.80	14.00	14.70	14.30	14.40	14.50	14.40					14.40	14.40	14.10	14.00	14.10	13.50	14.10
n	10	10	9	10	9	9	9	9	9	7	7								10	9	9	9	9	9	9
Mean	13.78	14.94	15.23	15.35	15.36	15.51	15.47	15.34	15.33	15.42	15.56								15.71	15.53	15.43	14.99	14.66	14.46	14.21
SD	0.72	0.88	0.77	0.85	0.98	0.96	0.93	0.86	0.75	0.80	0.94								0.82	0.66	0.76	0.73	0.79	0.67	0.59
delta		1.16	1.45	1.57	1.59	1.74	1.70	1.56	1.55	1.65	1.78								1.93	1.75	1.65	1.22	0.88	0.69	0.43

1L																									
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	14.00	14.90	14.60	15.20	15.50	15.35	15.40	15.45	15.70	15.50	15.40	15.70	16.05						16.05	16.30	16.00	13.40	14.80	13.40	12.95
2	13.50	14.90	14.80	14.90	15.00	15.00	15.40	15.10	15.30	15.30	15.30	15.65	15.50						15.30	15.50	15.20	14.50	14.60	14.20	13.90
3	14.50	15.80	14.70	15.10	15.30	15.55	15.30	15.30	15.60	15.80	16.00	15.80	16.00	15.55					15.55	15.50	15.30	15.10	14.80	14.20	13.70
4	13.80	14.90	15.00	15.10	15.20	15.10	15.20	15.20	15.40	15.30	15.60	15.55	15.75						15.75	15.75	15.50	14.70	14.70	14.55	13.55
5	14.30	15.00	15.40	15.70	15.40	15.60	15.30	15.10	15.50	15.30	15.60								15.60	15.45	15.15	15.00	15.00	14.50	14.10
6	15.10	16.60	16.20	16.10	16.30	16.50	16.40	16.60	16.60	16.90	16.90	16.90	17.20	17.40					17.40	16.50	16.35	16.00	15.50	14.90	14.80
7	12.90	13.90	14.30	14.35	14.45	14.50	14.60	14.60	14.55	14.70	14.70	14.70	14.70	14.60	14.65				14.65	14.55	14.55	14.10	13.75	13.20	12.90
8	14.10	15.00	13.70	14.90	15.20	15.60	15.20	15.80	15.80	15.70	16.00	16.20	16.50						16.50	16.20	16.20	15.70	15.40	15.00	14.60
9	13.80	15.00	14.80	15.00	15.30	15.20	15.20	15.20	15.20	15.50	15.50	15.40	15.30	15.40	15.60	15.40	15.40	15.30	15.30	15.00	14.30	15.60	14.20	13.60	13.50
10	11.20	13.30	13.40	13.60	13.50	13.80	14.00	13.70	13.90	14.10	14.00								14.00	13.50	13.40	13.10	12.60	12.30	
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	9
Mean	13.72	14.93	14.69	15.00	15.12	15.22	15.20	15.21	15.36	15.41	15.50								15.61	15.43	15.20	14.72	14.54	13.99	13.78
SD	1.06	0.90	0.80	0.68	0.73	0.72	0.61	0.75	0.73	0.72	0.78								0.94	0.90	0.92	0.97	0.85	0.85	0.65
delta		1.21	0.97	1.28	1.40	1.50	1.48	1.49	1.64	1.69	1.78								1.89	1.71	1.48	1.00	0.82	0.27	0.06

Table A 1.5 Blood Hct_a (%) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery						
		Time (min)																							
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	40.55	45.80	46.10	46.80	46.40	47.55	46.30	46.75	47.35										47.35	46.95	46.70	45.70	45	43.4	41.45
2	39.85	45.65	46.25	47.05	46.00	46.45	46.55	44.15	46.40										46.40	43.60	44.75	43.50	42.75	42.55	41.85
3	43.95	47.95	48.15	48.35	48.10	49.00	48.65	48.35	49.00	48.45	48.40	48.20	48.45	48.55	48.75	49.05	49.90	49.50	49.50	48.60	47.35	48.75	46.85	46.65	45.75
4	39.65	43.15	44.05	44.10	43.95	44.10	44.50	43.10	44.05	45.00	45.20	45.40	45.70	45.30	46.10				46.10	44.30	45.05	43.45	42.05	39.25	37.90
5	44.00	45.20	45.90	46.10	45.80	45.60	46.10	45.35	46.20	46.15	46.75	46.30	46.95						46.95	46.10	45.55	44.85	43.75	44.7	44.10
6	43.40	47.90	47.85	48.25	48.85	48.35	48.45	47.85	48.30	49.20	49.15	48.90	48.75	49.00	49.40	50.55			50.55	49.85	49.65	47.35	46.2	43.8	42.75
7	39.20	43.15	43.45	43.40	43.80	44.65	44.95	44.80	44.75	45.35	45.75	45.75	46.00	45.90	46.40				46.40	45.45	45.45	44.80	43.2	42.6	41.20
8	43.00	45.85	46.60	47.75	47.95	47.15	47.90	47.65	48.55	48.50	49.20								49.20	48.40	47.85	47.70	46.5	44.85	43.35
9	41.40	45.30	46.30	46.90	45.50	45.90	46.40	45.20	46.30	46.40	46.90	46.40	47.10	47.30	49.00				49.00	46.00	45.70	44.40	43.70	42.00	40.50
10	38.30	42.40	42.80	42.90	42.40	42.90	42.80	42.30	42.40	43.10	43.10	43.60	43.70	43.20					43.20	42.80	42.4	40.00	39.30	36.80	36.80
n	10	10	10	10	10	10	10	10	10	10	8	8							10	10	10	10	10.00	10.00	10.00
Mean	41.33	45.24	45.75	46.16	45.88	46.17	46.26	45.55	46.33	46.52	46.81								47.47	46.21	46.05	45.05	43.93	42.66	41.57
SD	2.12	1.89	1.78	2.00	2.07	1.93	1.83	2.06	2.11	2.08	2.11								2.15	2.29	1.97	2.53	2.32	2.85	2.71
delta		3.91	4.42	4.83	4.55	4.83	4.93	4.22	5.00	5.19	5.48								6.14	4.88	4.72	3.72	2.60	1.33	0.24

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	39.85	44.48	45.10	46.50	46.20	47.45	46.80	46.75	47.35										47.35	46.95	46.70	45.70	45.2	43.4	42.45
2	40.40	44.70	45.00	45.80	45.40	45.75	45.30	44.75	45.45	45.15	45.45	46.30	46.00						46.00	46.4	44.75	44.7	44.10	42.40	42.10
3	39.30	45.30	46.05	46.65	47.00	47.00	47.45	46.75	47.15	42.20	47.40	47.50	46.70	48.05					48.05	46.5	46.85	46.85	44.40	43.65	42.35
4	39.45	42.55	43.30	44.00	43.35	43.75	44.00	43.75	44.35	44.70	44.80	44.60	45.50						45.50	45.1	44.4	44.40	42.35	40.30	38.20
5	41.85	45.45	44.85	47.10	45.20	45.45	46.30	44.50	46.40	46.45	46.30								46.30	45.2	44.75	44.45	44.00	42.80	40.80
6	42.70	45.80	46.85	46.50	46.25	46.50	47.10	47.15	47.75	48.00	48.65	48.30	48.88	48.20					48.20	47.00	47.00	45.60	44.35	42.50	42.60
7	37.95	41.50	42.25	43.05	42.85	43.30	42.85	42.60	43.30	43.15	43.50	43.60	43.55	43.7	43.05				43.05	44.50	42.80	41.50	40.65	38.50	38.05
8	41.10	43.60	44.40	43.50	40.50	45.60	45.50	42.70	46.00	45.40	37.05	46.70	45.95						45.95	45.80	46.30	43.65	43.40	42.05	41.20
9	39.60	43.40	43.40	44.00	43.70	43.60	43.30	43.40	43.10	43.10	44.40	43.90	44.20	44.00	44.50	44.40	43.70	44.50	44.50	44.00	42.40	42.40	45.60	37.60	37.60
10	36.00	39.40	40.60	41.20	40.70	41.10	41.20	40.50	40.80	41.10	40.90								40.90	40.6	40.3	38.70	37.70	36.70	36.50
n	10	10	10	10	10	10	10	10	10	9	9								10	10	10	10	10	10	10
Mean	39.82	43.62	44.18	44.83	44.12	44.95	44.98	44.29	45.17	44.36	44.27								45.58	45.21	44.63	43.80	43.18	40.99	40.19
SD	1.91	2.01	1.84	1.96	2.29	1.97	2.07	2.14	2.24	2.17	3.52								2.27	1.91	2.23	2.38	2.39	2.54	2.34
delta		3.80	4.36	5.01	4.29	5.13	5.16	4.46	5.35	4.54	4.45								5.76	5.38	4.81	3.97	3.35	1.17	0.36

Table A 1.6 Blood Hct_v (%) at rest, during and following high-intensity cycling exercise

2L

		Exercise																Recovery						
		Time (min)																						
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	40.45	43.05	44.35	46.60	45.80	46.65	46.10	46.10	46.40										46.40	46.30	47.20	44.30	44.50	42.35	40.65
2	41.65	43.15	45.05	46.05	46.00	46.30	45.90	45.25	44.75										44.75	46.15	45.65	43.90	42.75	41.80	41.20
3	42.50	47.45	48.15	47.60	48.45	48.70	48.55	47.90	48.45	47.85	47.30	46.65	47.60	48.90	49	47.7	49.3	49.45	49.45	48.95	47.60	47.70	47.20	46.05	45.20
4	39.50	42.85	43.60	44.40	43.80	44.35	43.15	43.65	43.15	43.00	44.00	43.40	43.70	45.45	46.30				46.30	44.60	44.30	42.50	39.10	43.90	37.80
5	43.20	46.25	46.50	47.25	47.05	46.60	46.40	46.30	46.10	45.60	46.90	47.55							47.55	46.80	46.65	45.05	44.00	43.85	43.70
6	40.00	47.55	47.00	48.05	48.10	47.70	49.00	48.25	46.60	47.00	49.15	47.85	49.30	49.40	49.70	49.90			49.90	48.10	48.25	47.35	46.45	44.50	45.35
7	39.85	43.45	44.65	43.45	43.60	44.25	44.95	45.10	44.90	45.00	45.25	45.80	45.15	45.45	45.75				45.75	45.55	45.35	44.75	43.95	42.95	41.40
8	41.20	41.85		44.90															44.90						
9	41.50	43.60	46.20	45.10	46.10	47.00	45.80	45.90	46.10	46.20	47.00	46.90	46.90	46.70	47.00				47.00	45.60	45.10	44.10	41.80	41.50	41.50
10	36.10	40.60	41.50	41.00	40.80	40.90	41.70	41.60	42.40	43.00	43.20	43.50	43.60	43.90					43.90	42.60	42.20	41.00	42.00	37.30	41.50
n	10	10	9	10	9	9	9	9	9	7	7								10	9	9	9	9	9	9
Mean	40.60	43.98	45.22	45.44	45.52	45.83	45.73	45.56	45.43	45.38	46.11								46.59	46.07	45.81	44.52	43.53	42.69	42.03
SD	1.97	2.34	2.00	2.15	2.43	2.33	2.31	2.04	1.85	1.87	2.07								1.96	1.86	1.87	2.11	2.47	2.47	2.38
delta		3.39	4.63	4.84	4.93	5.23	5.13	4.97	4.83	4.78	5.52								5.99	5.48	5.22	3.92	2.93	2.09	1.44

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	39.80	42.95	41.80	43.70	44.50	44.35	44.15	44.70	45.15	44.75	44.70	45.45	46.15						46.15	47.10	46.35	38.05	43.70	40.05	37.65
2	40.05	44.40	44.10	44.70	45.00	44.70	45.75	45.25	45.60	45.80	46.05	46.45	46.55						45.55	45.70	45.4	43.35	42.90	41.85	41.90
3	41.85	46.00	43.80	44.70	45.00	46.60	45.70	45.50	46.60	46.80	47.35	46.85	47.30	46.75					46.75	46.20	45.95	46.00	43.55	42.00	41.10
4	39.50	43.60	43.50	43.75	44.15	43.80	44.25	44.10	44.10	44.55	44.90	45.20	45.10						45.10	45.10	44.95	43.00	42.35	40.35	39.20
5	43.15	45.10	46.35	47.25	46.90	46.60	46.40	46.05	46.00	46.55	46.30								46.30	46.50	45.85	45.30	44.60	43.20	42.00
6	42.10	46.85	46.65	45.05	46.95	46.45	46.85	47.50	47.15	48.20	48.25	47.95	48.85	48.90					48.90	46.70	46.95	45.40	44.10	42.65	42.20
7	38.35	41.45	42.40	42.25	42.55	42.55	43.00	42.65	42.60	42.85	43.30	43.20	43.15	43.40	43.10				43.10	43.25	43.05	41.50	40.55	38.90	38.35
8	40.75	44.15	39.70	43.70	44.35	45.50	44.70	46.20	46.25	45.75	46.50	47.50	48.20						48.20	47.30	47.20	45.60	44.90	43.50	42.20
9	39.50	43.20	42.70	43.70	44.20	44.30	44.10	43.50	44.00	44.30	44.80	44.70	43.90	44.40	44.70	44.60	45.00	44.60	44.60	43.20	41.50	45.00	41.30	39.40	39.50
10	32.90	39.60	39.80	40.20	40.20	41.40	41.80	41.40	41.70	42.10	42.00								42.00	40.1	39.7	39.10	37.70	37.00	
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	9
Mean	39.80	43.73	43.08	43.90	44.38	44.63	44.67	44.69	44.92	45.17	45.42								45.67	45.12	44.69	43.23	42.57	40.89	40.46
SD	2.82	2.12	2.35	1.84	1.96	1.75	1.56	1.82	1.78	1.84	1.87								2.11	2.28	2.48	2.84	2.20	2.10	1.79
delta		3.94	3.29	4.11	4.59	4.83	4.88	4.89	5.12	5.37	5.62								5.87	5.32	4.90	3.44	2.77	1.10	0.66

Table A 1.7 Plasma $[Na^+]_a$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery					
		Time (min)																						
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	138.4	142.6	142.2	142.0	143.1	143.3	143.1	141.6	143.5	144.5	144.2								144.2	142.9	142.7	141.2	139.8	140.1	139.0
2	138.4	146.7	146.1	146.5	146.3	146.3	143.2	142.5	145.1										145.1		141.9	141.3	139.1	138.4	137.0
3	135.5	138.8	138.4	136.9	138.1	138.1	138.2	139.3	139.2	139.4	141.1	139.3	140.5	141.5	142.1	143.1	142.7	143.3	142.3	143.2	144.6	138.7	138.1	138.2	138.5
4	137.3	138.5	136.7	139.2	141.3	140.7	142.0	140.6	142.1	144.1	140.6	144.1	144.2	143.7	144.7				144.7	140.8	140.6	138.9	138.1	137.9	136.0
5	137.7	141.4	140.6	141.4	142.3	141.6	140.0	138.5	140.4	141.1	142.4	141.8	142.5						142.5	140.3	138.4	138.0	137.2	137.5	137.7
6	140.7	144.9	144.6	141.9	144.5	144.6	144.9	142.9	142.6	143.7	143.4	145.1	145.4	144.4	142.4	142.2			142.2	140.7	143.4	143.0	140.3	141.3	140.9
7	138.8	142.8	142.3	143.1	144.9	146.0	146.5	145.4	147.9	149.0	149.6	150.5	150.3	153.8	153.3				153.3	149.8	147.4	147.0	145.8	146.5	143.6
8	139.4	144.6	145.7	145.7	145.8	146.2	146.4	144.3	147.4	148.3	148.9								148.9	147.0	145.7	143.6	141.9	141.1	141.7
9	137.6	141.2	141.3	142.2	142.1	142.9	142.5	139.8	142.8	143.4	141.6	142.7	143.7	144.2	143.3				143.3	140.4	140.4	138.8	138.0	138.7	137.1
10	140.0	144.2	144.0	141.3	142.9	143.7	143.8	140.8	144.1	146.8	146.3	147.7	146.8	143.8					143.8	140.7	141.7	141.2	140.0	141.2	138.4
n	10	10	10	10	10	10	10	10	10	9	9								10	9	10	10	10	10	10
Mean	138.4	142.6	142.2	142.0	143.1	143.3	143.1	141.6	143.5	144.5	144.2								145.0	142.9	142.7	141.2	139.8	140.1	139.0
SD	1.5	2.7	3.1	2.8	2.4	2.7	2.6	2.2	2.8	3.2	3.3								3.5	3.4	2.7	2.8	2.5	2.7	2.4
delta		4.2	3.8	3.6	4.8	5.0	4.7	3.2	5.1	6.1	5.9								6.7	4.5	4.3	2.8	1.5	1.7	0.6

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	138.3	141.5	141.6	141.2	141.6	142.4	142.1	141.6	141.9	141.9	143.3								143.3	141.7	141.1	139.4	138.5	138.6	137.6
2	137.6	141.1	142.0	141.5	142.6	142.8	142.9	143.4	140.8	134.7	139.8	139.5	141.5						141.5	140.9	140.1	137.9	138.9	137.0	137.8
3	139.3	140.7	140.5	140.2	140.1	139.7	140.9	139.2	140.7	141.3									141.3			133.1	134.6	134.7	134.9
4	133.3	139.4	137.6	137.1	137.5	139.7	139.2	137.7	138.8	142.0	144.2	143.7	145.8						145.8	143.1	143.0	142.3	142.0	141.6	136.2
5	137.4	139.4	141.6	141.4	142.1	143.7	141.3	140.8	141.7	139.5	139.9								139.9	139.0	138.6	137.2	133.0	136.2	134.8
6	138.3	140.5	140.5	140.6	140.4	140.8	141.4	142.5	143.2	144.2	144.3	143.3	144.0	143.6					143.6	142.3	141.6	144.0	139.4	140.2	138.7
7	141.3	143.7	143.5	143.3	143.5	144.2	143.8	143.8	143.6	144.0	143.8	144.2	143.1	143.8	144.0				144.0	142.1	141.7	140.6	139.5	138.7	139.3
8	138.5	142.1	141.9	142.4	142.0	142.5	141.8	141.1	141.5	142.6	144.7	143.9	144.3						144.3	143.0	141.7	140.8	140.6	140.7	140.5
9	139.1	142.5	142.9	141.3	143.2	144.2	143.7	143.3	142.4	144.0	144.9	144.9	144.0	142.1	144.7	142.4	143.4	144.0	144.0	141.4	140.6	137.4	137.6	137.7	137.0
10	139.9	144.3	144.1	143.4	143.4	143.7	143.8	142.3	144.0	144.5	144.9								144.9	141.9	141.4	141.4	140.6	140.4	139.3
n	10	10	10	10	10	10	10	10	10	10	9								10	9	9	10	10	10	10
Mean	138.3	141.5	141.6	141.2	141.6	142.4	142.1	141.6	141.9	141.9	143.3								143.3	141.7	141.1	139.4	138.5	138.6	137.6
SD	2.1	1.7	1.8	1.8	1.9	1.7	1.5	2.0	1.6	3.0	2.0								1.8	1.2	1.2	3.1	2.8	2.2	1.9
delta		3.2	3.3	3.0	3.4	4.1	3.8	3.3	3.6	3.6	5.0								5.0	3.4	2.8	1.1	0.2	0.3	-0.7

Table A 1.8 Plasma $[Na^+]_v$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery					
		Time (min)																						
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	140.0	142.0	144.5	147.0	148.1	144.5	145.5	143.8	145.1										145.1		143.0	142.5	139.9	138.8	138.4
2	140.0	142.0	144.5	147.0	148.1	144.5	145.5	143.8	145.1										145.1		143.0	142.5	139.9	138.8	138.4
3	138.2	138.9	138.4	138.2	138.7	138.8	141.4	138.9	138.5	140.0	142.0	140.9	140.3	141.3	142.5	142.3	142.9	143.6	144.6	143.4	140.4	140.0	140.1	139.7	140.0
4	138.4	134.7	131.3	141.2	141.8	141.8	141.4	141.8	141.8	142.2	143.4	143.7	146.0	144.9	144.8				144.8	144.7	141.5	140.5	138.7	135.6	134.3
5	137.7	138.8	137.6	141.0	141.0	139.4	139.7	139.5	140.8	141.1	140.4	140.5							140.5	140.5	140.4	138.1	138.7	138.4	137.7
6	140.6	144.1	144.5	143.7	144.9	144.6	145.7	145.4	145.0	144.8	145.2	146.5	146.3	148.0	148.3	149.5			149.5	146.5	145.2	144.6	143.2	142.7	141.1
7	137.2	144.6	144.2	143.7	144.6	145.3	146.8	146.2	147.3	148.3	147.7	149.1	151.2	151.1	151.1				151.1	150.5	148.0	148.3	147.9	144.0	143.6
8	140.9	141.5	143.0	144.3															144.3						
9	138.1	140.9	143.1	142.2	142.9	143.3	143.7	141.6	143.0	144.1	142.7	144.4	144.3	144.5	144.4				144.4	141.8	141.2	140.0	140.2	139.2	139.0
10	140.9	142.8	141.2	141.7	143.3	144.1	142.8	144.9	144.9	145.5	146.9	146.4	146.3	145.0					145.0	143.0	142.9	142.1	141.7	142.5	140.0
n	10	10	10	10	9	9	9	9	9	7	7								10	7	9	9	9	9	9
Mean	139.2	141.0	141.2	143.0	143.7	142.9	143.6	142.9	143.5	143.7	144.0								145.4	144.3	142.8	142.1	141.1	140.0	139.2
SD	1.4	2.9	4.3	2.7	3.1	2.4	2.4	2.6	2.7	2.8	2.7								2.9	3.3	2.5	3.0	2.9	2.6	2.5
delta		1.8	2.0	3.8	4.5	3.7	4.4	3.7	4.3	4.5	4.9								6.3	5.2	3.7	2.9	2.0	0.8	0.0

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	137.3	140.3	140.1	142.6	142.2	142.8	142.8	141.7	141.8	141.8	143.6	143.3	144.6						144.6	143.7	142.4	140.4	139.0	139.7	139.7
2	138.4	140.7	141.0	142.2	142.4	143.8	145.6	141.7	140.8	133.8	140.2	142.4	143.4						143.4	140.1	138.7	139.0	137.3	138.3	137.4
3	141.5	141.1	140.0	141.1	140.3	140.0	140.0	141.5	140.5	142.6									142.6				136.2	135.8	137.0
4	134.3	138.6	137.5	138.0	137.1	139.7	139.5	137.8	142.6	144.1	144.5	145.1	145.9						145.9	144.9	144.4	143.2	143.3	137.7	137.0
5	138.4	139.2	140.5	141.9	142.1	141.0	142.4	142.2	142.0	139.9	139.9								139.9	140.1	139.3	138.7	136.9	135.7	134.6
6	139.7	141.0	141.1	141.7	141.4	141.9	142.3	143.3	144.1	144.1	145.1	144.9	145.3	144.4					144.4	143.7	143.3	141.1	139.8	139.8	139.2
7	141.8	142.9	144.1	143.8	143.2	143.9	143.6	143.6	143.4	143.4	144.1	144.2	143.9	144.3	144.8				144.8	144.5	142.1	140.7	140.0	139.8	139.4
8	139.8	142.2	141.9	142.4	141.9	142.5	141.7	142.0	142.1	143.0	144.1	143.9	144.8						144.8	145.4	143.6	141.7	141.0	141.1	138.8
9	138.8	141.1	141.4	142.7	144.3	144.7	145.4	144.4	145.4	145.7	145.9	146.5	146.0	145.4	144.8	144.1	146.1	145.3	145.3	143.9	142.8	137.3	137.9	138.5	138.0
10	141.1	140.5	141.7	144.8	144.4	144.6	145.3	144.7	144.5	146.4	148.4								148.4	144.9	144.0	143.1	142.5	141.3	
n	10	10	10	10	10	10	10	10	10	10	9								10	9	9	9	10	10	9
Mean	139.1	140.8	140.9	142.1	141.9	142.5	142.9	142.3	142.7	142.5	144.0								144.4	143.5	142.3	140.6	139.4	138.8	137.9
SD	2.2	1.3	1.7	1.8	2.1	1.8	2.2	2.0	1.6	3.6	2.6								2.2	2.0	2.0	2.0	2.4	2.0	1.6
delta		1.7	1.8	3.0	2.8	3.4	3.8	3.2	3.6	3.4	4.9								5.3	4.4	3.2	1.5	0.3	-0.3	-1.2

Table A 1.9 Plasma $[Ca^{2+}]_a$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery						
		Time (min)																							
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.18	1.27	1.28	1.31	1.30	1.29	1.24	1.24	1.27										1.27		1.25	1.23	1.21	1.19	1.18
2	1.21	1.27	1.30	1.30	1.30	1.29	1.29	1.26	1.28										1.28	1.21	1.20	1.22	1.23	1.23	1.23
3	1.21	1.25	1.24	1.23	1.23	1.23	1.22	1.21	1.21	1.22	1.21	1.20	1.20	1.21	1.21	1.22	1.22	1.22	1.24	1.24	1.24	1.20	1.19	1.17	1.20
4	1.21	1.27	1.23	1.25	1.26	1.25	1.24	1.22	1.24	1.27	1.26	1.27	1.28	1.27	1.29				1.29	1.24	1.24	1.21	1.19	1.20	1.18
5	1.19	1.22	1.22	1.21	1.20	1.19	1.19	1.15	1.16	1.16	1.18	1.18	1.20						1.20	1.18	1.17	1.12	1.14	1.14	1.14
6	1.19	1.25	1.24	1.23	1.24	1.24	1.24	1.19	1.22	1.22	1.21	1.22	1.21	1.19	1.19	1.18			1.18	1.14	0.99	1.20	1.18	1.18	1.17
7	1.20	1.23	1.25	1.24	1.27	1.26	1.27	1.26	1.27	1.28	1.26	1.28	1.28	1.30	1.31				1.31	1.29	1.25	1.26	1.24	1.24	1.20
8	1.21	1.24	1.26	1.26	1.25	1.22	1.24	1.20	1.25	1.27	1.30								1.30	1.30	1.28	1.25	1.24	1.19	1.18
9	1.19	1.23	1.25	1.23	1.21	1.21	1.21	1.20	1.22	1.23	1.25	1.24	1.23	1.23	1.25				1.25	1.19	1.20	1.16	1.14	1.15	1.14
10	1.19	1.21	1.23	1.22	1.20	1.21	1.21	1.18	1.19	1.24	1.20	1.24	1.22	1.21					1.21	1.16	1.18	1.13	1.12	1.11	1.11
n	10	10	10	10	10	10	10	10	10	8	8								10	9	10	10	10	10	10
Mean	1.20	1.24	1.25	1.25	1.25	1.24	1.24	1.21	1.23	1.24	1.23								1.25	1.22	1.20	1.20	1.19	1.18	1.17
SD	0.01	0.02	0.02	0.03	0.04	0.03	0.03	0.04	0.04	0.04	0.04								0.04	0.06	0.08	0.05	0.04	0.04	0.03
delta		0.05	0.05	0.05	0.05	0.04	0.04	0.01	0.03	0.04	0.04								0.06	0.02	0.00	0.00	-0.01	-0.02	-0.02

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.19	1.21	1.22	1.21	1.20	1.20	1.19	1.17	1.16	1.18	1.18	1.18	1.20						1.20	1.18	1.17	1.15	1.16	1.17	1.17
2	1.18	1.25	1.24	1.24	1.23	1.23	1.23	1.25	1.27	1.26	1.27	1.28	1.28						1.28	1.27	1.25	1.23	1.20	1.21	1.20
3	1.08	1.23	1.23	1.24	1.24	1.25	1.24	1.21	1.25	1.25	1.21	1.21	1.22	1.24					1.24	1.20	1.21	1.17	1.18	1.18	1.11
4	1.21	1.23	1.24	1.25	1.25	1.27	1.28	1.29	1.30	1.27	1.27	1.27	1.29						1.29	1.26	1.25	1.26	1.24	1.22	1.20
5	1.21	1.22	1.22	1.23	1.20	1.25	1.23	1.23	1.24	1.22	1.21								1.21	1.21	1.20	1.17	1.18	1.21	1.19
6	1.19	1.21	1.21	1.21	1.20	1.19	1.19	1.21	1.21	1.23	1.24	1.23	1.21	1.16					1.16	1.22	1.20	1.22	1.17	1.18	1.18
7	1.19	1.24	1.24	1.23	1.22	1.22	1.21	1.21	1.21	1.21	1.21	1.21	1.19	1.21	1.20				1.20	1.22	1.22	1.21	1.19	1.19	1.19
8	1.16	1.15	1.18	1.19	1.10	1.20	1.19	1.11	1.18	1.21	1.20	1.20	1.20						1.20	1.20	1.20	1.17	1.15	1.14	1.14
9	1.21	1.24	1.25	1.22	1.24	1.25	1.24	1.23	1.21	1.22	1.22	1.22	1.20	1.21	1.24	1.21	1.22	1.22	1.22	1.22	1.21	1.19	1.20	1.20	1.20
10	1.15	1.22	1.22	1.22	1.21	1.20	1.21	1.17	1.20	1.20	1.21								1.21	1.19	1.18	1.18	1.16	1.17	1.17
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	10
Mean	1.18	1.22	1.23	1.22	1.21	1.23	1.22	1.21	1.22	1.23	1.22								1.22	1.22	1.21	1.20	1.18	1.19	1.18
SD	0.04	0.03	0.02	0.02	0.04	0.03	0.03	0.05	0.04	0.03	0.03								0.04	0.03	0.03	0.03	0.03	0.02	0.03
delta		0.04	0.05	0.05	0.03	0.05	0.04	0.03	0.05	0.05	0.04								0.04	0.04	0.03	0.02	0.01	0.01	0.00

Table A 1.10 Plasma $[Ca^{2+}]_v$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery				
		Time (min)																					
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	1.19	1.26	1.28	1.28	1.28	1.26	1.26	1.25	1.26										1.26		1.27	1.22	1.21	1.20	1.17
2	1.23	1.25	1.26	1.25	1.30	1.26	1.24	1.23	1.24										1.24	1.26	1.27	1.22	1.21	1.22	1.22
3	1.21	1.27	1.25	1.24	1.25	1.24	1.23	1.22	1.21	1.22	1.20	1.20	1.20	1.22	1.22	1.19	1.21	1.23	1.24	1.21	1.19	1.20	1.19	1.21	1.21
4	1.23	1.26	1.30	1.28	1.25	1.26	1.24	1.23	1.22	1.25	1.26	1.25	1.28	1.28	1.29				1.29	1.28	1.25	1.21	1.17	1.18	1.16
5	1.17	1.22	1.14	1.24	1.21	1.20	1.19	1.16	1.15	1.15	1.17	1.19							1.19	1.20	1.21	1.16	1.16	1.16	1.14
6	1.17	1.29	1.26	1.27	1.26	1.26	1.25	1.24	1.25	1.27	1.25	1.23	1.28	1.28	1.31	1.31			1.31	1.23	1.24	1.20	1.19	1.17	1.17
7	1.22	1.28	1.27	1.27	1.28	1.28	1.28	1.27	1.30	1.31	1.27	1.28	1.29	1.30	1.30				1.30	1.29	1.27	1.28	1.26	1.19	1.21
8	1.18	1.17	1.19	1.20	1.22	1.22	1.24	1.21	1.23										1.20	1.21	1.20	1.18	1.16	1.17	1.15
9	1.17	1.18	1.23	1.17	1.21	1.21	1.21	1.17	1.20	1.21	1.22	1.22	1.21	1.21	1.21				1.21	1.19	1.18	1.17	1.14	1.16	1.18
10	1.12	1.17	1.18	1.16	1.17	1.20	1.19	1.19	1.22	1.24	1.26	1.26	1.25	1.23					1.23	1.16	1.15	1.13	1.11	1.14	1.07
n	10	10	10	10	10	10	10	10	10	7	7								10	9	10	10	10	10	10
Mean	1.19	1.24	1.24	1.24	1.24	1.24	1.23	1.22	1.23	1.24	1.23								1.25	1.23	1.22	1.20	1.18	1.18	1.17
SD	0.03	0.05	0.05	0.04	0.04	0.03	0.03	0.03	0.04	0.05	0.04								0.04	0.04	0.04	0.04	0.04	0.02	0.04
delta		0.05	0.05	0.05	0.05	0.05	0.04	0.03	0.04	0.05	0.04								0.06	0.04	0.03	0.01	-0.01	-0.01	-0.02

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	1.21	1.27	1.26	1.28	1.28	1.28	1.28	1.26	1.27	1.27	1.29	1.27	1.28						1.28	1.30	1.30	1.26	1.24	1.22	1.22
2	1.19	1.25	1.23	1.22	1.22	1.25	1.26	1.24	1.27	1.26	1.27	1.28	1.28						1.28	1.25	1.23	1.22	1.21	1.18	1.19
3	1.16	1.25	1.21	1.19	1.19	1.21	1.17	1.22	1.19	1.27	1.22	1.22	1.23	1.25					1.25	1.21	1.18	1.15	1.14	1.16	1.09
4	1.21	1.25	1.26	1.27	1.27	1.29	1.29	1.29	1.26	1.29	1.28	1.29	1.29						1.29	1.29	1.27	1.26	1.24	1.20	1.21
5	1.22	1.25	1.27	1.29	1.28	1.26	1.28	1.28	1.26	1.23	1.24								1.24	1.23	1.21	1.20	1.21	1.21	1.21
6	1.16	1.26	1.25	1.21	1.22	1.22	1.21	1.22	1.23	1.24	1.26	1.24	1.23	1.23					1.23	1.21	1.20	1.19	1.17	1.17	1.17
7	1.20	1.24	1.27	1.26	1.25	1.25	1.24	1.24	1.24	1.24	1.24	1.24	1.23	1.25	1.26				1.26	1.24	1.23	1.21	1.20	1.20	1.19
8	1.17	1.21	1.15	1.17	1.19	1.21	1.20	1.21	1.22	1.21	1.19	1.22	1.24						1.24	1.24	1.22	1.19	1.17	1.16	1.15
9	1.18	1.25	1.25	1.27	1.25	1.27	1.26	1.26	1.25	1.25	1.26	1.25	1.23	1.24	1.24	1.24	1.26	1.25	1.25	1.24	1.19	1.20	1.18	1.19	1.19
10	1.07	1.20	1.22	1.21	1.22	1.25	1.26	1.24	1.24	1.26	1.28								1.28	1.25	1.22	1.20	1.18	1.16	
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	9
Mean	1.18	1.24	1.24	1.24	1.24	1.25	1.25	1.25	1.24	1.25	1.25								1.26	1.25	1.23	1.21	1.19	1.19	1.18
SD	0.04	0.02	0.04	0.04	0.03	0.03	0.04	0.03	0.02	0.02	0.03								0.02	0.03	0.04	0.03	0.03	0.02	0.04
delta		0.07	0.06	0.06	0.06	0.07	0.07	0.07	0.07	0.08	0.08								0.08	0.07	0.05	0.03	0.02	0.01	0.00

Table A 1.11 Plasma $[Cl^-]_a$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery				
		Time (min)																					
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	102.0	106.0	106.0	107.0	106.0	107.0	108.0	105.0	107.0										107.0		104.0	103.0	103.0	102.0	104.0
2	102.0	105.0	105.0	105.0	104.0	104.0	103.0	102.0	103.0										103.0	100.0	104.0	100.0	100.0	101.0	101.0
3	100.0	102.0	103.0	102.0	103.0	103.0	103.0	102.0	103.0	103.0	103.0	102.0	103.0	104.0	105.0	106.0	106.0	106.0	103.0	104.0	105.0	100.0	100.0	102.0	101.0
4	101.0	104.0	105.0	103.0	103.0	104.0	103.0	102.0	103.0	103.0	105.0	105.0	103.0	104.0	104.0				104.0	101.0	100.0	101.0	101.0	100.0	101.0
5	103.0	105.0	105.0	105.0	105.0	104.0	103.0	103.0	104.0	105.0	104.0	105.0	105.0						105.0	103.0	103.0	104.0	102.0	103.0	104.0
6	103.0	105.0	106.0	105.0	105.0	105.0	105.0	103.0	104.0	105.0	106.0	106.0	107.0	107.0	107.0	107.0			107.0	102.0	102.0	102.0	102.0	103.0	103.0
7	106.0	105.0	106.0	106.0	107.0	107.0	107.0	106.0	107.0	107.0	108.0	108.0	109.0	108.0	109.0				109.0	104.0	104.0	103.0	103.0	103.0	105.0
8	105.0	109.0	109.0	108.0	108.0	108.0	108.0	107.0	109.0	109.0	110.0								110.0	105.0	103.0	103.0	102.0	104.0	105.0
9	106.0	109.0	107.0	109.0	108.0	109.0	108.0	106.0	108.0	109.0	109.0	109.0	109.0	110.0	110.0				110.0	105.0	104.0	105.0	106.0	106.0	106.0
10	105.0	107.0	106.0	107.0	107.0	106.0	106.0	103.0	105.0	106.0	107.0	106.0	106.0	107.0					107.5	103.0	103.0	105.0	105.0	105.0	105.0
n	10	10	10	10	10	10	10	10	10	8	8								10	9	10	10	10	10	10
Mean	103.3	105.7	105.8	105.7	105.6	105.7	105.4	103.9	105.3	105.9	106.5								106.6	103.0	103.2	102.6	102.4	102.9	103.5
SD	2.1	2.2	1.5	2.2	1.9	2.0	2.3	1.9	2.3	2.4	2.4								2.7	1.7	1.4	1.8	2.0	1.8	1.9
delta		2.40	2.50	2.40	2.30	2.40	2.10	0.60	2.00	2.58	3.20								3.25	-0.30	-0.10	-0.70	-0.90	-0.40	0.20

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	104.0	105.0	105.0	105.0	104.0	104.0	104.0	102.0	104.0	106.0	106.0	107.0	106.0						106.0	101.0	100.0	101.0	101.0	101.0	103.0
2	108.0	102.0	102.0	102.0	101.0	100.0	100.0	99.0	99.0	99.0	102.0	103.0	103.0	102.0					102.0	101.0	99.0	100.0	99.0	100.0	104.0
3	103.0	105.0	106.0	106.0	106.0	105.0	105.0	104.0	104.0	104.0	105.0	106.0	105.0						105.0	105.0	102.0	100.0	101.0	101.0	102.0
4	102.0	103.0	105.0	104.0	104.0	101.0	101.0	101.0	101.0	101.0	102.0								102.0	102.0	102.0	100.0	101.0	102.0	103.0
5	104.0	107.0	108.0	107.0	107.0	107.0	106.0	107.0	107.0	106.0	106.0	106.0	107.0	108.0					108.0	102.0	102.0	100.0	103.0	103.0	103.0
6	104.0	105.0	106.0	104.0	105.0	105.0	105.0	105.0	105.0	106.0	106.0	105.0	107.0	106.0	107.0				107.0	103.0	103.0	103.0	103.0	103.0	103.0
7	108.0	111.0	110.0	110.0	114.0	108.0	108.0	110.0	108.0	109.0	121.0	108.0	109.0						109.0	106.0	104.0	104.0	103.0	104.0	105.0
8	106.0	108.0	109.0	110.0	108.0	107.0	108.0	108.0	107.0	109.0	108.0	107.0	107.0	107.0	107.0	108.0	108.0	108.0	108.0	105.0	105.0	105.0	106.0	106.0	106.0
9	105.0	106.0	106.0	105.0	105.0	106.0	105.0	104.0	105.0	106.0	106.0								106.0	103.0	103.0	103.0	103.0	104.0	103.0
10	107.0	110.0	110.0	109.0	111.0	110.0	109.0	108.0	109.0	110.0									110.0	107.0	106.0	107.0	107.0	108.0	108.0
n	10	10	10	10	10	10	10	10	10	10	9								10	10	10	10	10	10	10
Mean	105.1	106.2	106.7	106.2	106.5	105.3	105.1	104.8	104.9	105.6	106.9								106.3	103.5	102.6	102.3	102.7	103.2	104.0
SD	2.1	2.9	2.5	2.7	3.7	3.1	2.9	3.5	3.1	3.5	5.6								2.7	2.1	2.1	2.5	2.4	2.4	1.8
delta		1.10	1.60	1.10	1.40	0.20	0.00	-0.30	-0.20	0.50	1.79								1.20	-1.60	-2.50	-2.80	-2.40	-1.90	-1.10

Table A 1.12 Plasma $[Cl^-]_v$ (mM) at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery						
		Time (min)																							
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	103.0	102.0	104.0	105.0	106.0	109.0	106.0	104.0	105.0										105.0	105.0	105.0	105.0	104.0	102.0	104.0
2	102.0	103.0	102.0	104.0	103.0	104.0	105.0	102.0	104.0										104.0	103.0	101.0	102.0	101.0	102.0	102.0
3	101.0	100.0	101.0	101.0	102.0	102.0	102.0	101.0	103.0	103.0	104.0	103.0	103.0	104.0	104.0	105.0	105.0	105.0	105.0	105.0	103.0	101.0	101.0	101.0	101.0
4	101.0	100.0	100.0	102.0	103.0	102.0	102.0	102.0	103.0	102.0	103.0	104.0	102.0	103.0	103.0				103.0	101.0	101.0	101.0	102.0	101.0	103.0
5	103.0	102.0	103.0	102.0	103.0	102.0	102.0	102.0	104.0	105.0	103.0	103.0							103.0	104.0	103.0	103.0	103.0	103.0	104.0
6	104.0	101.0	101.0	101.0	102.0	102.0	103.0	102.0	103.0	103.0	103.0	105.0	105.0	103.0	104.0	104.0			104.0	105.0	104.0	103.0	102.0	103.0	103.0
7	105.0	104.0	104.0	104.0	104.0	105.0	105.0	105.0	105.0	105.0	106.0	106.0	106.0	106.0	106.0				106.0	105.0	105.0	104.0	103.0	105.0	104.0
8	106.0	108.0	107.0	108.0	108.0	107.0	107.0	108.0	107.0										108.0	105.0	105.0	103.0	103.0	103.0	104.0
9	106.0	107.0	107.0	109.0	107.0	108.0	108.0	107.0	107.0	109.0	109.0	109.0	110.0	109.0	110.0				110.0	107.0	106.0	105.0	107.0	107.0	105.0
10	107.0	104.0	103.0	104.0	104.0	105.0	103.0	105.0	102.0	102.0	102.0	101.0	102.0	103.0					103.0	106.0	105.0	105.0	106.0	104.0	106.0
n	10	10	10	10	10	10	10	10	10	7	7								10	10	10	10	10	10	10
Mean	103.8	103.1	103.2	104.0	104.2	104.6	104.3	103.8	104.3	104.1	104.3								105.1	104.6	103.8	103.2	103.2	103.1	103.6
SD	2.1	2.7	2.4	2.7	2.1	2.7	2.2	2.4	1.7	2.5	2.4								2.3	1.6	1.8	1.5	2.0	1.9	1.4
delta		-0.70	-0.60	0.20	0.40	0.80	0.50	0.00	0.50	0.34	0.49								1.30	0.80	0.00	-0.60	-0.60	-0.70	-0.20

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fatigue	+1	+2	+5	+10	+20	+30
1	101.0	102.0	102.0	102.0	102.0	103.0	102.0	101.0	101.0	102.0	102.0	104.0	104.0						104.0	103.0	102.0	102.0	101.0	101.0	101.0
2	104.0	103.0	104.0	103.0	104.0	103.0	102.0	102.0	102.0	103.0	102.0	103.0	103.0						103.0	102.0	102.0	101.0	100.0	102.0	103.0
3	104.0	100.0	101.0	102.0	102.0	100.0	102.0	99.0	100.0	99.0	102.0	102.0	102.0	101.0					101.0	101.0	101.0	102.0	102.0	101.0	106.0
4	103.0	104.0	105.0	105.0	105.0	105.0	105.0	103.0	103.0	104.0	105.0	105.0	104.0						104.0	103.0	102.0	101.0	101.0	102.0	102.0
5	101.0	101.0	100.0	100.0	100.0	100.0	99.0	100.0	100.0	100.0	101.0								101.0	101.0	102.0	100.0	101.0	101.0	101.0
6	105.0	103.0	103.0	104.0	104.0	105.0	105.0	105.0	106.0	105.0	105.0	106.0	105.0	105.0					105.0	104.0	104.0	103.0	103.0	104.0	104.0
7	104.0	102.0	103.0	102.0	103.0	103.0	103.0	103.0	104.0	104.0	104.0	104.0	104.0	104.0	104.0				104.0	103.0	104.0	104.0	103.0	103.0	103.0
8	107.0	105.0	109.0	108.0	107.0	105.0	106.0	106.0	105.0	105.0	107.0	106.0	105.0						108.0	106.0	104.0	104.0	103.0	103.0	103.0
9	107.0	105.0	105.0	105.0	105.0	106.0	106.0	104.0	105.0	106.0	105.0	106.0	107.0	107.0	107.0	107.0	108.0	108.0	108.0	106.0	107.0	105.0	106.0	106.0	107.0
10	109.0	104.0	103.0	104.0	103.0	102.0	102.0	101.0	102.0	103.0	103.0								103.0	101.0	101.0	103.0	103.0	103.0	102.0
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	10
Mean	104.5	102.9	103.5	103.5	103.5	103.2	103.2	102.4	102.8	103.1	103.6								104.1	103.0	102.9	102.5	102.3	102.6	103.2
SD	2.6	1.7	2.5	2.2	2.0	2.1	2.3	2.2	2.1	2.2	1.9								2.4	1.9	1.9	1.6	1.7	1.6	2.0
delta		-1.60	-1.00	-1.00	-1.00	-1.30	-1.30	-2.10	-1.70	-1.40	-0.90								-0.40	-1.50	-1.60	-2.00	-2.20	-1.90	-1.30

Table A 1.13 Plasma pH_a at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery				
		Time (min)																					
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.44	7.29	7.27	7.24	7.24	7.21	7.21	7.21	7.22										7.22	7.18	7.18	7.16	7.20	7.29	7.40
2	7.41	7.38	7.38	7.37	7.39	7.41	7.43	7.40	7.43	7.47	7.49	7.52	7.46						7.46	7.34	7.34	7.33	7.36	7.38	7.39
3	7.44	7.38	7.39	7.37	7.38	7.37	7.38	7.39	7.39	7.39	7.36	7.36	7.38	7.38	7.38	7.36	7.34	7.35	7.32	7.28	7.30	7.30	7.34	7.38	7.41
4	7.43	7.33	7.31	7.30	7.31	7.32	7.31	7.31	7.34	7.33	7.32	7.31	7.31	7.31	7.30				7.30	7.29	7.25	7.27	7.30	7.35	7.40
5	7.42	7.39	7.37	7.37	7.37	7.37	7.38	7.38	7.41	7.42	7.41	7.40	7.38						7.38	7.33	7.30	7.31	7.34	7.37	7.41
6	7.44	7.38	7.38	7.39	7.39	7.39	7.39	7.41	7.43	7.43	7.42	7.40	7.38	7.40	7.39	7.36			7.36	7.27	7.25	7.26	7.32	7.38	7.41
7	7.42	7.35	7.34	7.34	7.34	7.34	7.35	7.35	7.36	7.38	7.37	7.38	7.37						7.33	7.28	7.26	7.27	7.30	7.35	7.39
8	7.39	7.34	7.29	7.28	7.28	7.27	7.27	7.27	7.26	7.26	7.23	7.38	7.37						7.23	7.18	7.12	7.11	7.13	7.24	7.31
9	7.40	7.37	7.34	7.36	7.38	7.38	7.38	7.38	7.39	7.39	7.38	7.37	7.38	7.36	7.33				7.33	7.29	7.29	7.30	7.33	7.38	7.39
10	7.44	7.35	7.35	7.35	7.36	7.36	7.38	7.40	7.41	7.38	7.38	7.38	7.37	7.35					7.35	7.34	7.33	7.34	7.36	7.38	7.42
n	10	10	10	10	10	10	10	10	10	9	9								10	10	10	10	10	10	10
Mean	7.42	7.36	7.34	7.34	7.34	7.34	7.35	7.35	7.36	7.38	7.37								7.33	7.28	7.26	7.27	7.30	7.35	7.39
SD	0.02	0.03	0.04	0.05	0.05	0.06	0.06	0.06	0.07	0.06	0.07								0.07	0.06	0.07	0.07	0.07	0.05	0.03
delta		-0.07	-0.08	-0.09	-0.08	-0.08	-0.07	-0.07	-0.06	-0.04	-0.05								-0.09	-0.15	-0.16	-0.16	-0.12	-0.07	-0.03

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.40	7.36	7.34	7.34	7.33	7.36	7.36	7.36	7.39										7.39	7.34	7.32	7.34	7.37	7.369	7.349
2	7.43	7.38	7.37	7.37	7.37	7.36	7.37	7.39	7.40	7.33	7.39	7.38	7.38	7.36					7.36	7.36	7.31	7.32	7.33	7.358	7.385
3	7.40	7.37	7.36	7.36	7.37	7.36	7.36	7.35	7.37	7.36	7.36	7.37	7.36						7.36	7.33	7.33	7.30	7.32	7.358	7.364
4	7.43	7.40	7.38	7.37	7.37	7.37	7.37	7.35	7.37	7.37	7.38								7.38	7.36	7.35	7.32	7.36	7.371	7.393
5	7.41	7.40	7.38	7.39	7.38	7.39	7.39	7.38	7.39	7.39	7.40	7.41	7.46	7.47					7.47	7.34	7.32	7.32	7.36	7.375	7.392
6	7.43	7.41	7.40	7.39	7.41	7.40	7.38	7.40	7.41	7.42	7.41	7.44	7.46	7.45	7.45				7.45	7.37	7.32	7.34	7.37	7.408	7.425
7	7.41	7.36	7.35	7.33	7.34	7.32	7.33	7.34	7.36	7.32	7.33	7.32	7.31						7.31	7.28	7.25	7.23	7.27	7.334	7.367
8	7.41	7.39	7.38	7.39	7.38	7.39	7.40	7.40	7.38	7.38	7.40	7.37	7.37	7.40	7.39	7.40	7.39	7.39	7.39	7.34	7.34	7.35	7.36	7.384	7.393
9	7.44	7.39	7.39	7.38	7.38	7.38	7.38	7.41	7.40	7.39	7.40								7.40	7.38	7.38	7.40	7.38	7.416	7.396
10	7.47	7.33	7.34	7.31	7.32	7.32	7.33	7.35	7.33	7.35									7.35	7.36	7.35	7.37	7.39	7.404	7.405
n	10	10	10	10	10	10	10	10	10	9	8								10	10	10	10	10	10	10
Mean	7.42	7.38	7.37	7.36	7.37	7.37	7.37	7.37	7.38	7.37	7.38								7.39	7.34	7.33	7.33	7.35	7.38	7.39
SD	0.02	0.03	0.02	0.03	0.03	0.03	0.02	0.03	0.02	0.03	0.03								0.05	0.03	0.03	0.04	0.04	0.03	0.02
delta		-0.04	-0.05	-0.06	-0.06	-0.06	-0.06	-0.05	-0.04	-0.05	-0.04								-0.04	-0.08	-0.10	-0.09	-0.07	-0.04	-0.04

Table A 1.14 Plasma pH_v at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery					
		Time (min)																						
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.39	7.25	7.23	7.21	7.20	7.37	7.25	7.37	7.38									7.18	7.18	7.18	7.16	7.19	7.28	7.36
2	7.37	7.34	7.33	7.33	7.37	7.36	7.37	7.34	7.34	7.36	7.37	7.37	7.37					7.37	7.36	7.34	7.33	7.34	7.36	7.38
3	7.37	7.31	7.32	7.32	7.34	7.35	7.36	7.36	7.38	7.37	7.37	7.35	7.37	7.37	7.36	7.35	7.35	7.32	7.33	7.23	7.30	7.29	7.31	7.37	7.36
4	7.35	7.30	7.25	7.26	7.27	7.28	7.27	7.29	7.29	7.29	7.28	7.27	7.25	7.26	7.25				7.25	7.23	7.23	7.23	7.28	7.32	7.35
5	7.42	7.37	7.35	7.35	7.35	7.36	7.36	7.36	7.36	7.38	7.38	7.38	7.38						7.38	7.33	7.31	7.30	7.33	7.36	7.39
6	7.37	7.30	7.29	7.27	7.33	7.32	7.34	7.34	7.34	7.36	7.34	7.34	7.32	7.27	7.25	7.21			7.21	7.19	7.24	7.25	7.28	7.37	7.40
7	7.38	7.32	7.30	7.29	7.24	7.26	7.30	7.31	7.32	7.35	7.37	7.35	7.35						7.28	7.26	7.27	7.28	7.30	7.35	7.37
8	7.36	7.31	7.27	7.24	7.25	7.35	7.32	7.33	7.33	7.41	7.46	7.35	7.36						7.53	7.26	7.27	7.28	7.30	7.35	7.37
9	7.38	7.34	7.34	7.34	7.35	7.36	7.36	7.36	7.37	7.36	7.36	7.35	7.35	7.34	7.33				7.33	7.28	7.28	7.30	7.33	7.36	7.38
10	7.41	7.35	7.34	7.31	7.32	7.31	7.30	7.34	7.32	7.32	7.31	7.30	7.28	7.24					7.24	7.31	7.32	7.34	7.35	7.31	7.33
n	10	10	10	10	10	10	10	10	10	9	9								10	10	10	10	10	10	10
Mean	7.38	7.32	7.30	7.29	7.30	7.33	7.32	7.34	7.34	7.35	7.36								7.31	7.26	7.27	7.28	7.30	7.34	7.37
SD	0.02	0.03	0.04	0.05	0.06	0.04	0.04	0.03	0.03	0.03	0.05								0.10	0.06	0.05	0.05	0.04	0.03	0.02
delta		-0.06	-0.08	-0.09	-0.08	-0.05	-0.06	-0.04	-0.04	-0.03	-0.02								-0.07	-0.12	-0.11	-0.10	-0.08	-0.04	-0.01

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.45	7.32	7.29	7.29	7.30	7.30	7.29	7.28	7.27	7.28	7.27	7.29	7.28						7.28	7.30	7.27	7.25	7.27	7.350	7.388
2	7.35	7.31	7.29	7.29	7.29	7.33	7.35	7.31	7.36										7.36	7.34	7.33	7.34	7.38	7.386	7.415
3	7.36	7.29	7.27	7.28	7.30	7.30	7.30	7.33	7.33	7.40	7.35	7.33	7.34	7.30					7.30	7.32	7.34	7.30	7.32	7.346	7.345
4	7.38	7.33	7.33	7.34	7.35	7.35	7.35	7.33	7.34	7.33	7.34	7.34	7.33						7.33	7.31	7.29	7.29	7.31	7.344	7.360
5	7.39	7.33	7.32	7.30	7.29	7.30	7.30	7.30	7.31	7.32	7.33								7.33	7.31	7.32	7.31	7.32	7.357	7.359
6	7.33	7.31	7.27	7.29	7.31	7.35	7.36	7.37	7.38	7.39	7.36	7.38	7.37	7.39					7.39	7.34	7.33	7.32	7.36	7.376	7.382
7	7.39	7.35	7.32	7.34	7.35	7.35	7.34	7.36	7.35	7.36	7.37	7.36	7.37	7.36	7.36				7.36	7.35	7.32	7.33	7.35	7.380	7.402
8	7.33	7.26	7.26	7.25	7.25	7.24	7.25	7.27	7.28	7.27	7.28	7.27	7.26						7.26	7.25	7.24	7.23	7.26	7.325	7.343
9	7.38	7.31	7.31	7.32	7.32	7.34	7.35	7.33	7.31	7.33	7.30	7.32	7.33	7.37	7.36	7.34	7.36	7.35	7.35	7.31	7.32	7.33	7.36	7.373	7.364
10	7.36	7.36	7.31	7.29	7.30	7.29	7.29	7.30	7.31	7.29	7.26								7.26	7.26	7.29	7.33	7.32	7.338	7.370
n	10	10	10	10	10	10	10	10	10	9	9								10	10	10	10	10	10	10
Mean	7.37	7.32	7.30	7.30	7.30	7.31	7.32	7.32	7.32	7.33	7.32								7.32	7.31	7.30	7.30	7.32	7.36	7.37
SD	0.04	0.03	0.02	0.03	0.03	0.03	0.04	0.03	0.03	0.05	0.04								0.04	0.03	0.03	0.04	0.04	0.02	0.02
delta		-0.06	-0.07	-0.08	-0.07	-0.06	-0.06	-0.06	-0.05	-0.04	-0.06								-0.05	-0.06	-0.07	-0.07	-0.05	-0.02	0.00

Table A 1.15 Blood $[Lac^-]_a$ at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery				
		Time (min)																					
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.64	6.86	7.82	8.79	9.33	10.00	10.50	10.30	11.00										11.00		11.10	10.60	9.94	7.64	5.01
2	0.59	2.51	4.57	5.94	6.69	5.67	3.89	7.30	5.48										5.48	4.39	6.44	5.59	4.30	2.81	1.82
3	0.92	2.08	2.86	3.69	3.86	3.69	3.77	3.65	3.83	3.71	4.30	4.24	4.37	4.58	5.06	5.64	6.16	5.63	7.05		7.19	7.22	6.23	3.95	2.85
4	0.45	2.66	4.02	4.29	4.36	4.36	4.47	4.24	4.61	5.00	5.60	6.23	6.71	7.39	7.94				7.94	7.50	7.20	6.69	5.65	3.54	2.27
5	0.53	2.24	3.34	4.05	4.31	4.89	5.11	5.00	5.11	5.14	5.57	5.86	6.14						6.14	6.53	6.62	6.16	5.18	3.26	2.27
6	0.51	2.48	3.43	3.26	3.16	3.27	3.25	3.10	2.86	3.33	3.73	3.92	5.63	5.91	6.10	6.64			6.64	7.80	7.56	7.43	6.22	3.99	2.70
7	0.74	1.56	1.68	1.74	2.68	3.43	4.13	3.91	4.13	4.39	5.13	5.75	6.38	7.00	7.55				7.55	7.71	7.86	7.47	6.24	3.60	2.37
8	0.30	2.83	5.74	6.96	7.43	7.15	7.77	7.86	8.41	8.81	9.72								9.72	10.40	10.60	10.30	9.24	6.85	4.65
9	0.39	1.33	2.59	2.58	2.47	2.68	2.66	2.41	2.62	3.32	3.86	4.57	4.79	5.61	6.14				6.14	5.93	5.42	4.75	3.44	1.88	1.28
10	0.38	2.36	2.96	3.38	3.33	3.69	3.71	3.21	3.31	3.72	4.44	5.37	5.76	6.32					6.32	5.97	5.65	4.98	4.19	3.07	2.34
n	10	10	10	10	10	10	10	10	10	8	8								10	8	10	10	10	10	10
Mean	0.55	2.69	3.90	4.47	4.76	4.88	4.93	5.10	5.14	4.68	5.29								7.40	7.03	7.56	7.12	6.06	4.06	2.76
SD	0.19	1.54	1.78	2.15	2.29	2.23	2.40	2.55	2.65	1.81	1.93								1.74	1.78	1.90	2.00	2.10	1.80	1.18
delta		2.14	3.35	3.92	4.22	4.34	4.38	4.55	4.59	4.13	4.75								6.85	6.48	7.02	6.57	5.52	3.51	2.21

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.51	1.66	2.50	3.18	3.23	3.14	3.03	3.02	2.69	3.06	3.50	4.21	4.76						4.76	5.06	4.74	4.48	3.54	2.04	1.35
2	0.51	2.13	3.10	3.73	3.97	3.83	4.22	4.22	4.16	4.13	4.78	4.86	5.06	5.30					5.30	4.91	5.37	5.19	4.47	2.89	2.16
3	0.60	2.03	3.07	3.52	3.66	3.77	3.93	3.98	3.95	4.19	4.53	4.85	5.24						5.24	5.39	5.15	5.20	4.13	2.63	1.12
4	0.37	2.14	3.77	5.30	5.95	5.70	5.66	5.27	5.48	5.51	5.72								5.72	5.50	5.46	5.45	4.72	3.05	2.16
5	0.33	1.16	2.05	2.24	2.27	2.31	2.27	2.44	2.87	3.32	3.63	3.90	4.36	4.62					4.62	4.76	4.50	4.02	3.02	1.87	1.24
6	0.81	1.82	2.76	3.34	3.39	3.63	3.73	3.74	3.84	3.90	4.18	4.45	4.71	4.88	5.03				5.03	5.29	5.59	5.26	4.19	2.39	1.61
7	0.60	3.63	4.92	5.50	5.43	6.12	6.20	5.78	6.36	6.54	5.98	7.64	8.16						8.16	8.24	8.16	7.89	6.69	4.21	2.84
8	0.72	1.98	2.40	2.50	2.47	2.27	2.16	1.73	2.00	2.23	2.51	2.72	2.87	3.21	3.45	3.79	3.98	4.20	4.20	3.61	3.58	3.18	1.88	1.34	1.04
9	0.85	3.73	4.65	5.25	5.13	5.27	5.36	4.80	4.94	5.07	5.42								5.42	4.96	4.93	4.59	3.70	2.56	1.99
10	0.85	3.68	4.71	5.27	4.71	4.79	4.60	4.34	4.32	4.59									4.32	4.92	4.88	4.39	3.65	2.02	1.65
n	10	10	10	10	10	10	10	10	10	10	9								10	10	10	10	10	10	10
Mean	0.62	2.40	3.39	3.98	4.02	4.08	4.12	3.93	4.06	4.25	4.47								5.28	5.26	5.24	4.97	4.00	2.50	1.72
SD	0.19	0.93	1.05	1.24	1.25	1.35	1.38	1.25	1.32	1.25	1.14								1.12	1.17	1.18	1.24	1.24	0.79	0.57
delta		1.78	2.78	3.37	3.41	3.47	3.50	3.32	3.45	3.64	3.86								4.66	4.65	4.62	4.35	3.38	1.88	1.10

Table A 1.16 Blood $[Lac^-]_v$ at rest, during and following high-intensity cycling exercise

2L

	Exercise																		Recovery				
	Time (min)																						
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.86	4.29	5.65	7.18	7.82	9.19	10.30	9.67	9.65										9.65		10.60	10.40	9.30	7.23	5.50
2	0.56	1.19	2.76	4.56	5.58	6.65	7.08	6.64	6.48										6.48	6.90	6.27	5.51	4.30	2.73	1.93
3	0.93	1.31	2.13	2.75	3.16	3.02	3.41	3.59	3.84	3.75	3.99	4.16	4.40	4.26	4.64	5.02	5.67	5.83	6.31		6.79	6.76	6.10	4.25	3.11
4	0.53	1.57	2.62	3.51	3.76	4.20	4.08	3.95	4.08	4.02	4.12	4.35	4.78	5.40	5.62				5.62		6.48	5.57	4.72	3.47	2.40
5	0.58	1.57	2.49	3.10	3.42	4.16	4.51	4.52	4.53	4.50	4.53	4.81							4.81	4.53	5.65	5.64	5.20	3.74	2.77
6	0.54	1.46	1.99	2.38	2.69	2.49	2.99	2.57	2.60	2.71	3.40	3.76	4.35	4.74	5.31	5.26			5.26	6.47	6.74	6.53	5.43	4.05	2.72
7	0.73	0.02	1.35	1.51	1.77	2.56	3.45	3.24	3.02	2.99	3.71	4.10	3.94	4.48	4.87				4.87	7.50	7.06	6.92	5.81	3.92	2.25
8	0.42	1.14	2.43	4.24	4.42	4.28	4.22	4.25	4.26										4.24	4.82	4.74	4.56	3.76	2.35	1.56
9	0.53	1.34	2.02	2.29	2.15	2.51	2.54	2.45	2.47	2.65	3.23	3.89	4.30	4.76	5.17				5.17	5.51	5.16	4.45	3.37	2.14	1.49
10	0.61	1.02	1.43	2.02	2.02	2.33	2.66	2.84	2.60	2.64	2.91	3.39	3.79	4.52					4.52	5.06	5.07	3.96	3.92	3.61	1.34
n	10	10	10	10	10	10	10	10	10	7	7								10	7	10	10	10	10	10
Mean	0.63	1.49	2.49	3.35	3.68	4.14	4.52	4.37	4.35	3.32	3.70								5.69	5.83	6.46	6.03	5.19	3.75	2.51
SD	0.16	1.08	1.21	1.65	1.87	2.22	2.41	2.23	2.22	0.76	0.56								1.57	1.14	1.67	1.83	1.70	1.42	1.21
delta		0.86	1.86	2.73	3.05	3.51	3.90	3.74	3.73	2.69	3.07								5.06	5.20	5.83	5.40	4.56	3.12	1.88

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fatigue**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.65	2.19	3.30	4.22	4.75	5.41	5.94	6.09	5.86	5.63	6.28	6.33	6.78						6.78	7.74	7.99	8.52	7.08	5.28	3.47
2	0.53	1.10	1.71	2.44	2.50	2.82	2.71	2.46	2.18	2.51	2.88	3.33	3.85						3.85	4.80	4.68	4.43	3.57	2.11	1.55
3	0.72	1.47	1.73	2.46	2.42	3.13	3.33	3.58	3.58	3.78	3.81	3.88	4.09	4.12					4.12	4.66	5.01	4.92	3.93	3.22	2.65
4	0.56	1.69	2.78	3.22	3.38	3.62	3.83	3.75	3.83	4.03	4.29	4.54	4.89						4.89	4.86	5.02	5.07	4.27	2.78	1.95
5	0.48	1.79	2.46	3.92	4.94	4.94	4.76	4.74	4.99	5.05	5.04								5.04	5.00	5.01	4.87	3.98	3.23	2.37
6	0.75	0.02	1.94	2.06	1.88	2.04	2.16	2.22	2.48	2.86	3.13	3.35	3.68	3.69					3.69	4.12	3.97	3.93	3.26	2.05	1.55
7	0.85	1.03	2.10	2.17	2.55	2.61	2.92	2.92	3.05	3.05	3.29	3.31	3.23	3.41	3.61				3.61	5.13	4.96	5.06	4.07	2.41	1.67
8	0.77	2.33	2.57	4.36	4.84	5.51	5.44	5.47	5.38	5.22	5.95	5.95	6.00						6.00	6.79	7.50	7.79	6.84	4.47	3.10
9	0.83	1.23	1.59	1.73	1.66	1.98	1.86	1.56	1.91	1.74	2.01	2.13	2.34	2.76	2.96	3.34	3.49	3.80	3.80	4.03	3.17	2.85	2.45	1.63	1.34
10	0.97	1.63	3.01	3.69	3.81	4.17	4.61	4.31	4.35	4.72	5.18								5.18	4.81	4.46	4.39	3.89	3.30	2.93
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	10
Mean	0.71	1.45	2.32	3.03	3.27	3.62	3.76	3.71	3.76	3.86	4.19								4.70	5.19	5.18	5.18	4.33	3.05	2.26
SD	0.16	0.66	0.59	0.97	1.25	1.33	1.39	1.46	1.37	1.30	1.40								1.08	1.17	1.48	1.71	1.48	1.13	0.75
delta		0.74	1.61	2.32	2.56	2.91	3.05	3.00	3.05	3.15	3.48								3.99	4.48	4.47	4.47	3.62	2.34	1.55

Table A 1.17 Plasma $[Glu^-]_a$ at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery						
		Time (min)																							
Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fat**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	5.15	4.94	5.13	5.03	5.35	5.50	5.80	6.76	6.86										6.86		7.19	7.23	6.90	6.41	5.85
2	4.36	4.40	4.30	4.16	4.20	3.25	2.17	5.03	3.51										3.51	3.13	4.54	4.20	3.76	3.60	3.57
3	5.28	4.89	4.75	4.92	4.70	4.83	4.73	4.70	4.78	4.66	4.75	4.74	4.75	4.80	4.57	4.73	4.72	3.86	4.73		4.51	4.92	4.93	4.99	2.85
4	5.01	4.88	5.48	5.74	5.50	5.20	5.47	5.59	5.69	5.67	5.44	5.56	5.49	5.58	5.60				5.60	6.42	6.43	6.22	5.63	4.80	4.22
5	5.34	4.60	4.39	4.36	4.39	4.43	4.61	4.70	4.70	4.61	4.60	4.51	4.40						4.40	4.46	4.74	4.52	4.56	4.68	5.23
6	5.47	3.96	3.63	3.44	3.59	3.81	3.99	4.24	4.19	4.27	2.21	4.25	4.18	4.20	4.15	4.10			4.10	5.41	5.37	5.23	4.87	4.17	4.21
7	5.06	4.42	4.53	4.67	4.73	4.51	4.47	4.44	4.49	4.37	4.39	4.43	4.41	4.47	4.50				4.50	4.67	5.09	5.25	4.98	4.91	4.68
8	4.61	4.65	4.86	4.73	4.70	4.76	4.75	4.98	5.09	4.99	5.02								5.02	6.25	6.69	6.80	6.10	5.37	4.91
9	4.32	4.36	4.69	4.63	4.51	4.22	4.18	4.33	4.39	4.35	4.19	4.27	4.27	4.23	4.21				4.21	4.82	5.01	5.09	4.85	4.41	4.14
10	4.79	4.87	5.16	5.27	5.23	5.05	4.98	4.81	5.12	4.94	4.91	5.10	4.93	4.99					4.99	5.69	5.73	5.27	5.31	5.24	5.05
n	10	10	10	10	10	10	10	10	10	10	8	8							10	8	10	10	10	10	10
Mean	4.94	4.60	4.69	4.70	4.69	4.56	4.52	4.96	4.88	4.73	4.44								4.79	5.11	5.53	5.47	5.19	4.86	4.47
SD	0.40	0.31	0.52	0.63	0.57	0.67	0.99	0.74	0.91	0.46	0.98								0.93	1.07	0.95	0.97	0.86	0.75	0.86
delta		-0.34	-0.25	-0.24	-0.25	-0.38	-0.42	0.02	-0.06	-0.21	-0.50								-0.15	0.17	0.59	0.53	0.25	-0.08	-0.47

1L

Subject	**Rest**	**2**	**5.5**	**9**	**12.5**	**16**	**19.5**	**21.5**	**22**	**22.5**	**23**	**23.5**	**24**	**24.5**	**25**	**25.5**	**26**	**26.5**	**Fat**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	4.27	4.67	4.64	4.59	4.32	4.08	4.18	4.46	4.38	4.42	4.18	4.15	4.22						4.22	4.91	4.85	4.64	4.49	4.24	4.22
2	4.71	5.15	5.14	5.12	4.92	4.88	5.00	4.88	5.08	4.33	4.98	4.96	4.96	4.87					4.87	5.03	5.07	5.23	5.47	5.19	4.99
3	4.28	4.58	4.64	4.82	4.69	4.50	4.92	5.09	5.11	5.05	4.97	5.04	5.02						5.02	5.02	5.39	5.35	4.94	4.80	3.58
4	4.68	4.88	4.82	5.00	5.13	5.31	5.72	5.63	5.79	5.75	5.75								5.75	5.60	5.79	5.98	5.99	5.61	5.17
5	4.59	4.15	4.13	3.97	3.82	3.80	3.59	3.65	3.66	3.82	3.69	3.69	3.87	3.76					3.76	4.07	4.13	3.91	3.88	3.94	3.93
6	4.82	4.43	4.58	4.49	4.35	4.51	4.76	4.74	4.70	4.73	4.41	4.39	4.40	4.28	4.31				4.31	4.45	4.82	4.94	4.68	4.45	4.30
7	5.91	4.05	4.29	4.35	3.93	4.24	4.51	4.13	4.46	4.38	3.43	4.35	4.41						4.41	4.61	4.92	4.67	4.25	3.96	4.22
8	5.17	5.23	5.22	5.21	4.92	4.48	4.74	4.77	4.64	4.65	4.60	4.73	4.63	4.61	4.44	4.41	4.34	4.39	4.39	4.75	4.95	5.10	4.78	4.96	4.82
9	5.38	5.34	5.02	4.48	4.27	4.10	4.09	4.32	4.17	4.15	4.02								4.02	4.28	4.33	4.03	4.10	4.22	4.45
10	4.60	5.21	5.06	4.95	4.84	4.97	4.93	5.03	5.08	5.19									5.19	5.01	5.27	5.15	5.12	4.72	4.29
n	10	10	10	10	10	10	10	10	10	10	9								10	10	10	10	10	10	10
Mean	4.84	4.77	4.75	4.70	4.52	4.49	4.64	4.67	4.71	4.65	4.45								4.59	4.77	4.95	4.90	4.77	4.61	4.40
SD	0.51	0.47	0.36	0.39	0.45	0.46	0.59	0.56	0.59	0.56	0.72								0.60	0.44	0.48	0.62	0.64	0.55	0.48
delta		-0.07	-0.09	-0.14	-0.32	-0.35	-0.20	-0.17	-0.13	-0.19	-0.39								-0.25	-0.07	0.11	0.06	-0.07	-0.23	-0.44

Table A 1.18 Plasma $[Glu^-]_v$ at rest, during and following high-intensity cycling exercise

2L

		Exercise																	Recovery				
		Time (min)																					
Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fat	+1	+2	+5	+10	+20	+30
1	5.00	4.84	4.71	4.79	4.94	5.18	5.71	6.48	6.42										6.42		6.80	6.86	6.59	6.39	5.65
2	4.43	4.05	3.96	4.05	3.96	4.04	4.14	4.48	4.36										4.36	4.51	4.66	4.11	3.68	3.51	3.44
3	4.43	4.34	4.40	4.51	4.73	4.47	4.59	4.55	4.76	4.59	4.57	4.52	4.77	4.67	4.64	4.58	4.73	4.51	4.62		4.58	4.80	4.82	5.04	4.70
4	4.50	4.37	4.89	5.38	5.12	5.08	5.19	5.32	5.31	5.27	5.15	5.11	5.08	5.21	5.22				5.22		6.07	5.79	5.26	4.80	4.13
5	5.17	4.75	4.38	4.42	4.41	4.51	4.62	4.60	4.56	4.52	4.48	4.54							4.54	4.53	4.63	4.52	4.52	4.71	4.98
6	4.22	3.29	2.96	3.10	3.40	3.58	3.79	3.95	3.89	3.91	4.17	3.83	4.00	4.00	3.98	3.64			3.64	4.42	5.01	4.92	4.64	3.99	4.04
7	4.19	0.16	3.86	4.13	4.08	4.16	4.31	4.07	4.02	4.00	4.17	4.15	3.96	4.01	4.12				4.12	4.68	4.89	5.09	4.80	4.79	3.91
8	4.30	4.02	3.98	4.03															4.03						
9	4.35	4.08	4.41	4.30	4.33	4.15	4.12	4.24	4.26	4.22	4.14	4.30	4.22	4.20	4.22				4.22	4.57	4.92	4.88	4.45	4.41	4.18
10	4.44	4.40	4.49	4.58	4.53	4.39	4.42	4.49	4.52	4.54	4.64	4.67	4.63	4.65					4.65	4.92	5.22	5.02	5.05	5.13	2.71
n	10	10	10	10	10	9	9	9	9	9	7	7							10	6	9	9	9	9	9
Mean	4.50	3.83	4.20	4.33	4.39	4.40	4.54	4.69	4.68	4.44	4.47								4.58	4.61	5.20	5.11	4.87	4.75	4.19
SD	0.32	1.36	0.55	0.59	0.53	0.50	0.59	0.78	0.78	0.46	0.36								0.77	0.18	0.75	0.80	0.78	0.80	0.86
delta		-0.67	-0.30	-0.17	-0.11	-0.11	0.04	0.18	0.17	-0.07	-0.03								0.08	0.10	0.69	0.61	0.36	0.25	-0.31

1L

Subject	Rest	2	5.5	9	12.5	16	19.5	21.5	22	22.5	23	23.5	24	24.5	25	25.5	26	26.5	Fat	+1	+2	+5	+10	+20	+30
1	4.91	5.03	5.03	5.17	5.32	5.44	5.48	5.76	5.65	5.55	5.69	5.64	5.62						5.62	6.00	6.20	6.82	6.54	6.07	5.71
2	4.41	4.60	4.46	4.33	4.26	4.08	4.14	4.21	4.21	4.27	4.29	4.12	4.11						4.21	4.72	4.71	4.61	4.36	4.11	4.08
3	4.25	4.43	4.23	4.27	4.38	4.46	4.37	4.47	4.63	4.68	4.58	4.63	4.62	4.48					4.48	4.74	4.96	5.02	5.05	4.85	4.56
4	4.49	4.46	4.55	4.71	4.50	4.49	4.75	4.86	4.91	4.90	4.90	4.88	4.87						4.47	5.02	5.24	5.36	4.96	4.69	4.56
5	4.73	4.80	4.86	5.41	5.08	5.36	5.58	5.53	5.68	5.72	5.66								5.66	5.59	5.68	5.84	5.91	5.69	5.29
6	3.81	3.80	3.76	3.64	3.64	3.63	3.69	3.67	3.66	3.75	3.75	3.61	3.72	3.69					3.69	3.83	3.87	3.82	3.83	3.89	3.78
7	3.91	3.10	3.92	3.57	3.91	3.88	4.30	4.35	4.41	4.43	4.14	4.16	4.03	4.10	4.05				4.05	4.35	4.51	4.94	4.49	4.12	4.17
8	4.91	3.83	3.36	4.00	4.08	3.87	4.03	4.34	4.28	4.34	4.08	4.07	4.05						4.05	4.36	4.73	4.87	4.36	4.11	4.22
9	4.75	4.83	4.89	4.95	4.79	4.51	4.62	4.53	4.70	4.29	4.47	4.46	4.45	4.54	4.30	4.37	4.39	4.37	4.37	4.32	4.50	4.92	4.96	4.82	4.56
10	4.51	4.99	4.70	4.31	4.05	3.95	4.03	4.07	4.08	4.08	4.28								4.28	3.90	4.06	3.91	3.86	3.98	
n	10	10	10	10	10	10	10	10	10	10	10								10	10	10	10	10	10	9
Mean	4.47	4.39	4.38	4.44	4.40	4.37	4.50	4.58	4.62	4.60	4.58								4.49	4.68	4.85	5.01	4.83	4.63	4.55
SD	0.39	0.62	0.55	0.62	0.53	0.62	0.62	0.64	0.65	0.63	0.65								0.65	0.70	0.71	0.88	0.86	0.75	0.61
delta		-0.08	-0.09	-0.03	-0.07	-0.10	0.03	0.11	0.15	0.13	0.12								0.02	0.22	0.38	0.54	0.36	0.17	0.08

Table A 1.19 MVC (Nm) pre-exercise and following high-intensity cycling exercise bouts and expressed as a percentage of pre-exercise

2L

									Expressed as a % of pre-exercise					
		pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	100%	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	leg length (cm)	MVC (Nm)							MVC (%)						
1	0.32	233.6	142.9	172.9	191.7	190.6	106.3	192.0	100	61.2	74.0	82.1	81.6	45.5	82.2
2	0.32	190.1	177.1	138.7	130.9	127.9	176.8	189.7	100	93.2	73.0	68.9	67.3	93.0	99.8
3	0.32	102.0	101.8	71.8	78.0	78.0	88.6	87.1	100	99.8	70.4	76.5	76.5	86.9	85.4
4	0.32	57.5	54.9	51.0	64.1	48.7	55.4	63.2	100	95.4	88.6	111.4	84.6	96.3	109.7
5	0.33	165.0	153.4	145.9	138.4	128.1	156.9	155.0	100	93.0	88.4	83.9	77.6	95.1	93.9
6	0.32	113.2	113.9	113.1	117.7	109.9	116.0	131.0	100	100.6	99.9	103.9	97.1	102.4	115.7
7	0.32	106.9	94.7	94.6	121.5	101.6	80.7	86.0	100	88.6	88.5	113.7	95.1	75.5	80.5
8	0.32	106.6	58.6	78.1	87.2	68.9	62.5	65.5	100	55.0	73.2	81.8	64.6	58.6	61.5
9	0.37	272.1	261.4	242.9	279.1	200.7	252.3	236.5	100	96.1	89.3	102.6	73.8	92.7	86.9
10	0.32	98.0	92.9	91.0	101.2	90.0	79.0	75.3	100	94.9	92.9	103.4	91.9	80.6	76.8
n	10	10	10	10	10	10	10	10		10	10	10	10	10	10
Mean	0.33	148.1	127.1	122.5	129.1	122.5	124.9	128.7	100	87.8	83.8	92.8	81.0	82.7	89.3
SD	0.02	63.2	56.2	52.6	59.1	53.9	59.3	56.4	0	16.1	10.2	15.9	11.2	18.2	16.1

1L

		pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	100%	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	leg length (cm)	MVC (Nm)							MVC (%)						
1	0.32	225.9	142.9	172.9	191.7	190.6	106.3	192.0	100	63.2	76.5	84.8	84.4	47.1	85.0
2	0.32	242.0	217.0	188.9	177.8	157.9	183.1	235.7	100	89.7	78.0	73.5	65.3	75.7	97.4
3	0.32	120.2	65.0	53.4	94.3	53.4	94.3	112.8	100	54.1	44.4	78.4	44.4	78.4	93.9
4	0.32	87.7	76.6	74.0	44.8	40.7	73.5	72.8	100	87.4	84.5	51.1	46.4	83.8	83.0
5	0.33	182.5	171.4	138.4	128.1	126.7	127.6	126.3	100	93.9	75.8	70.2	69.4	69.9	69.2
6	0.32	118.3	103.5	101.5	113.4	100.0	109.5	108.4	100	87.4	85.7	95.9	84.5	92.5	91.6
7	0.32	100.2	69.9	116.4	102.7	91.2	96.0	89.1	100	69.8	116.2	102.5	91.0	95.8	89.0
8	0.32	116.9	82.2	51.8	45.2	45.5	67.7	78.4	100	70.3	44.3	38.7	38.9	57.9	67.1
9	0.37	252.2	225.9	272.1	219.6	261.4	279.1	247.7	100	89.6	107.9	87.1	103.6	110.7	98.2
10	0.32	95.5	89.8	85.4	94.5	82.4	88.8	97.0	100	94.1	89.5	99.0	86.3	93.1	101.6
n	10	10	10	10	10	10	10	10		10	10	10	10	10	10
Mean	0.33	143.9	85.6	111.5	120.0	115.2	124.0	135.8	100	80.0	80.3	78.1	71.4	80.5	87.6
SD	0.02	56.9	41.9	63.8	53.5	64.1	57.9	58.8	0	14.3	23.1	20.7	22.2	18.9	11.8

Table A 1.20 Familiarisation of the ramp protocol at 50, 60, 70, 80, 90 and 100% of stimulator output at rest

Familiarisation

% Stimulator Output	50%			60%			70%			80%						90%						100%					
Stimulation	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV%	1	2	3	mean	SD	CV%	1	2	3	mean	SD	CV%
Subject	Twitch (Nm)															Twitch (Nm)						Twitch (Nm)					
1	18.22	17.16	16.52	22.44	22.40	24.05	23.02	29.63	29.87	33.71	32.98	34.05	33.58	0.55	1.64	33.52	33.54	35.52	34.19	1.15	3.36	34.18	35.24	35.54	34.98	0.72	2.04
2	13.89	12.73	12.52	16.76	13.32	12.46	19.12	19.08	18.75	21.76	21.69	23.96	22.47	1.29	5.74	23.06	23.76	24.36	23.73	0.65	2.73	23.91	23.50	24.08	23.83	0.30	1.24
3	2.10	2.12	1.94	3.39	2.94	3.04	2.94	6.01	5.86	11.79	11.99	14.42	12.73	1.46	11.47	13.90	12.28	14.36	13.52	1.10	8.11	13.63	14.15	14.30	14.03	0.35	2.48
4	2.23	2.25	2.25	3.21	2.93	3.11	5.36	4.96	4.97	9.84	9.76	10.97	10.19	0.68	6.64	9.70	10.25	10.65	10.20	0.48	4.70	10.37	10.06	10.69	10.37	0.32	3.05
5	2.47	2.30	2.39	3.80	3.50	3.64	5.10	4.90	4.48	12.83	12.58	13.31	12.90	0.37	2.86	12.75	13.62	13.57	13.31	0.49	3.69	12.82	13.04	13.84	13.23	0.54	4.07
6	1.78	1.73	1.55	3.85	3.76	3.95	5.59	5.36	5.54	32.57	33.74	33.84	33.39	0.71	2.12	34.67	34.49	35.28	34.81	0.41	1.18	35.20	35.55	35.71	35.49	0.26	0.73
7	1.65	1.82	1.82	3.65	3.95	4.05	5.21	5.18	4.88	12.18	12.95	13.81	12.98	0.82	6.30	14.50	13.72	14.78	14.33	0.55	3.82	15.01	15.27	15.38	15.22	0.19	1.25
8	3.99	6.80	8.32	3.10	4.27	3.33	7.94	6.19	6.40	6.16	6.41	7.87	6.81	0.92	13.55	7.65	6.96	7.75	7.45	0.43	5.77	7.76	7.49	7.62	7.62	0.13	1.74
9	1.87	2.21	2.25	7.21	6.87	6.80	10.88	10.06	10.35	18.50	17.03	18.81	18.12	0.95	5.24	17.21	17.61	18.70	17.84	0.77	4.31	19.23	18.61	19.24	19.02	0.36	1.90
10	3.17	4.64	5.44	8.38	8.87	8.72	16.08	15.76	17.26	31.12	31.80	32.20	31.71	0.55	1.72	33.52	32.21	33.17	32.96	0.68	2.06	33.82	33.04	34.31	33.72	0.64	1.89
n	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	5.14	5.38	5.50	7.58	7.28	7.32	10.12	10.71	10.83	19.05	19.09	20.32	19.49	0.83	4.25	20.05	19.84	20.81	20.23	0.67	3.31	20.59	20.60	19.43	20.75	0.38	1.83
SD	5.88	5.39	5.29	6.72	6.26	6.63	6.93	8.32	8.49	10.22	10.32	9.98	10.17	0.34	4.08	10.42	10.36	10.54	10.43	0.26	1.96	10.52	10.62	11.52	10.61	0.19	0.97

Table A 1.21 Pre-exercise 1 Hz stimulations separated by 3 s at 50, 60, 70, 80, 90 and 100% of magnetic stimulator output

2L

Stimulator Output	50%			60%			70%			80%						90%						100%					
Stimulation	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV%	1	2	3	mean	SD	CV%	1	2	3	mean	SD	CV%
Subject	Twitch (Nm)															Twitch (Nm)						Twitch (Nm)					
1	18.22	17.16	16.52	22.41	22.44	22.40	23.53	23.02	24.05	29.75	30.63	32.87	31.08	1.61	5.18	33.51	32.98	34.05	33.24	0.38	1.14	33.51	33.24	36.54	34.43	1.83	5.32
2	9.38	10.10	9.15	13.73	13.63	12.68	19.61	20.91	20.86	26.38	27.16	34.78	29.44	4.64	15.77	33.51	33.10	34.18	33.64	0.76	2.27	33.39	32.48	34.69	33.52	1.11	3.31
3	1.87	2.07	2.12	3.19	3.24	3.06	6.01	5.81	5.35	12.26	11.28	12.89	12.15	0.81	6.69	13.13	13.26	13.94	13.44	0.43	3.23	14.71	13.34	14.63	14.23	0.77	5.41
4	2.25	2.48	2.04	2.97	2.80	3.19	5.33	4.83	4.66	9.66	10.78	10.89	10.44	0.68	6.54	10.79	10.85	11.90	11.18	0.63	5.60	10.42	10.68	10.78	10.62	0.19	1.75
5	5.32	2.63	2.82	9.50	10.55	9.80	12.88	14.55	14.85	16.96	17.98	19.15	18.03	1.10	6.10	17.06	16.96	18.60	17.54	0.92	5.22	16.56	17.02	18.02	17.20	0.75	4.35
6	6.73	6.79	6.61	8.03	9.44	9.43	15.34	15.36	15.13	29.47	31.83	32.75	31.35	1.69	5.40	32.03	31.97	35.39	33.13	1.96	5.91	35.89	35.74	35.95	35.86	0.11	0.30
7	1.27	1.35	1.28	2.85	2.76	2.36	5.47	5.68	5.63	8.63	8.83	9.36	8.94	0.38	4.26	11.14	10.52	14.49	12.05	2.14	17.72	14.22	14.28	15.37	14.62	0.65	4.43
8	3.41	3.07	3.02	3.82	3.93	4.03	4.72	5.00	5.03	5.46	5.50	5.73	5.57	0.15	2.64	5.67	5.85	6.45	5.99	0.41	6.78	5.89	6.20	6.50	6.19	0.31	4.93
9	3.37	3.13	3.07	4.67	3.82	4.20	8.71	7.50	7.90	10.85	10.20	10.92	10.66	0.39	3.69	10.82	11.45	11.28	11.36	0.12	1.03	11.80	12.05	13.24	12.36	0.77	6.20
10	2.23	2.32	2.45	6.29	6.03	6.12	8.24	7.95	7.66	10.80	11.93	11.98	11.57	0.67	5.80	12.99	12.10	13.95	13.02	1.31	10.02	14.27	14.76	14.36	14.46	0.26	1.80
n	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	5.40	5.11	4.91	7.75	7.87	7.73	10.98	11.06	11.11	16.02	16.61	18.13	16.92	1.21	7.17	18.07	17.90	19.42	18.46	0.90	4.90	19.07	18.98	20.01	19.35	0.67	3.48
SD	5.16	5.00	4.74	6.22	6.36	6.21	6.61	6.87	7.13	9.14	9.72	11.10	9.96	1.31	3.60	10.70	10.56	10.87	10.64	0.69	5.00	10.90	10.66	11.27	10.93	0.52	1.92

1L

Stimulation	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV%	1	2	3	mean	SD	CV%	1	2	3	mean	SD	CV%
Subject	Twitch (Nm)															Twitch (Nm)						Twitch (Nm)					
1	17.30	17.16	17.17	22.96	24.05	24.06	26.32	23.02	23.03	30.65	31.63	33.99	32.09	1.72	5.35	33.51	34.05	34.52	34.03	0.51	1.49	33.73	33.72	36.53	34.66	1.62	4.68
2	9.38	10.16	9.31	13.86	13.55	12.62	19.67	20.89	20.86	26.37	30.27	31.71	29.45	2.76	9.38	33.41	33.13	34.10	33.55	0.50	1.49	36.25	34.53	43.69	38.16	4.87	12.77
3	2.70	2.26	2.84	4.55	4.88	4.23	5.55	6.15	6.20	7.64	9.53	9.71	8.96	1.14	12.76	12.14	11.08	12.27	11.83	0.65	5.52	12.66	12.35	13.76	12.92	0.74	5.72
4	2.17	2.46	2.56	4.97	5.09	5.24	7.75	7.88	8.72	12.78	11.96	12.14	12.30	0.43	3.50	12.17	12.67	13.68	12.84	0.77	5.99	13.49	13.27	13.75	13.50	0.24	1.77
5	2.47	2.25	2.21	3.80	3.38	3.62	4.64	4.82	4.31	13.01	13.76	13.09	13.29	0.41	3.11	13.00	13.84	14.91	13.91	0.96	6.87	15.96	14.78	16.88	15.87	1.05	6.62
6	6.43	9.23	7.44	8.13	8.80	9.18	18.25	16.29	15.71	31.84	32.83	34.94	33.20	1.59	4.78	34.83	35.25	35.27	35.12	0.24	0.70	36.55	35.80	37.11	36.49	0.66	1.80
7	2.58	2.66	2.53	4.40	4.37	4.16	7.36	6.63	6.91	12.65	12.77	13.96	13.13	0.73	5.52	13.75	13.87	13.94	13.85	0.10	0.71	14.19	14.78	16.17	15.05	1.02	6.76
8	4.66	5.06	6.57	7.28	6.94	6.78	7.18	7.09	7.73	7.86	7.85	8.76	8.15	0.52	6.39	8.88	8.81	9.12	8.94	0.16	1.82	7.99	8.51	8.86	8.45	0.44	5.17
9	3.32	3.16	3.07	4.54	3.87	4.15	8.73	7.50	7.80	9.90	10.80	10.34	10.35	0.45	4.35	11.43	10.82	11.48	11.24	0.37	3.30	11.99	12.48	13.49	12.65	0.76	6.01
10	2.56	2.40	2.60	6.63	6.54	6.24	9.66	9.73	9.07	11.83	12.16	12.84	12.28	0.51	4.19	13.65	13.31	13.53	13.50	0.17	1.28	14.16	15.20	15.65	15.00	0.76	5.09
n	10	10	10	10	10	10	10	10	10	10	10	11	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	5.36	5.68	5.63	8.11	8.15	8.03	11.51	11.00	11.03	16.45	17.36	16.77	17.32	1.03	5.92	18.68	18.68	19.28	18.88	0.44	2.35	19.70	19.54	21.59	20.28	1.22	6.00
SD	4.78	5.00	4.77	6.00	6.34	6.29	7.27	6.58	6.49	9.38	9.97	11.20	10.02	0.78	2.98	10.61	10.79	10.71	10.70	0.29	2.35	11.13	10.63	12.43	11.36	1.34	3.06

Table A 1.22 Q_{twpot} force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

2L

									Expressed as a % of pre-exercise					
		pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	100%	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	leg length (cm)	Twitch (Nm)							Twitch (%)						
1	0.32	62.7	19.4	11.0	29.9	15.0	6.2	28.3	100	30.9	17.6	47.7	23.9	9.8	45.1
2	0.32	49.1	38.7	32.9	12.1	28.1	28.1	39.9	100	78.9	67.0	24.7	57.2	57.2	81.4
3	0.32	16.9	14.0	14.1	9.3	7.7	13.5	16.9	100	83.0	83.6	55.2	45.3	79.9	99.9
4	0.32	23.6	19.7	12.2	9.1	10.5	11.0	19.6	100	83.6	51.9	38.7	44.3	46.4	83.2
5	0.33	27.5	21.3	20.5	18.5	15.9	12.9	16.8	100	77.6	74.5	67.4	57.8	46.8	61.0
6	0.32	46.9	44.5	40.2	37.7	30.7	33.1	46.8	100	94.8	85.6	80.2	65.3	70.4	99.7
7	0.32	13.0	9.2	8.4	5.8	3.7	4.8	6.9	100	70.4	64.6	44.3	28.5	36.8	52.9
8	0.32	10.8	4.7	3.3	6.3	5.4	7.7	6.4	100	43.1	30.8	57.9	50.1	71.5	59.2
9	0.37	17.7	12.4	13.7	12.7	12.5	10.3	10.4	100	69.9	77.4	72.1	70.9	58.3	58.6
10	0.32	19.6	19.5	17.8	19.6	15.7	15.5	15.0	100	99.2	90.8	99.8	80.1	79.0	76.6
n	10.00	10	10	10	10	10	10	10		10	10	10	10	10	10
Mean	0.33	25.0	20.4	18.1	14.6	14.5	15.2	19.9	100	73.1	64.4	58.8	52.3	55.6	71.8
SD	0.02	13.2	12.5	11.0	9.4	8.9	8.8	13.4	0	21.4	24.2	21.9	17.8	21.7	19.2

1L

		pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	100%	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	leg length (cm)	Twitch (Nm)							Twitch (%)						
1	0.32	46.6	30.2	16.8	10.2	6.8	20.9	25.9	100	64.9	36.1	21.8	14.6	44.9	55.5
2	0.32	18.5	16.8	10.0	5.7	5.7	4.4	9.4	100	90.4	53.9	30.7	30.7	23.7	50.9
3	0.32	14.6	11.7	5.6	14.0	6.1	8.4	13.8	100	80.1	38.1	96.2	41.5	57.5	94.4
4	0.32	21.4	16.9	11.9	11.6	13.7	11.3	12.0	100	79.0	55.7	54.3	64.1	52.8	55.7
5	0.33	13.3	12.5	8.2	4.6	5.5	6.1	8.2	100	94.0	61.9	34.7	41.2	45.7	61.6
6	0.32	58.3	58.0	51.9	42.3	26.9	30.1	36.2	100	99.5	89.0	72.6	46.2	51.7	62.1
7	0.32	17.0	10.9	10.1	9.7	5.3	6.3	12.1	100	63.8	59.1	57.0	31.2	37.2	71.2
8	0.32	8.1	7.5	2.6	3.4	1.9	1.9	4.4	100	92.8	32.6	41.8	23.8	23.5	54.5
9	0.37	21.6	19.9	19.0	17.6	13.6	14.1	11.2	100	91.9	88.0	81.3	63.0	65.5	51.9
10	0.32	17.9	16.7	13.2	13.8	13.0	11.4	13.7	100	93.3	73.7	77.2	72.6	63.9	76.8
n	10.00	10	10	10	10	10	10	10		10	10	10	10	10	10
Mean	0.33	23.7	20.1	14.9	13.3	9.8	11.5	14.7	100	85.0	58.8	56.8	42.9	46.6	63.5
SD	0.02	15.1	13.9	13.1	10.6	6.9	8.1	8.9	0	12.5	20.2	24.6	18.9	14.9	13.7

Table A 1.23 Doublet force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

2L

									Expressed as a % of pre-exercise					
		pre-exercise	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**100%**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	leg length (cm)	Doublet (Nm)							**Doublet (%)**						
1	0.32	104.4	30.5	20.3	64.5	30.1	13.0	51.8	100	29.2	19.4	61.7	28.8	12.4	49.6
2	0.32	100.0	80.3	42.6	39.9	44.9	45.0	75.6	100	80.3	42.6	39.9	44.9	45.0	75.6
3	0.32	26.3	13.7	13.2	15.2	52.2	52.9	18.0	100	52.1	50.2	57.7	198.1	200.9	68.2
4	0.32	38.2	56.1	58.1	43.8	39.7	39.8	41.4	100	146.8	152.0	114.5	103.9	104.2	108.3
5	0.33	68.7	48.7	47.3	45.4	38.8	44.0	45.2	100	70.9	68.8	66.0	56.4	64.1	65.8
6	0.32	82.4	78.4	72.4	62.0	51.1	62.9	67.3	100	95.1	87.9	75.3	62.0	76.3	81.6
7	0.32	23.8	9.8	8.5	8.7	9.6	15.9	13.9	100	41.0	35.7	36.6	40.5	66.8	58.4
8	0.32	18.7	15.0	14.3	8.2	6.7	12.7	17.9	100	80.5	76.8	43.7	35.7	67.8	96.0
9	0.37	28.4	15.0	14.3	13.6	13.5	16.8	13.7	100	52.9	50.5	47.9	47.8	59.2	48.4
10	0.32	35.2	32.0	36.3	35.5	28.1	28.1	29.7	100	90.8	103.1	100.8	79.8	79.8	84.4
n	10.00	10	10	10	10	10	10	10		10	10	10	10	10	10
Mean	0.33	52.6	38.0	32.7	33.7	31.5	33.1	37.4	100	74.0	68.7	64.4	69.8	77.6	73.6
SD	0.02	31.4	25.3	20.8	20.1	15.9	17.3	21.4	0	33.6	38.6	26.0	50.3	49.4	19.5

1L

		pre-exercise	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**100%**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	leg length (cm)	Doublet (Nm)							**Doublet (%)**						
1	0.32	89.4	39.2	46.1	28.0	16.2	42.0	65.0	100	43.9	51.6	31.4	18.1	47.0	72.7
2	0.32	26.0	7.3	13.0	10.7	23.9	16.0	17.6	100	28.0	49.8	41.0	91.9	61.5	67.8
3	0.32	55.8	13.7	6.5	39.5	22.4	19.4	57.9	100	24.6	11.6	70.8	40.1	34.7	103.6
4	0.32	52.8	13.8	14.2	32.4	41.5	29.2	25.1	100	26.0	27.0	61.4	78.5	55.2	47.6
5	0.33	27.3	20.3	17.3	13.5	12.9	16.0	13.9	100	74.4	63.4	49.3	47.4	58.6	51.0
6	0.32	98.3	86.3	78.3	69.4	44.4	55.3	57.1	100	87.8	79.6	70.6	45.2	56.2	58.1
7	0.32	51.8	35.8	21.8	19.4	11.8	21.5	23.5	100	69.1	42.0	37.5	22.8	41.5	45.5
8	0.32	20.0	26.0	21.7	21.7	13.9	16.6	17.6	100	130.3	108.4	108.4	69.5	83.3	88.4
9	0.37	26.3	26.0	29.2	28.6	21.4	22.0	20.1	100	98.8	110.7	108.6	81.1	83.6	76.3
10	0.32	32.5	36.0	28.6	24.7	21.9	21.2	25.7	100	110.7	88.0	76.1	67.5	65.2	79.1
n	10.00	10	10	10	10	10	10	10		10	10	10	10	10	10
Mean	0.33	48.0	30.4	27.6	28.8	23.0	25.9	32.4	100	69.4	63.2	65.5	56.2	58.7	69.0
SD	0.02	26.0	21.2	19.8	15.8	10.8	12.3	18.5	0	37.8	33.2	27.3	25.2	16.0	18.9

Table A 1.24 20 Hz Tetani (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

2L

							Expressed as a % of pre-exercise			
		pre-exercise	Bout 6	Fatigue	+10 min	+30 min	100%	Bout 6	Fatigue	+10 min	+30 min
Subject	leg length (cm)	Tetani (Nm)					Tetani (%)				
1	0.32	139.1	63.1	58.0	40.0	96.2	100	45.4	41.7	28.7	69.1
2	0.32	109.6	80.3	48.0	48.0	97.8	100	73.3	43.8	43.8	89.3
3	0.32	86.9	54.5	78.1	84.6	88.4	100	62.7	89.8	97.4	101.7
4	0.32	167.0	141.5	100.4	141.2	158.1	100	84.7	60.1	84.6	94.7
5	0.33	154.1	119.6	104.5	120.3	134.8	100	77.6	67.9	78.1	87.5
6	0.32	139.2	136.2	112.9	100.9	112.3	100	97.8	81.1	72.5	80.6
7	0.32	81.9	35.7	46.2	61.8	69.3	100	43.5	56.3	75.4	84.6
8	0.32	40.1	24.2	26.1	26.4	43.3	100	60.5	65.1	65.9	108.1
9	0.37	171.1	93.2	93.2	108.9	55.2	100	54.5	54.5	63.7	32.3
10	0.32	51.0	47.5	40.5	43.1	47.1	100	93.2	79.3	84.4	92.4
n	10	10	10	10	10	10	10	10	10	10	10
Mean	0.33	114.0	79.6	70.8	77.5	90.3	100	69.33	63.97	69.45	84.02
SD	0.02	44.9	39.7	29.2	37.1	35.9	0	19.11	15.91	20.31	21.15

1L

		pre-exercise	Bout 6	Fatigue	+10 min	+30 min	100%	Bout 6	Fatigue	+10 min	+30 min
Subject	leg length (cm)	Tetani (Nm)					Tetani (%)				
1	0.32	113.0	46.1	43.1	31.7	89.9	100	40.8	38.1	28.0	79.6
2	0.32	41.5	20.4	11.9	30.6	36.0	100	49.2	28.8	73.6	86.8
3	0.32	109.1	67.7	88.4	55.1	63.4	100	62.0	81.0	50.5	58.1
4	0.32	155.3	142.4	140.4	105.6	90.4	100	91.7	90.5	68.0	58.2
5	0.33	144.7	80.9	47.7	75.1	118.6	100	55.9	33.0	51.9	82.0
6	0.32	191.1	150.2	121.6	133.3	136.8	100	78.6	63.6	69.8	71.6
7	0.32	95.5	74.1	63.3	63.1	56.6	100	77.5	66.3	66.1	59.2
8	0.32	43.4	39.8	30.6	36.0	41.5	100	91.6	70.3	82.9	95.5
9	0.37	58.1	57.4	48.8	42.3	47.0	100	98.9	84.1	72.8	81.0
10	0.32	54.9	43.9	44.6	35.2	38.2	100	79.9	81.3	64.2	69.5
n	10	10	10	10	10	10	10	10	10	10	10
Mean	0.33	100.7	72.3	64.0	60.8	71.8	100	72.6	63.7	62.8	74.1
SD	0.02	49.0	40.7	38.6	33.0	33.7	0	19.7	22.6	15.6	13.0

Table A 1.25 Q_{twpot} vastus medialis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	Latency (ms)							Latency (%)						
1	5	5	5	5	5	5	5	100	100	100	100	100	100	100
2	6	7	7	7	7	5	6	100	111	111	111	111	84	95
3	5	5	8	5	6	5	6	100	94	150	100	111	94	106
4	5	5	5	4	5	5	6	100	114	100	93	107	107	121
5	5	5	4	5	5	5	5	100	94	81	94	94	88	88
6	6	7	6	6	6	6	6	100	111	89	89	89	89	89
7	4	4	4	4	4	4	4	100	100	100	108	100	108	92
8	6	7	6	6	6	6	5	100	118	106	106	106	106	94
9	4	5	4	5	4	4	4	100	108	100	115	100	100	100
10	7	8	8	5	7	7	7	100	125	125	75	100	100	100
n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	5.37	5.80	5.73	5.27	5.46	5.20	5.27	100	107.32	106.21	99.12	101.77	97.63	98.52
SD	0.90	1.36	1.57	0.80	0.97	0.74	0.87	0	10.34	19.28	11.88	6.94	8.52	9.86

1L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	Latency (ms)							Latency (%)						
1	5	6	6	6	5	5	5	100	106	106	106	100	100	100
2	6	7	6	6	6	7	6	100	105	100	100	95	105	95
3	6	5	5	5	6	5	5	100	94	94	88	100	94	88
4	5	5	5	5	5	6	6	100	107	107	109	107	121	121
5	5	5	5	5	5	5	5	100	88	94	100	100	100	100
6	6	5	5	5	6	6	6	100	88	88	88	100	100	106
7	4	4	4	4	3	4	4	100	100	100	100	91	100	109
8	5	6	5	7	5	5	5	100	113	100	125	100	100	88
9	5	5	5	5	5	5	5	100	100	100	88	100	100	100
10	4	4	5	5	4	3	4	100	92	117	117	100	83	92
n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	5.13	5.10	5.13	5.21	5.10	5.17	5.10	100	99.27	100.62	102.12	99.28	100.41	99.85
SD	0.80	0.94	0.69	0.86	0.82	0.97	0.79	0	8.61	8.00	12.55	4.17	9.42	10.37

Table A 1.26 Q_{twpot} vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	Amplitude (mV)							**Amplitude (%)**						
1	3	3	3	3		3	3	100	100	100	100		104	100
2	6	1	1	0	1	1	2	100	10	10	8	24	16	31
3	1	1	0	1		1	1	100	65	33	69		65	93
4	2	1	0	1	1	2	2	100	48	10	24	82	82	96
5	7	7	6	6	6	6	6	100	98	94	92	81	86	92
6	2	2	2	1	1	2	2	100	90	81	52	29	90	100
7	2	2	1	1	1	2	2	100	78	70	67	67	71	98
8	0	0	0	0	0	0	0	100	44	32	47	35	48	62
9	3	1	2	2	1	2	3	100	46	57	73	29	68	87
10	1	0	0	0	0	0	0	100	47	43	34	39	50	45
n	10	10	10	10	10	10	10	10	10	10	10	8	10	10
Mean	2.84	1.85	1.67	1.70	1.40	1.95	2.28	100	62.72	52.97	56.72	48.20	68.10	80.53
SD	2.10	1.96	1.98	1.91	1.76	1.70	1.75	0	28.78	32.77	29.38	24.37	25.12	25.27

1L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	Amplitude (mV)							**Amplitude (%)**						
1	6	7	6	6	7	6	6	100	106	102	100	107	93	100
2	3	1	1	1	2	1	2	100	48	28	24	80	48	80
3	2	2	1	1	1	1	3	100	70	40	55	40	50	135
4	9				3	4	5	100				30	40	51
5	4	5	3	3	3	5	5	100	114	75	69	72	111	111
6	3	1	3	2	2	2	3	100	35	97	95	65	79	97
7	4	3	3	3	2	2	3	100	80	84	92	57	57	73
8	1	0	1	0	0	0	1	100	73	100	73	67	73	100
9	4	3	3	3	3	4	4	100	84	95	89	92	113	103
10	0	0	0	0	0	0	0	100	78	86	76	54	78	60
n	10	9	9	9	10	10	10	10	9	9	9	10	10	10
Mean	3.62	2.47	2.37	2.34	2.37	2.59	3.11	100	76.47	78.49	74.83	66.45	74.15	90.94
SD	2.70	2.18	1.99	1.96	1.92	1.93	1.90	0	24.70	26.78	23.88	23.23	25.76	25.04

Table A 1.27 Q_{twpot} vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	**Area (mV.s)**							**Area (%)**						
1	23	23	38	38	23	23	26	100	100	165	165	100	100	113
2	30	30	30	30	22	29	30	100	100	100	100	73	97	100
3	12	15	15	17		17	13	100	125	125	142		142	108
4	16	15	15	15	10	14	12	100	94	94	94	63	88	75
5	37	36	32	33	28	30	32	100	97	86	89	76	81	86
6	13	12	8	5	5	9	8	100	92	62	38	38	69	62
7	25	17	16	16	18	18	23	100	68	64	64	72	72	92
8	13	2	2	2	2	2	2	100	15	15	15	15	15	15
9	18	15	15	12	14	19	20	100	83	83	67	78	106	111
10	14	13	13	13	13	14	15	100	93	93	93	93	100	107
n	10	10	10	10	9	10	10	10	10	10	10	9	10	10
Mean	20.10	17.80	18.40	18.10	15.00	17.50	18.10	100	86.79	88.76	86.72	67.55	86.91	87.00
SD	8.44	9.65	11.31	11.87	8.59	8.55	9.77	0	28.87	39.58	44.46	26.24	32.44	30.25

1L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	**Area (mV.s)**							**Area (%)**						
1	37	32	31	33	28	33	35	100	86	84	89	76	89	95
2	22	11	15	15	17	20	20	100	50	68	68	77	91	91
3	15	14	14	14	13	15	17	100	93	93	93	87	100	113
4	26				22	22	27	100				85	85	104
5	28	25	17	21	18	25	27	100	89	61	75	64	89	96
6	16	14	15	17	11	16	16	100	88	94	106	69	100	100
7	34	30	30	29	21	17	20	100	88	88	85	62	50	59
8	13	12	8	8	7	16	15	100	92	62	62	54	123	115
9	40	19	33	37	29	29	26	100	48	83	93	73	73	65
10	15	12	12	12	12	13	14	100	80	80	80	80	87	93
n	10	9	9	9	10	10	10	10	9	9	9	10	10	10
Mean	24.60	18.78	19.44	20.67	17.80	20.60	21.70	100	79.41	79.12	83.48	72.54	88.62	93.17
SD	9.96	8.20	9.29	10.09	7.28	6.59	6.80	0	17.80	12.75	13.84	10.44	18.93	18.41

Table A 1.28 Q_{twpot} vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	**Duration (ms)**							**Duration (%)**						
1	33	34	36	36	37	37	26	100	101	108	108	110	110	79
2	28	24	23	22	59	42	27	100	86	82	79	212	151	95
3	19	13	15	18		9	8	100	71	80	95		50	43
4	12	11	11	11	19	15	10	100	97	94	93	163	131	86
5	20	23	30	30	33	27	22	100	111	148	148	161	133	108
6	20	26	18	17	27	22	21	100	128	89	84	131	107	102
7	72	72	76	75	74	72	73	100	100	106	104	103	100	101
8	31	41	36	55	42	42	27	100	130	115	177	134	134	85
9	29	22	18	19	24	35	30	100	76	63	67	83	122	103
10	32	28	33	38	37	40	30	100	89	105	121	116	126	95
n	10	10	10	10	9	10	10	10	10	10	10	9	10	10
Mean	29.60	29.37	29.63	32.12	38.96	34.17	27.28	100	98.98	98.98	107.37	134.66	116.46	89.71
SD	16.35	17.19	18.51	19.90	17.51	17.58	17.65	0	19.74	23.13	33.38	38.93	27.78	18.88

1L	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**	**pre-exercise**	**Bout 1**	**Bout 3**	**Bout 6**	**Fatigue**	**+10 min**	**+30 min**
Subject	**Duration (ms)**							**Duration (%)**						
1	34	33	32	33	35	29	34	100	97	92	95	103	85	100
2	30	30	27	20	40	31	27	100	100	91	68	134	104	91
3	11	21	17	17	18	18	10	100	188	153	153	156	162	91
4	15				16	15	15	100				107	100	100
5	22	20	15	32	33	30	20	100	90	67	145	149	133	90
6	27	21	31	36	34	37	20	100	77	115	132	126	134	72
7	57	60	65	62	59	51	56	100	106	115	109	104	90	99
8	41	43	51	51	54	53	42	100	103	123	123	131	127	102
9	19	19	33	21	23	24	19	100	104	179	111	121	129	104
10	45	50	50	47	52	46	42	100	111	111	104	115	102	93
n	10	9	9	9	10	10	10	10	9	9	9	10	10	10
Mean	30.20	33.15	35.78	35.48	36.43	33.40	28.60	100	108.44	116.11	115.50	124.58	116.68	94.12
SD	14.42	14.94	16.48	15.29	15.14	13.17	14.61	0	31.59	33.39	26.09	18.36	23.99	9.23

Table A 1.29 Q_{twpot} vastus lateralis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	rest	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Latency (ms)							Latency (%)						
1	4	4	4			4	4	100	108	100			100	108
2	6	5	1	1	5	5	5	100	84	21	21	84	79	84
3	5				6		5	100				120		107
4	5	5	6	5		5	5	100	107	113	107		107	107
5	5	7	7	7	7	7	7	100	131	131	131	131	125	131
6	7	6	6	6		6	6	100	86	81	81		81	81
7	4	4	4	4	4	4	4	100	100	100	100	108	100	92
8	5	6	6	6	6	6	6	100	129	129	129	129	129	129
9	5	5	5	5	4	4	5	100	93	93	100	87	87	93
10	5	5	5	4	7	5	5	100	100	100	93	143	107	107
n	10	9	9	8	9	10	10	10	9	9	8	7	9	10
Mean	5.10	5.26	4.78	4.83	5.11	5.23	5.23	100	104.23	96.50	95.17	114.55	101.55	103.88
SD	0.94	0.95	1.62	1.70	0.91	0.92	0.92	0	16.75	32.60	34.43	22.52	17.67	16.92

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	rest	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Latency (ms)							Latency (%)						
1	7	7	7	7	7	7	7	100	105	100	105	100	100	100
2	6	7	7	6	6	6	6	100	105	105	100	95	100	100
3	5	5	7	7	11			100	106	140	147	220		
4	5				4	5	7	100				87	93	140
5	6		7	6	5	5	5	100		117	94	83	78	78
6	4	4	4	6	6	5	3	100	100	92	150	142	125	83
7	4	4	4	4	4	5	4	100	100	100	92	92	117	108
8	5	5	6	5	5	5	5	100	100	129	114	100	114	114
9	5	5	5	6	5	5	5	100	100	100	113	100	100	100
10	4	4	4	4	5	4	5	100	100	108	108	125	100	117
n	10	8	9	9	10	9	9	10	8	9	9	10	9	9
Mean	5.10	5.12	5.63	5.74	5.73	5.19	5.30	100	102.03	110.06	113.65	114.31	103.01	104.49
SD	0.98	1.19	1.34	1.18	2.04	0.85	1.20	0	2.82	15.61	21.08	41.19	13.98	18.51

Table A 1.30 Q_{twpot} vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)							Amplitude (%)						
1	5	5	4		4		5	100	100	85		82		100
2	6	3	3	3	2	3	5	100	57	55	51	38	57	85
3	2					0	0	100					23	23
4	3	1	0	1	1		1	100	48	13	35	33		52
5	9	5	6	6	5	5	6	100	59	68	71	53	55	68
6	2	2	2	1	1		1	100	111	117	55	55		41
7	2	1	1	1	1	2	2	100	57	72	55	76	82	93
8	3	0	0	0	0	1	0	100	14	10	16	12	19	15
9	5	4	3	5	4	3	5	100	80	76	117	77	69	105
10	1	0	0	0	0	1	1	100	17	38	30	28	105	107
n	10	10	9	9	8	9	7	10	9	9	8	9	7	10
Mean	3.48	2.36	2.29	2.24	1.98	2.05	2.55	100	60.26	59.40	53.80	50.45	58.61	68.99
SD	2.39	1.83	1.95	2.33	1.62	1.67	2.20	0	32.93	34.55	31.01	24.43	30.50	34.36

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	rest	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)							Amplitude (%)						
1	6	5	6	6	5	5	6	100	86	100		78		100
2	3	3	3	3	2	3	3	100	89	89	93	70	100	93
3	0	0	0	0	0			100	100	133	67	67		
4	5				1	2	4	100				13	52	96
5	7		5	5	4	5	5	100		76	78	67	72	83
6	1	0	0	0	1	1	1	100	25	42	46	58	65	84
7	1	1	1	1	1	1	1	100	58	46	49	54	93	77
8	3	2	1	2	3	2	2	100	70	55	76	96	71	90
9	1	1	1	1	1	1	1	100	97	97	66	110	63	110
10	1	0	0	0	0	0	1	100	44	41	50	33	69	98
n	10	8	9	9	10	9	9	10	8	9	8	10	8	9
Mean	2.69	1.53	1.97	2.04	1.66	2.28	2.71	100	71.19	75.43	65.43	64.64	73.09	92.43
SD	2.28	1.69	2.13	2.23	1.69	1.84	2.08	0	26.99	32.10	16.39	28.12	15.87	10.02

Table A 1.31 Q_{twpot} vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Area (mV.s)							Area (%)						
1	32	32	24		24		21	100	100	75		75		66
2	28	24	18	22	14	24	27	100	86	64	79	50	86	96
3	19					17	18	100					89	95
4	19	14	12	12	12		18	100	74	63	63	63		95
5	65	65	115	80	51	114	114	100	100	177	123	78	175	175
6	16	14	14	13	13		16	100	88	88	81	81		100
7	14	9	16	15	14	16	16	100	64	114	107	100	114	114
8	19	12	12	13	12	13	13	100	63	63	68	63	68	68
9	36	22	24	35	20	26	38	100	61	67	97	56	72	106
10	14	12	12	13	12	14	14	100	86	86	93	86	100	100
n	10	9	9	8	9	7	10	10	9	9	8	9	7	10
Mean	26.20	22.67	27.44	25.38	19.11	32.00	29.50	100	80.13	88.52	88.96	72.48	100.79	101.52
SD	15.62	17.49	33.18	23.40	12.66	36.49	30.61	0	15.20	37.12	20.12	15.88	36.44	30.08

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Area (mV.s)							Area (%)						
1	65	66	60	60	51	65	65	100	102	92	92	78	100	100
2	22	18	17	18	11	22	18	100	82	77	82	50	100	82
3	15	13	13	12	12			100	87	87	80	80		
4	19				14	12	14	100				74	63	74
5	31		23	26	30	24	28	100		74	84	97	77	90
6	16	11	12	12	14	16	16	100	69	75	75	88	100	100
7	10	6	16	15	15	17	17	100	60	160	150	150	170	170
8	18	16	15	23	23	14	22	100	89	83	128	128	78	122
9	15	11	12	19	13	16	17	100	73	80	127	87	107	113
10	15	12	12	12	12	13	15	100	80	80	80	80	87	100
n	10	8	9	9	10	9	9	10	8	9	9	10	9	9
Mean	22.60	19.13	20.00	21.89	19.50	22.11	23.56	100	80.12	89.86	99.72	91.09	97.97	105.71
SD	15.91	19.28	15.41	15.14	12.57	16.56	16.12	0	12.88	26.92	27.52	28.44	30.51	28.27

Table A 1.32 Q_{twpot} vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Duration (ms)							Duration (%)						
1	40	40	36		35		31	100	100	90		87		78
2	27	39	37	42	34	39	40	100	143	134	154	123	143	145
3	24					14	12	100					57	51
4	24	14	11	15	12		12	100	57	47	61	51		51
5	55	52	56	60	51	46	50	100	96	102	110	93	84	92
6	13	24	23	22	25		13	100	185	174	172	192		97
7	41	53	64	65	75	69	67	100	127	156	157	181	166	163
8	34	17	27	27	31	39	28	100	51	79	79	93	115	83
9	38	24	27	32	34	44	46	100	64	71	83	89	116	120
10	35	28	32	38	35	40	37	100	81	90	110	100	114	105
n	10	9	9	8	9	7	10	10	9	9	8	9	7	10
Mean	33.07	32.37	34.67	37.63	36.89	41.38	33.60	100	100.43	104.94	115.78	112.39	113.46	98.66
SD	11.58	14.29	16.43	17.73	17.51	16.09	18.23	0	44.18	41.57	40.95	46.15	35.88	36.46

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Duration (ms)							Duration (%)						
1	51	66	74	61	51	52	51	100	130	146	120	101	102	100
2	25	22	22	22	27	25	22	100	89	89	89	109	100	89
3	12	17	20	24	16			100	141	162	195	130		
4	17				22	18	11	100				129	104	63
5	19		17	18	35	26	22	100		90	95	183	134	116
6	21	13	18	17	35	40	22	100	62	87	83	167	192	103
7	49	46	56	38	25	27	23	100	93	113	77	51	55	47
8	27	36	41	45	35	27	38	100	132	149	166	129	100	139
9	35	35	35	40	38	31	30	100	98	100	113	108	89	85
10	28	38	40	41	58	33	31	100	135	144	148	206	119	110
n	10	8	9	9	10	9	9	10	8	9	9	10	9	9
Mean	28.53	34.04	36.00	34.15	34.27	31.11	27.70	100	109.79	120.02	120.53	131.20	110.62	94.54
SD	13.00	16.95	19.28	14.60	12.75	9.91	11.48	0	28.22	30.09	40.77	44.68	37.33	27.78

Table A 1.33 Doublet vastus medialis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Latency (ms)							Latency (%)						
1	4	5	5	6	5	5	5	100	115	115	138	115	110	108
2	6	6	6	5	7	6	6	100	106	106	83	122	106	100
3	5	5	8	8	6	7	6	100	94	144	144	106	138	113
4	5	8	5	8	8	7	9	100	160	100	160	153	147	180
5	5	6	5	5	4	5	5	100	106	94	88	81	88	88
6	5	6	6	5	6	5	6	100	113	106	100	119	100	119
7	6	5		4	5	4	5	100	88	0	71	82	65	94
8	5	6	7	7	9	7	6	100	113	125	125	163	125	113
9	5	5	4	5	4	5	4	100	100	93	100	93	107	93
10	5	5	5	7	7	7	7	100	100	100	133	133	133	133
n	10	10	9	10	10	10	10	10	10	10	10	10	10	10
Mean	5.20	5.67	5.63	5.87	6.07	5.78	5.90	100	108.8	96.4	111.5	117.0	111.9	114.6
SD	0.48	0.99	1.06	1.35	1.51	1.26	1.34	0	20.8	39.7	30.3	29.3	26.3	28.5

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Latency (ms)							Latency (%)						
1	4	5	3	5	3	5	5	100	123	77	115	62	123	115
2	6	6	6	6	6	6	6	100	100	100	100	94	100	106
3	5	6	6	5	5	5	5	100	113	106	100	100	100	100
4	5	5			8	6	5	100	94	0	0	144	113	94
5	5	5	6	5	5	5	6	100	100	106	100	100	100	106
6	4	7	6	2	6	6	5	100	200	155	64	155	155	145
7	5	4	5	4	5	4	5	100	81	100	69	94	81	100
8	7	7	5	6	5	5	5	100	100	80	95	80	80	80
9	5	6	6	6	6	5	5	100	113	113	113	113	100	100
10	5	4	4	4	4	3	4	100	86	86	93	93	71	93
n	10	10	9	9	10	10	10	10	10	10	10	10	10	10
Mean	5.20	5.60	5.22	4.93	5.30	5.20	5.30	100	109.52	93.92	81.41	107.98	99.97	102.65
SD	0.83	1.02	0.93	1.29	1.26	0.80	0.51	0	35.51	41.05	34.32	24.99	24.24	17.89

Table A 1.34 Doublet vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)							Amplitude (%)						
1	5	3	3	1	4		5	100	64	62	26	92	0	115
2	8	7	2	2	2	4	9	100	82	23	21	21	52	104
3	2	2	1	1	1	1	3	100	85	45	30	50	30	115
4	2	1	2	1	1	2	1	100	53	100	53	35	85	73
5	4	4	8	7	7	8	4	100	89	183	158	169	192	103
6	2	1	2	2	1	1	2	100	60	87	140	60	73	93
7	2	2		2	3	2	3	100	72	0	74	141	111	141
8	2	0	0	0	0	0	0	100	9	8	5	14	9	9
9	2	2	2	2	2	2	3	100	81	75	100	73	101	117
10	2	0	0	0	0	1	0	100	20	22	21	13	57	24
n	10	10	9	10	10	9	10	10	10	10	10	10	10	10
Mean	3.1	2.16	2.15	1.83	2.13	2.45	3.05	100	61.2	60.2	67.0	64.1	78.9	86.6
SD	2.1	2.0	2.3	1.9	2.2	2.5	2.6	0	29.0	58.3	55.3	55.9	53.3	44.0

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)							Amplitude (%)						
1	8	7	7	8	7	7	8	100	87	88	93	83	86	99
2	10	3	5	5	5	5	6	100	34	51	47	48	51	56
3	5	4	5	2	2	5	5	100	85	98	40	38	108	110
4	16	11	13	12	15	15	4	100	67	84	75	98	93	28
5	5	4	3	4	4	5	6	100	80	63	83	88	105	135
6	2	3	2	2	2	2	2	100	120	100	102	86	102	98
7	4	3	2	2	2	3	3	100	67	60	50	49	72	89
8	1	1	1	0	1	1	1	100	38	40	32	41	36	39
9	4	4	4	4	3	5	4	100	87	86	87	79	133	104
10	2	0	0	0	0	0	0	100	17	18	8	10	17	10
n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	5.68	3.85	4.20	3.83	4.07	4.81	4.02	100	66.15	66.54	58.24	59.48	79.65	74.23
SD	4.52	3.05	3.80	3.58	4.48	4.11	2.52	0	32.02	27.70	30.47	29.31	38.08	42.54

Table A 1.35 Doublet vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Area (mV.s)							Area (%)						
1	34	16	20	7	30		32	100	47	59	21	88		94
2	49	3	12	14	6	18	51	100	6	24	29	12	37	104
3	5	10	4	2	6	2	5	100	200	80	40	120	40	100
4	10	4	10	4	2	2	4	100	40	100	40	20	20	40
5	18	15	32	33	33	33	13	100	83	178	183	183	183	72
6	7	8	11	10	6	6	5	100	114	157	143	86	86	71
7	16	14		15	25	27	36	100	88		94	156	169	225
8	2	2	2	2	4	3	2	100	100	100	100	200	150	100
9	9	7	5	12	5	8	12	100	78	56	133	56	89	133
10	9	3	3	5	5	11	4	100	33	33	56	56	122	44
n	10	10	9	10	10	9	10	10	10	9	10	10	9	10
Mean	15.90	8.20	11.00	10.40	12.20	12.22	16.40	100	78.94	87.46	83.80	97.69	99.52	98.46
SD	14.72	5.33	9.71	9.25	12.04	11.38	17.10	0	54.12	55.02	54.14	69.60	60.20	55.92

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Area (mV.s)							Area (%)						
1	33	26	33	29	34	26	30	100	79	100	88	103	79	91
2	64	19	33	29	35	33	34	100	30	52	45	55	52	53
3	14	10	14	7	5	15	14	100	71	100	50	36	107	100
4	16	34			7	6	16	100	213			44	38	100
5	19	17	20	20	18	24	27	100	89	105	105	95	126	142
6	5	14	11	11	9	11	12	100	280	220	220	180	220	240
7	28	30	21	15	21	15	29	100	107	75	54	75	54	104
8	15	12	7	10	12	17	17	100	80	47	67	80	113	113
9	25	31	28	42	27	31	23	100	124	112	168	108	124	92
10	7	2	3	2	2	2	2	100	29	43	29	29	29	29
n	10	10.0	9.0	9.0	10.0	10.0	10.0	10	10	9	9	10	10	10
Mean	22.60	19.50	18.89	18.33	17.00	18.00	20.40	100	113.64	94.17	92.17	77.83	95.78	108.08
SD	16.99	10.46	10.99	12.85	11.96	10.34	9.90	0	83.20	57.79	68.06	46.83	60.46	59.52

Table A 1.36 Doublet vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Duration (ms)							Duration (%)						
1	22	21	25	18	32		28	100	97	117	82	146	0	128
2	23	24	39	30	36	14	14	100	107	174	131	157	63	62
3	16	24	20	13	20	13	8	100	153	128	81	130	85	53
4	24	20	26	20	13	13	14	100	86	109	86	54	56	59
5	20	18	29	27	33	25	15	100	90	144	131	161	125	75
6	20	26	30	18	17	13	12	100	128	148	88	85	63	62
7	44	45		46	39	46	43	100	103	0	105	89	106	99
8	46	44	43	43	46	73	40	100	96	94	94	100	158	87
9	27	22	18	41	30	33	45	100	81	66	154	111	122	170
10	45	32	42	58	53	52	37	100	70	93	130	119	115	81
n	10	10	9	10	10	9	10	10	10	10	10	10	10	10
Mean	28.5	27.60	30.24	31.33	31.80	31.37	25.70	100	101.22	107.30	108.16	115.15	89.40	87.65
SD	11.64	9.62	9.30	15.09	12.71	21.42	14.48	0	24.11	51.76	25.84	34.62	34.55	35.83

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Duration (ms)							Duration (%)						
1	25	23	34	27	31	23	27	100	93	137	109	124	92	108
2	25	30	35	29	37	35	31	100	117	139	113	145	139	124
3	16	17	16	24	17	15	14	100	106	100	148	104	96	90
4	24	27			37	29	25	100	112	0	0	151	120	104
5	20	14	18	17	29	18	16	100	72	92	87	145	88	80
6	20	38	20	24	42	35	22	100	192	98	118	210	173	110
7	43	45	46	44	44	43	42	100	105	107	102	101	100	97
8	43	42	44	48	51	44	47	100	98	103	112	119	103	111
9	23	31	36	44	36	17	19	100	131	154	189	154	74	80
10	45	45	45	45	45	46	46	100	101	101	101	100	103	103
n	10	10	9	9	10	10	10	10	10	10	10	10	10	10
Mean	28.47	31.33	32.78	33.48	36.70	30.58	29.00	100	112.83	103.19	107.80	135.24	108.91	100.62
SD	10.80	11.22	11.94	11.56	9.60	11.80	12.28	0	31.80	42.77	50.55	35.41	29.81	14.68

Table A 1.37 Doublet vastus lateralis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Latency (ms)							Latency (%)						
1	4	5	4	4	4		5	100	133	108	100	100	0	133
2	5	6	6	5	5	5	5	100	106	106	100	94	94	88
3	5	8	10	5	6	5	8	100	160	207	100	113	107	167
4	8	7	5	5	8	5	8	100	96	65	61	100	70	109
5	7	7	7	7		7	7	100	105	95	100	0	105	105
6	6		7		6	7	8	100	0	105	0	89	105	132
7	4	5	4	4		5	5	100	115	92	92	0	108	108
8	10	3	6	6	6	6	6	100	26	58	58	58	58	58
9	5	5	4	5	5	4	4	100	107	87	93	93	87	87
10	5	5	5	5	3	5	7	100	100	100	100	67	100	133
n	10.0	9	10	9	8	9	10	10	10	10	10	10	10	10
Mean	6.00	5.74	5.80	5.07	5.25	5.52	6.40	100	94.8	102.4	80.5	71.5	83.2	111.8
SD	1.91	1.62	1.85	0.95	1.33	0.97	1.62	0	47.5	40.4	32.6	41.0	33.7	30.8

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Latency (ms)							Latency (%)						
1	7	8	7	7	7	7	7	100	105	95	95	91	100	100
2	6	6	6	8	9	8	6	100	112	100	141	165	147	106
3	10	8	6	8	8	6	6	100	79	62	83	79	59	62
4	5	8			5	5	6	100	153	0	0	100	100	127
5	6	5	5	5	5	6	5	100	82	88	88	94	100	94
6	5	6	4	5	5	5	4	100	106	75	94	94	100	69
7	4	4	4	4	4	5	5	100	92	100	100	100	115	115
8	5	5	5	2	5	5	5	100	114	100	50	114	114	114
9	6	6	6	5	5	6	5	100	100	100	89	89	100	89
10	6	7	4	6	6	7	6	100	111	72	100	100	117	100
n	10	10	9	9	10	10	10	10	10	10	10	10	10	10
Mean	5.97	6.17	5.22	5.67	6.00	6.07	5.63	100	105.5	79.3	84.0	102.6	105.2	97.6
SD	1.54	1.29	1.00	1.83	1.51	1.12	0.96	0	20.7	31.1	36.9	23.6	22.0	20.3

Table A 1.38 Doublet vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)							Amplitude (%)						
1	6	2	3	5	6		2	100	29	49	94	104		39
2	5	2	3	2	2	3	2	100	40	52	50	44	55	48
3	3	4	1	1	1	1	1	100	132	36	36	40	40	20
4	3	3	1	2	2	1	1	100	100	34	57	53	34	31
5	7	8	5	7		7	6	100	114	68	95		102	83
6	1		1		1	1	1	100		55	0	61	55	55
7	2	2	1	2		3	3	100	101	60	79		130	130
8	1	0	0	1	0	0	0	100	47	34	69	46	43	35
9	5	5	3	4	3	4	5	100	109	70	85	60	92	97
10	1	0	1	1	1	1	1	100	12	43	44	62	77	93
n	10	9	10	9	8	9	10	10	9	10	10	8	9	10
Mean	3.47	3.00	1.87	2.74	2.01	2.41	2.19	100	75.98	50.17	60.93	58.84	69.79	63.02
SD	2.08	2.45	1.44	2.16	1.82	2.19	1.83	0	43.70	13.29	29.75	20.13	32.60	35.65

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)							Amplitude (%)						
1	12	11	7	6	5	12	14	100	88	54	48	38	100	111
2	10	6	4	8	4	8	8	100	60	39	81	38	81	77
3	4	3	2	3	4	5	5	100	75	41	72	94	137	131
4	15	15			15	16	16	100	100			95	101	101
5	7	4	4	6	4	5	5	100	60	52	80	53	67	73
6	2	2	1	1	1	1	0	100	97	43	34	61	38	27
7	5	4	3	2	1	3	4	100	70	58	47	26	51	80
8	7	3	3	2	2	2	2	100	36	34	29	31	31	29
9	3	1	1	1	1	4	1	100	45	28	49	42	137	43
10	1	0	1	1	1	0	1	100	48	59	100	65	48	57
n	10	10	9	9	10	10	10	10	10	9	9	10	10	10
Mean	6.70	4.92	2.60	3.35	3.70	5.61	5.58	100	67.85	45.14	59.98	54.13	78.97	72.84
SD	4.77	4.74	1.98	2.67	4.10	5.02	5.33	0	21.99	10.94	24.19	24.53	38.86	34.79

Table A 1.39 Doublet vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL								Expressed as a % of pre-exercise						
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Area (mV.s)							Area (%)						
1	47	32	27	24	15		29	100	68	57	51	32		62
2	26	14	19	16	16	19	21	100	54	73	62	62	73	81
3	26	29	4	6	6	6	3	100	112	15	23	23	23	12
4	26	24	6	7	6	6	19	100	92	23	27	23	23	73
5	87	76	53	74		72	56	100	87	61	85	0	83	64
6	6		2		4	3	3	100		33		67	50	50
7	30	17	13	17		26	29	100	57	43	57	0	87	97
8	6	3	2	2	3	3	6	100	50	33	33	50	50	100
9	39	30	40	31	23	28	37	100	77	103	79	59	72	95
10	11	4	4	5	6	11	12	100	36	36	45	55	100	109
n	10	9	10	9	8	9	10	10	9	10	9	10	9	10
Mean	30.4	25.44	17.00	20.22	9.88	19.33	21.50	100	70.3	47.9	51.4	37.0	62.3	74.2
SD	23.99	21.80	17.81	22.34	7.20	21.94	16.88	0	23.8	26.1	21.8	24.9	27.4	29.1

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Area (mV.s)							Area (%)						
1	88	75	74	47	53	87	105	100	85	84	53	60	99	119
2	51	40	22	49	20	49	39	100	78	43	96	39	96	76
3	19	14	10	12	12	18	18	100	74	53	63	63	95	95
4	15	7			7	8	9	100	47			47	53	60
5	34	23	19	25	18	22	22	100	68	56	74	53	65	65
6	10	5	4	3	6	5	5	100	50	40	30	60	50	50
7	30	32	17	7	17	33	25	100	107	57	23	57	110	83
8	21	27	23	41	22	19	19	100	129	110	195	105	90	90
9	24	15	7	15	15	24	16	100	63	29	63	63	100	67
10	10	5	5	8	6	5	6	100	50	50	80	60	50	60
n	10	10	9	9	10	10	10	10	10	9	9	10	10	10
Mean	30.20	24.30	20.11	23.00	17.60	27.00	26.40	100	74.9	57.9	75.2	60.6	80.8	76.6
SD	23.77	21.40	21.47	18.19	13.74	25.01	29.38	0	26.4	24.5	50.5	17.3	23.5	20.8

Table A 1.40 Doublet vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL									Expressed as a % of pre-exercise					
2L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Duration (ms)							Duration (%)						
1	44	17	26	30	29		15	100	39	60	69	67		34
2	13	21	23	25	28	17	23	100	166	179	197	221	132	179
3	37	41	12	19	20	18	14	100	111	33	52	55	49	37
4	15	16	19	37	34	20	14	100	107	122	239	220	133	89
5	43	41	43	43		41	40	100	95	99	99		96	93
6	17		16		18	15	13	100		96		106	92	76
7	25	37	46	46		26	37	100	149	186	185		105	151
8	18	25	25	27	29	28	29	100	135	135	145	160	153	158
9	39	23	35	36	40	41	41	100	60	91	93	102	104	104
10	47	75	33	60	52	52	42	100	161	71	128	111	111	89
n	10	9	10	9	8	9	10	10	9	10	9	8	9	10
Mean	29.67	32.85	27.73	35.78	31.21	28.67	26.63	100	113.47	107.12	134.29	130.21	108.28	101.18
SD	13.40	18.51	11.31	12.39	10.79	12.97	12.49	0	43.97	49.39	62.90	63.77	29.70	48.72

1L	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min	pre-exercise	Bout 1	Bout 3	Bout 6	Fatigue	+10 min	+30 min
Subject	Duration (ms)							Duration (%)						
1	34	32	43	41	43	34	36	100	95	127	121	128	100	107
2	24	24	21	23	26	23	19	100	100	85	93	108	95	77
3	28	27	26	24	23	26	27	100	94	92	86	80	91	95
4	22	32			38	28	24	100	147	0	0	173	126	111
5	25	27	19	21	19	18	17	100	108	78	84	78	72	69
6	13	31	33	25	30	34	18	100	236	254	192	231	259	136
7	22	45	42	45	46	44	39	100	203	187	200	204	197	176
8	37	41	35	32	38	34	35	100	111	96	87	104	93	95
9	37	35	32	36	37	42	37	100	95	87	98	102	115	102
10	36	43	45	43	43	43	44	100	120	126	121	121	120	124
n	10	10	9	9	10	10	10	10	10	10	10	10	10	10
Mean	27.73	33.60	32.85	32.15	34.37	32.40	29.63	100	130.82	113.20	108.29	132.92	126.54	109.11
SD	7.88	7.19	9.40	9.38	9.22	8.89	9.96	0	49.93	68.12	57.16	52.33	57.62	30.85

Table A 1.41 20Hz Tetani vastus medialis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Latency (ms)				Latency (%)			
1	5	6	4	4	100	113	-20	-20
2	6	6	4	6	100	6	-33	-6
3	5	8		5	100	60		-7
4	5	8		6	100	44		6
5	5	6	5	5	100	6	-6	0
6	6	6	6	6	100	6	0	0
7	5	3	1	5	100	-38	-75	-12
8	6	7	6	5	100	5	-5	-26
9	5	4	4	5	100	-7	-7	0
10	6.67	6.67	5.00	3.33	100	0.00	-25.00	-50.01
n	10	10	8	10	10	10	8	10
Mean	5.53	6.03	4.42	4.83	100	19.54	-21.50	-11.47
SD	0.60	1.34	1.35	0.73	0	42.34	24.44	16.82

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Latency (ms)				Latency (%)			
1	3	7		2	100	150	-100	-13
2	6	6		6	100	-6	-100	0
3	6	5	5	5	100	-12	-6	-6
4	5	3	5		100	-29	7	
5	5	6	5	5	100	13	7	-7
6	5	5	6	6	100	-6	6	6
7	6	4	5	4	100	-35	-18	-35
8	6	4	5	5	100	-33	-11	-11
9	7	5	5	5	100	-20	-30	-20
10	5	5	5	7	100	0	0	33
n	10	10	8	9	10	10	10	9
Mean	5.27	4.93	5.13	5.00	100	2.25	-24.46	-5.77
SD	1.03	0.96	0.33	1.23	0	54.16	41.53	18.90

Table A 1.42 20Hz Tetani vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)				Amplitude (%)			
1	5	5	6	5	100	87	109	102
2	9	6	6	8	100	64	66	96
3	1	1		2	100	67	0	171
4	15	1		15	100	5	0	103
5	8	4	4	7	100	53	56	88
6	3	3	3	3	100	79	86	100
7	3	2	2	3	100	61	65	100
8	6	3	3	4	100	56	57	75
9	3	3	2	2	100	86	76	73
10	0.37	0.34	0.73	0.59	100	93.72	200.00	161.48
n	10	0	0	8	10	10	10	10
Mean	5.36	2.65	3.40	5.16	100	65.07	71.46	106.99
SD	4.12	1.69	1.71	4.12	0	25.44	56.67	33.15

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)				Amplitude (%)			
1	7	5		7	100	67	0	103
2	6	3		5	100	47	0	75
3	5	4	4	5	100	78	95	98
4	2	2	1		100	84	53	
5	6	5	5	5	100	91	94	87
6	4	4	2	2	100	99	64	65
7	3	2	2	2	100	74	67	74
8	6	0	0	0	100	6	7	7
9	3	2	6	5	100	63	212	160
10	1	1	1	1	100	-5	-11	-6
n	10	10	8	9	10	10	10	9
Mean	4.11	2.66	2.74	3.48	100	60.48	57.99	73.78
SD	1.89	1.50	2.02	2.09	0	34.81	67.20	49.99

Table A 1.43 20Hz Tetani vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Area (mV.s)				Area (%)			
1	67	34	47	44	100	51	70	66
2	49	28	30	49	100	57	61	100
3	6	5		10	100	83		167
4	13	12		7	100	92		54
5	30	17	14	26	100	57	47	87
6	15	11	12	13	100	73	80	87
7	34	5	9	33	100	15	26	97
8	25	10	24	25	100	40	96	100
9	11	4	9	9	100	36	82	82
10	8.00	3.00	3.00	5.00	100	37.50	37.50	62.50
n	10	10	8	10	10	10	8	10
Mean	25.80	12.90	18.50	22.10	100	54.21	62.48	90.09
SD	18.79	10.02	13.50	15.06	0	23.69	24.01	31.40

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Area (mV.s)				Area (%)			
1	37	31		39	100	84		105
2	25	18		29	100	72		116
3	21	11	10	19	100	52	48	90
4	7		6		100		86	0
5	24	20	21	15	100	83	88	63
6	19	19	8	10	100	100	42	53
7	22	14	10	12	100	64	45	55
8	24	6	6	6	100	25	25	25
9	34	11	21	33	100	32	62	97
10	8	8	9	8	100	100	113	100
n	10	9	8	9	10	9	8	10
Mean	22.10	15.33	11.38	19.00	100	68.05	63.46	70.36
SD	9.04	7.21	5.74	11.22	0	27.23	29.26	37.92

Table A 1.44 20Hz Tetani vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Duration (ms)				Duration (%)			
1	28	34	34	30	100	120	120	108
2	28	29	30	28	100	105	108	100
3	19	24		21	100	130		114
4	18	20		22	100	107		122
5	19	25	18	23	100	132	95	123
6	21	25	23	21	100	116	106	97
7	31	33	48	44	100	106	154	143
8	16	46	33	35	100	282	204	216
9	25	43	26	27	100	173	104	107
10	23.33	33.33	35.00	33.33	100	142.86	150.00	142.86
n	10	10	8	10	10	10	8	10
Mean	22.87	31.20	30.79	28.53	100	141.47	130.16	127.34
SD	4.74	8.06	8.50	7.13	0	53.48	36.85	35.10

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Duration (ms)				Duration (%)			
1	35	41		38	100	116		107
2	18	27		29	100	145		156
3	12	25	13	15	100	205	103	119
4	9	17	18		100	200	212	
5	15	21	14	15	100	135	93	100
6	25	26	31	23	100	103	124	92
7	29	37	31	32	100	129	108	111
8	19	33	27	28	100	172	144	149
9	17	44	17	15	100	254	96	85
10	35	43	43	35	100	124	124	100
n	10	10	8	9	10	10	8	9
Mean	21.57	31.43	24.42	25.56	100	158.26	125.41	113.25
SD	8.75	9.12	9.99	8.47	0	48.23	38.65	24.61

Table A 1.45 20Hz Tetani vastus lateralis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Latency (ms)				Latency (%)			
1	5	5	6		100	100	113	0
2	7	6	4	4	100	95	55	65
3	6	5	8		100	94	147	0
4	8	8	5		100	96	63	0
5	7	7	5	8	100	100	68	109
6	4	6	6	6	100	155	173	164
7	5	4	3	3	100	79	71	64
8	4	4	3	6	100	92	62	138
9	5	5	4	4	100	94	75	81
10	7	5	5	5	100	75	75	75
n	10	10	10	7	10	10	10	10
Mean	5.73	5.50	4.90	5.24	100	97.91	90.17	69.67
SD	1.32	1.23	1.56	1.49	0	21.58	40.41	57.63

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Latency (ms)				Latency (%)			
1	5	3	7		100	57	143	0
2	4	6	6		100	142	150	0
3	5	7	8	10	100	125	156	181
4	5	5	7	3	100	93	133	60
5	7	6	5	4	100	77	68	59
6	6	4	4	5	100	72	72	78
7	4	5	6	4	100	145	155	100
8	12	6	6	5	100	50	50	44
9	5	6	7	6	100	129	143	129
10	3	2	3	5	100	70	100	150
n	10	10	10	8	10	10	10	10
Mean	5.60	4.93	5.87	5.21	100	96.07	117.02	80.12
SD	2.40	1.37	1.33	1.90	0	35.99	40.56	60.39

Table A 1.46 20Hz Tetani vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)				Amplitude (%)			
1	6	4	5	6	100	71	88	100
2	6	3	4	5	100	53	76	82
3	1	1		1	100	70		100
4	15	15		15	100	98		101
5	14	10	11	12	100	71	78	90
6	4	2	3	3	100	58	81	74
7	3	3	3	3	100	101	101	101
8	5	2	4	4	100	40	65	81
9	4	4	4	5	100	104	108	115
10	3	3	3	3	100	88	98	98
n	10	10	8	8	10	10	8	10
Mean	6.11	4.71	4.64	5.74	100	75.48	86.72	94.18
SD	4.42	4.13	2.40	4.32	0	21.74	14.52	12.21

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Amplitude (mV)				Amplitude (%)			
1	7	5		5	100	76		79
2	7	4		8	100	59		107
3	6	3	4	6	100	46	63	104
4	3	1	3		100	31	87	
5	6	5	5	6	100	84	86	95
6	1	1	1	1	100	97	88	105
7	3	1	2	2	100	51	96	88
8	6	2	3	5	100	37	40	79
9	2	2	3	3	100	68	131	144
10	3	2	3	3	100	66	100	100
n	10	10	8	9	10	10	8	9
Mean	4.50	2.68	2.99	4.44	100	61.46	86.39	100.14
SD	2.15	1.60	1.18	2.04	0	20.84	26.52	19.67

Table A 1.47 20Hz Tetani vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Area (mV.s)				Area (%)			
1	32	30	32	32	100	94	100	100
2	30	11	20	22	100	37	67	73
3	6	7		6	100	117	0	100
4	9	6		15	100	67	0	167
5	85	47	74	87	100	55	87	102
6	16	10	14	13	100	63	88	81
7	24	5	6	30	100	21	25	125
8	21	5	3	5	100	24	14	24
9	34	20	29	40	100	59	85	118
10	21	11	12	23	100	52	57	110
n	10	10	8	10	10	10	10	10
Mean	27.80	15.20	23.75	27.30	100	58.74	52.29	99.96
SD	20.99	12.94	21.25	22.60	0	29.54	39.02	37.04

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Area (mV.s)				Area (%)			
1	38	34		45	100	89		118
2	50	22		39	100	44	0	78
3	21	3	19	29	100	14	90	138
4	17	4	24		100	24	141	0
5	27	29	28	25	100	107	104	93
6	4	4	4	5	100	100	100	125
7	26	7	8	15	100	27	31	58
8	36	16	15	12	100	44	42	33
9	36	21	36	16	100	58	100	44
10	20	19	20	20	100	95	100	100
n	10	10	8	9	10	10	9	10
Mean	27.50	15.90	19.25	22.89	100	60.34	78.64	78.76
SD	12.35	10.49	9.73	12.23	0	34.89	44.57	44.43

Table A 1.48 20Hz Tetani vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL					Expressed as a % of pre-exercise			
2L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Duration (ms)				Duration (%)			
1	30	32	28	29	100	107	93	99
2	28	14	22	21	100	50	77	76
3	18	31		20	100	167		111
4	19	22		32	100	120		171
5	36	26	32	34	100	71	88	94
6	22	15	15	17	100	67	67	76
7	30	37	46	46	100	122	152	151
8	18	30	34	33	100	167	189	181
9	28	45	40	45	100	162	144	160
10	38	40	45	35	100	104	117	91
n	10	10	8	10	10	10	8	10
Mean	26.77	29.17	32.67	31.17	100	113.74	115.97	120.99
SD	6.90	9.69	10.30	9.14	0	42.51	42.34	40.56

1L	pre-exercise	Fatigue	+10 min	+30 min	pre-exercise	Fatigue	+10 min	+30 min
Subject	Duration (ms)				Duration (%)			
1	36	52		42	100	142		115
2	19	21		19	100	107		97
3	14	25	21	26	100	179	148	183
4	13	28	30		100	224	237	
5	19	15	19	24	100	82	100	127
6	22	23	33	29	100	108	154	135
7	40	36	32	33	100	90	79	83
8	27	31	26	25	100	114	96	94
9	19	43	32	24	100	221	166	124
10	28	47	33	35	100	165	118	124
n	10	10	8	9	10	10	8	9
Mean	23.73	32.03	28.21	28.48	100	143.02	137.12	120.08
SD	8.61	11.30	5.42	6.62	0	51.87	50.60	29.57

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Appendix G

MUSCLE BIOPSY & ARTERIAL CATHETERISATION QUESTIONNAIRE

Chapter 4

NAME: _____

ADDRESS: _____

DATE: _____ **AGE:** _____ **years**

1. Have you or your family suffered from any tendency to bleed excessively? (eg. Haemophilia) or bruise very easily? Yes No Don't Know

   If yes, please elaborate

   _____

2. Are you allergic to local anaesthetic? Yes No Don't Know

   If yes, please elaborate

   _____

3. Do you have any skin allergies? Yes No Don't Know

   If yes, please elaborate

   _____

4. Have you any other allergies? Yes No Don't Know

   If yes, please elaborate

   _____

5. Are you currently on any medication? Yes No

   If yes, what is the medication?

   _____

6. Do you have any other medical problems? Yes No

If yes, please elaborate

_____

7. Have you ever fainted when you had an injection or blood sample taken?

Yes No Don't know

If yes, please elaborate

_____

8. Have you previously had heparin infused or injected? Yes No Don't know

If yes, please elaborate

_____

9. Do you or other members of your family have Raynauds disease, or suffer from very poor circulation in the fingers,

leading to painful fingers that turn white/blue? Yes No Don't know

If yes, please elaborate

_____

To the best of my knowledge, the above questionnaire has been completely accurately and truthfully.

Signature: _____ Date: _____

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Appendix H

INFORMATION TO PARTICIPANTS INVOLVED IN RESEARCH
Chapter 4

You are invited to participate

You are invited to participate in a research project entitled **"The effects of an oral dose of digoxin on potassium regulation in muscle and blood, skeletal muscle Na+,K+-ATPase and muscle fatigability during and following cycling exercise in healthy young adults".**
This project is being conducted by student researchers Trevor Farr and Tania Atanasovska as part of a PhD study at Victoria University under the supervision of Professor Michael McKenna from the Institute of Sport, Exercise and Active Living, within the College of Sport and Exercise Science / ISEAL.

Project explanation

Digoxin is an important drug taken by many patients with moderate to severe heart failure. The major action of digoxin is on the heart, where it increases the force of contraction of the heart muscle and increases the amount of blood pumped out to the rest of the body. This action occurs as a result of digoxin blocking (inhibiting) a protein known as the Na^+,K^+-ATPase (or NaK pump) in the heart. The NaK pump is also located in skeletal muscle cells, where it is vital in preserving muscle potassium levels and the capacity for repeated contractions. Exercise causes a rapid and pronounced increase in potassium concentration in blood. Immediately following exercise, this rapidly reverses such that potassium concentration declines below resting levels. Changes in potassium concentration have been linked to muscle fatigue. Numerous studies in rat muscles have shown that minor blocking of NaK pump impairs muscle performance. This study will investigate in healthy young adults the acute effects of oral digoxin on potassium concentration in the blood at rest, during cycle exercise and post-exercise; on NaK pump in muscle; and on exercise performance and muscle fatigue.

What will I be asked to do?

Participants will comprise 14 healthy male and female adults between ages of 18-35 years. Participants are expected to be healthy and recreationally active. The study will be conducted at Victoria University in the Exercise Physiology Laboratory, Building P, Footscray Park. Prospective participants will be screen prior to entry into the study.
Participants will visit the laboratory on five separate occasions. The first visit will consist of participant pre-screening procedures, incremental exercise (VO2 peak) test and protocol familiarisation. The second and third visits will comprise of the variability tests. The fourth and fifth visit will involve the experimental trials with and without oral digoxin.

Visit 1: Pre-screening: Participants will be screened prior to entry in the study. Participants will be required to complete the standard Victoria University Cardiovascular Risk Questionnaire, the Catheterization and Muscle Biopsy Questionnaire and give Informed Consent (appendix 2). Prospective participants will be asked by the investigators to complete the standard questionnaires. Those potential participants that circle the "Yes" response on the questionnaire will be further questioned by the Principal Investigator to ascertain the reliability/severity of any possible contraindication. Prospective participants will be undergo a venous blood sample to ensure participants have no abnormal plasma electrolyte concentrations, or

plasma creatinine and urea levels, which might indicate impaired kidney function. A full ECG will also be measured at rest for 5 minutes to ensure heart rhythm and electrical activity of the heart is normal and blood pressure will be measured. These results will be examined by one of the clinical investigators (usually Dr. Robert Smith). Only participants deemed healthy will be given approval to participate. An incremental exercise test will be performed on an electrically braked cycle ergometer to determine VO2 peak.

Familiarisation: After a 30 min rest following the incremental VO2 peak test, participants will then be familiarised with the exercise protocol undertaken during the placebo / digoxin trial. The familiarisation will consist of 60 % of VO2 peak for 1 min and 95 % of VO2 peak for 1 min followed by a maximal "all-out" effort until fatigue. This will give participants insight into physical efforts required on trial days.

Visit 2 & 3: Variability tests: Participants will be requested to undergo variability testing of the protocol. Each variability visit should last no more than 15 min. These tests will be repeated, separated by 5-7 days, to document the variability of each participant during the exercise. This is important since it allows us to establish the exact variability of the exercise test undertaken by the participants.

Visit 4 & 5: Experimental trials with either placebo or digoxin intervention
The fourth and fifth visit will comprise of the participant performing the experimental trial with placebo or oral digoxin administration. Participants will be required to complete the protocol consisting of 1 min at 60 % VO2 peak, 1 min at 95 % VO2 peak followed by a maximal "all-out" effort until volitional fatigue on a cycle ergometer. Blood and muscle samples will be collected at rest, during exercise and in recovery. Following a 2 week period for males and a 4 week period for females, participants will be required to return to the laboratory and repeat the exercise trial with either placebo or digoxin. The order of doing the trials will be randomly chosen. The greater time between trials for females is to ensure females are in the same phase of the menstrual cycle during the second trial. This design is chosen to ensure no digoxin carry-over effects on the subsequent trial. Verbal encouragement will be given to each participant to give a maximal effort during each trial. Prospective participants will dedicate approximately 8-10 hrs of their time in total.

What will I gain from participating?

You will gain information on your aerobic fitness (oxygen consumption and heart rate) during the exercise and other physiological parameters such as lactates, pH, and potassium concentration; will better understand fitness tests and the procedures and protocols associated with research.
Participants will be reimbursed according to their participation, allowing a subject to receive compensation for their time if they decide to withdraw from the study prior to completion. They will receive payment of:

- $0 if they withdraw from the study after the variability test. VO_2 peak tests carry a commercial value of $200-300 per test in the public domain and provide valuable information about fitness capabilities of the individual undertaking the test. As such, should a participant choose to withdraw from the study after the preliminary test, not monetary honorarium will be given as the information obtained is of great value.
- $ 100 cash or $100 gift voucher from Coles / Myer for completion of one experimental trial
- $ 200 cash or $200 gift voucher from Coles /Myer for completion of the whole study / two experimental trials.

How will the information I give be used?

No persons other than the investigators will be given access to your individual information. Records will be kept in filing cabinets in locked rooms. Any published data, oral presentations or written reports will not include your name. You will have access to your own results. No persons other than the chief and student investigators will be given access to the questionnaire, or any individual subject information.

What are the potential risks of participating in this project?

Exercise Testing & Vasovagal episodes: To ensure participants safety during exercise testing and training, the procedures will be terminated immediately before completion if any of the following criteria are present:

- Participant wishes to stop.
- Participant experiences chest pain, severe shortness of breath or any other pain related to, or caused by exercise.
- Participant wishes to continue but there are abnormal changes in ECG or other signs of metabolic, cardio-respiratory or thermo-regulatory distress (e.g. facial pallor).
- Participants sweating responses are inappropriate to the environmental conditions in the laboratory.

In addition, participants will be closely supervised and monitored at all times during exercise and testing sessions. Participants' heart rate and rhythm will be monitored continuously throughout and following all exercise trials involving blood sampling, using a Mortara ECG. This is a standard clinical physiological monitoring system complying with all relevant safety standards. A qualified medical practitioner will be in attendance. Investigator/s will follow the standard VU Management Plan. If the participants' condition does not improve an ambulance will be called.

Muscle Biopsy: Injection of a local anaesthetic in the skin and subcutaneous tissue overlying the muscle is used to minimise pain. The soreness is due to slight bleeding within the muscle and will be treated by ice, compression and elevation. An ice pack will be applied over the biopsy site after the biopsy procedure to minimise any bleeding and therefore soreness. The risk of localised altered skin sensation is minimised by (i) the choice of biopsy site – the site that is used above the vastus lateralis muscle avoids major branches of subcutaneous sensory nerve branches and (ii) using the smallest possible incision in the skin. The risk of infection is managed by the whole procedure being performed under local sterile conditions. Overall risks are minimised by the biopsy procedure being performed by a qualified and experienced medical practitioner. This has been safely conducted in our laboratory on many occasions.

Arterial and venous punctures and catheterisation using narrow gauge teflon external sleeve catheters are painful during the puncture, but well tolerated subsequently. Serious complications such as bleeding, arterial spasm, thrombosis (blood clot), and infection are theoretically possible, but rare. With arterial and venous sampling, we will follow standard clinical practice in which non-heparinised saline under pressure is used to keep the catheter patent. Arterial catheterisation and blood sampling have previously been safely undertaken in our laboratory at VU without incident in numerous separate studies; with all cannulations performed by experienced medical practitioners.

Digoxin side effects are expected to be minimal but might include nasal congestion / sinusitis, headache, tiredness, dry mouth, body aches and pain, nausea, increased tendency to bruise, joint pain, vomiting, mental impairment, sleepiness. We anticipate that digoxin may cause a small decrease in heart rate and possibly a decrease in blood pressure.

Toxic levels (i.e. overdose) of digoxin may cause severe heart rhythm disturbances, confusion and vision changes, but this is highly unlikely to occur, given that we will use only a low dose in a single tablet, thus preventing accidental overdose. In the very unlikely instance that digoxin toxicity does occur an ambulance will be called immediately and participants will be taken to the nearest hospital emergency centre.

Peripheral magnetic stimulation is a well-established and accepted technique, routinely performed on healthy individuals in the VU Exercise Physiology Laboratory. While lying on the bed a magnetic stimulator a double 50-mm coil (producing two overlapping circular fields) will be used to stimulate the subject's quadriceps. Magnetic stimulation is usually painless for the subject. In some cases, subjects may experience the sensation of muscle cramping and minimal muscle soreness but such side effects are acute and usually last for the remainder of the trial at most.

How will this project be conducted?

Participants will comprise 14 healthy male and female adults between ages of 18-35 years. Participants are expected to be healthy and recreationally active. Participant Information sheets will be mailed out or given directly to interested individuals. Participants will initially have all of the procedures and risks explained to them in understandable language by one of the investigators. If they choose to participate in the study they will be required to sign the consent form. The study will be conducted at Victoria University in the Exercise Physiology Laboratory, Building P, Footscray Park.

Participants will visit the laboratory on five separate occasions. The first visit will consist of participant pre-screening procedures, incremental exercise (VO2 peak) test and protocol familiarisation. The second and third visits will comprise of the variability tests. The fourth and fifth visit will involve the experimental trials with digoxin or placebo intervention.

Visit 1: Pre-screening: Visit 1: Pre-screening: Participants will be screened prior to entry in the study. Participants will be required to complete the standard Victoria University Cardiovascular Risk Questionnaire, the Catheterization and Muscle Biopsy Questionnaire and give Informed Consent (appendix 2). Prospective participants will be asked by the investigators to complete the standard questionnaires. Those potential participants that circle the "Yes" response on the questionnaire will be further questioned by the Principal Investigator to ascertain the reliability/severity of any possible contraindication. Prospective participants will undergo a venous blood sample to ensure participants have no abnormal plasma electrolyte concentrations, or plasma creatinine and urea levels, which might indicate impaired kidney function. A 12 Lead ECG will also be measured at rest for 5 minutes to ensure heart rhythm and electrical activity of the heart is normal and blood pressure will be measured. These results will be examined by one of the clinical investigators (usually Dr. Robert Smith). Only participants deemed healthy will be given approval to participate.
Inclusion criteria: Only low risk healthy participants will be included, defined as a person having no cardiovascular risk factors, not suffering from any cardiovascular, metabolic or respiratory disease / condition, bleeding disorders, thyroid disease, skin or anaesthetic allergies or musculoskeletal injuries. Prospective participants will also be free from taking any medication except for the contraceptive pill for females. Females will be encouraged to use condoms in addition to the contraceptive pill.
Exclusion criteria: Participants presenting with or suffering from cardiovascular risk factors, cardiovascular or respiratory condition / disease (e.g. asthma, hypertension, cardiac arrhythmias), bleeding disorders, eating disorders, skin or anaesthetic allergies or musculoskeletal injuries that may be aggravated by the exercise protocol, or pregnancy. Prospective participants taking prescribed medications such as beta-

agonists, cardiac glycosides, and diuretics will be excluded from this study due to the ability to influence potassium concentration.

Incremental exercise testing: An incremental exercise test will be performed on an electrically braked cycle ergometer at a cadence of 60-70 revs per minute to determine VO2 peak. For females the test will commence at 25 watts (W) and for males at 50 watts (W) and will increase by a further 25 W every minute until volitional exhaustion. Expired gases will be analysed using a custom-made metabolic cart.

Familiarisation: After a 30 min rest following the incremental VO2 peak test, participants will then be familiarised with the exercise protocol undertaken during the placebo / digoxin trial. The familiarisation will consist of 60 % of VO2 peak for 1 min and 95 % of VO2 peak for 1 min followed by a maximal "all-out" effort until volitional fatigue. This will give participants insight into physical efforts required on trial days. Participants will also have their quadriceps muscle stimulated in order to familiarise the participant with the peripheral magnetic stimulation technique.

Variability test: Participants will be requested to undergo variability testing of the protocol. Each variability visit should last no more than 15 min. These tests will be repeated, separated by 5-7 days, to document the variability of each participant during the exercise test. This is important since it allows us to establish the exact variability of the exercise test undertaken by the participants.

Visit 4 & 5: Experimental trials with placebo or digoxin intervention

The fourth and fifth visit will comprise of the participant performing the experimental trial with placebo or digoxin infusion. Participants will be required to complete the protocol consisting of 1 min at 60 % VO2 peak, 1 min at 95 % VO2 peak followed by a maximal "all-out" effort until volitional fatigue on a cycle ergometer. Blood sampling, muscle sampling and peripheral magnetic stimulation data will be collected at rest, during exercise and in recovery. Following a 1 week period for males and a one month period for females, participants will be required to return to the laboratory and repeat the exercise trial with either placebo or digoxin. The extended period for females is to ensure females are in the same phase of the menstrual cycle during the second trial. This design is chosen to ensure no drug / exercise carry-over effects on the subsequent trial and to ensure participants are able to give an 'all-out' effort during exercise. Verbal encouragement will be given to each participant to give a maximal effort during each trial.

Procedures:

Electrocardiography (ECG)

Heart rate and rhythm will be monitored and recorded continuously during and after each trial by 12-lead ECG. ECG electrodes will be adhered to the skin at ten sites on the chest. Patient cable leads are attached to the electrode and the transmitter will be fitted on the waist of the subjects with a belt. The transmitter telemetered signals to a compatible PC, will allow continuous ECG monitoring before, during and after each trial. To ensure low levels of movement artefact, electrodes will be fastened to the participants bodies with medical adhesive tape. Chest hair will also be shaved and cleaned to ensure signals are not impeded. There is no discomfort associated with the application, wearing and removal of the ECG electrodes. ECG recordings will be continuously monitored and recorded by the medical practitioner Dr Robert Smith.

Arterial cannulation – blood sampling and analyses

Upon arrival to the laboratory during the fourth and fifth visit, a cannula will be inserted into the radial artery of the right arm. The procedure will be performed by Dr Robert Smith, Western Hospital, Melbourne. The arterial cannula will be attached to sterile extension tubing set; this will also be attached to a

pressurised sterile isotonic saline bag (0.9 % Sodium Chloride) to enable rapid, repeated blood sampling whilst participants exercise freely during the trial. Approximately 20 minutes following cannulation, a resting blood sample of arterial blood will be drawn from the participant. Following the first (resting) blood sample, subjects 0.5 mg of oral digoxin / placebo will be administered to the participant. Participants' will rest in a supine position for 1 h to ensure full bioavailability of digoxin has taken effect. Approximately 10 min prior to exercise, participants will undergo a muscle biopsy, and peripheral magnetic stimulation and the second arterial blood sample will be taken. Subjects will then move to the cycle ergometer where a seated pre-exercise sample will be taken immediately prior to exercise commencing. During exercise, arterial blood sampling will be collected every 30 sec during exercise at 60 % and 95 % VO_2 peak bouts; and every 15 seconds for the first 2 minutes and every 30 seconds thereafter until volitional fatigue during the maximal 'all-out' exercise bout. Post-exercise blood samples will be collected at 1, 2, 3, 5, 10, 20, 30, 40, 50, 60 min during recovery. Multiple samples are required to accurately measure the time course of these changes, which is an important aim of this study. The drawing of blood will be conducted by principal and or associate investigators.

Oral Digoxin / placebo administration-
Approximately 20 min following arterial cannulation and 1 hr before exercise commences, an oral dose of 0.5 mg digoxin or placebo in the form of a tablet will be administered to participants by Dr Robert Smith. The digoxin will be administered 1 hr before exercise to ensure the digoxin has had time to enter the blood and bind to the muscles.

Muscle biopsy
Dr Mitch Anderson will perform all muscle biopsy procedures in this study. A total of 4 muscle biopsies will be collected; 2 per trial. Muscle biopsies will be collected at rest and at the end of exercise. All muscle biopsies will be taken at a constant depth from the vastus lateralis muscle, which is heavily involved in leg cycling exercise. After an injection of a local anaesthetic into the skin and fascia (2% Xylocaine), a small incision will be made and muscle samples (100-150mg) taken. All muscle samples will be placed in cryotubes and immediately frozen in liquid nitrogen in order to snap freeze samples for later analyses.

Maximal Voluntary Contraction (MVC) test
Participants perform a series of maximal voluntary contractions (MVC; isometric knee extensions) of 4 s duration whilst lying supine on a bed with the knee flexed at 90° and the leg passively stabilised to prevent lateral motion. A non-elastic ankle strap attached to a force transducer and amplifier measures thigh muscle force. This test has been done routinely in research within the Exercise Physiology laboratory.

Peripheral Magnetic Stimulation
While seated on the cycle ergometer, a magnetic stimulator coil will be used to stimulate the subject's thigh muscles. The area of stimulation associated with the largest thigh twitch and associated electrical signal will be determined by positioning the coil head high onto the quadriceps muscle. To determine supramaximal quadriceps stimulation, three single twitches every 30 s at 50, 60, 70, 80, 85, 90, 95, and 100% of maximal power output of the stimulator will be collected. To assess fatigue, the stimulus power set at 100% of maximum, single twitches at 1Hz and paired twitches at a frequency of 20 Hz will be performed. The same procedure and stimulator intensity will be used throughout the experiment. The potentiated quadriceps twitch is shown to be more sensitive for detecting fatigue than is the non-potentiated twitch, particularly when the degree of fatigue is small. Accordingly, we will measure Q_{tw} force 4 s after a 4-s MVC of the quadriceps via three single and three paired twitches during the 1 min of rest between bouts. The twitch responses to each stimulus will be analysed for peak force, contraction time, maximal rate of force development, one-half relaxation time, and maximal relaxation rate. The entire

fatigue assessment procedure will be performed before (~10 min) and immediately after the cycle exercise.

Who is conducting the study?

Principal Investigator:
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Any queries about your participation in this project may be directed to the Chief Investigator listed above. If you have any queries or complaints about the way you have been treated, you may contact the Research Ethics and Biosafety Manager, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 or phone (03) 9919 4148.

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

Appendix I

CONSENT FORM FOR PARTICIPANTS INVOLVED IN RESEARCH
Chapter 4

INFORMATION TO PARTICIPANTS:
We would like to invite you to be a part of a study into…
" The effects of an oral dose of digoxin on potassium regulation in muscle and blood, skeletal muscle Na+, K+ -ATPase and muscle fatigability during and following cycling exercise in healthy young adults".

This project is being conducted by student researchers Miss Tania Atanasovska and Mr Trevor Farr as part of a PhD at Victoria University under the supervision of Professor Michael J. McKenna, Dr Aaron Petersen, Dr Robert Smith and Professor Henry Krum.
CERTIFICATION BY SUBJECT
I,
of
certify that I am at least 18 years old* and that I am voluntarily giving my consent to participate in the study:
" The effects of an oral dose of digoxin on potassium regulation in muscle and blood, skeletal muscle Na+, K+ -ATPase and muscle fatigability during and following cycling exercise in healthy young adults"
being conducted at Victoria University by: Professor Michael McKenna

I certify that the objectives of the study, together with any risks and safeguards associated with the procedures listed hereunder to be carried out in the research, have been fully explained to me by: Trevor Farr and that I freely consent to participation involving the below mentioned procedures:

- VO_2 MAX TEST, FAMILIARISATION TEST
- VARIABILITY TESTS
- ORAL DIGOXIN / PLACEBO INTAKE
- BLOOD AND MUSCLE SAMPLING
- MAGNETIC STIMULATION
- ECG RECORDINGS
- CYCLING EXERCISE AT VARIOUS INTENSITIES

I certify that I have had the opportunity to have any questions answered and that I understand that I can withdraw from this study at any time and that this withdrawal will not jeopardise me in any way.

I have been informed that the information I provide will be kept confidential.

Signed:

Date:

Any queries about your participation in this project may be directed to the Chief Investigator
Professor Michael J McKenna
Ph: 03 9919 4499
Mob: 0432 757 859

If you have any queries or complaints about the way you have been treated, you may contact the Research Ethics and Biosafety Manager, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 or phone (03) 9919 4148.
[*please note: Where the participant/s are aged under 18, separate parental consent is required; where the participant/s are unable to answer for themselves due to mental illness or disability, parental or guardian consent may be required.]

Appendix J
Individual Raw Data
Chapter 4

Table A 2.1 Plasma [K^+]a (mM) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin

	Pre-exercise			Exercise											Recovery										
	Time (min)																								
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	6.0	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	3.70	3.80	4.00	4.60	4.80	5.40	5.80	6.30	6.60	6.80	7.00					7.00	5.20	3.90	3.70	3.40	3.40	3.50	3.60	3.60	3.70	3.80
2	4.00	3.90	4.20	4.80	4.90	5.10	5.50	5.80								5.80	4.90	3.90	3.80	3.70	4.00	3.80	3.80	4.00	4.10	4.00
3	3.90	3.80	3.80	4.60	5.10	5.10	5.60	5.80	5.40							5.40	4.80	3.70	3.40	3.30	3.60	3.70	3.70	3.80	3.80	3.80
4	3.90	4.00	4.30	4.50	4.90	5.40	5.70	5.90	6.30	6.60	6.60					6.60	4.60	3.80	3.60	3.60	3.70	3.80	3.80	3.80	3.80	3.90
5	3.90	3.80	4.00	4.50	4.50	5.40	6.20	6.80	7.00	7.30						7.30	5.00	4.00	3.70	3.60	3.50	3.70	3.80	3.70	3.70	3.80
6	4.10	4.00	4.30	4.80	5.30	5.30	5.00	5.70	6.10	6.90	7.20	6.70				6.70	5.30	4.20	3.70	3.50	3.70	3.80	3.90	3.90	3.90	4.00
7	4.10	4.20	4.60	5.00	5.30	5.60	6.10	6.50	6.70	7.00	7.00	7.00				7.00	5.10	4.10	3.80	3.70	3.80	3.80	3.90	3.60	3.80	3.70
8	4.00	3.90	4.40	4.60	4.90	5.10	5.30	5.80	6.00	6.10	6.30	6.40	6.40	6.30		6.30	4.50	3.80	3.70	3.60	3.60	3.80	3.70	3.80	3.80	3.90
9	4.10	4.20	4.40	4.60	4.90	5.40	5.50	5.80	6.10	6.10	6.40					6.40	4.90	4.10	3.90	3.90	4.00	4.20	4.30	4.50	4.60	4.60
10	3.60	3.70	3.80	4.30	4.70	5.00	5.30	5.80	5.40	5.60	5.90	6.30				6.30	4.50	4.00	3.70	3.50	3.60	3.70	3.70	3.70	3.80	3.80
n	10	10	10	10	10	10	10	10	9	8						10	10	10	10	10	10	10	10	10	10	10
Mean	3.93	3.93	4.18	4.63	4.93	5.28	5.60	6.02	6.18	6.55						6.48	4.88	3.95	3.70	3.58	3.69	3.78	3.82	3.84	3.90	3.93
SD	0.17	0.17	0.27	0.19	0.25	0.19	0.37	0.38	0.55	0.57						0.58	0.28	0.16	0.13	0.17	0.20	0.18	0.19	0.26	0.27	0.25

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	6.0	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	3.80	3.80	3.90	4.30	4.80	5.10	5.50	5.90	6.10	6.30	6.50	6.80				6.80	4.90	3.60	3.50	3.30	3.30	3.50	3.50	3.60	3.90	4.00
2	4.30	4.10	4.40	5.00	5.20	5.70	5.90	6.50								6.50	4.80	4.10	3.80	3.80	3.90	3.90	3.90	4.00	3.90	4.00
3	3.70	3.70	4.00	4.40	4.80	5.30	5.80	5.80	6.30	6.70						6.70	4.60	3.80	3.30	3.40	3.50	3.70	3.60	3.60	3.80	3.70
4	3.90	3.80	4.20	4.60	5.00	5.40	5.70	6.00	6.50	6.20	6.70					6.70	5.00	4.00	3.50	3.50	3.60	3.80	3.90	3.80	3.80	3.80
5	3.70	4.00	4.10	4.80	5.00	5.30	5.90	6.10	6.40	7.30						7.30	5.10	4.10	3.70	3.60	3.80	3.90	4.00	4.00	4.00	4.20
6	4.30	4.10	4.10	4.70	4.80	5.30	5.70	5.90	6.20	6.40	6.70					6.70	5.70	3.80	3.40	3.30	3.60	3.70	3.80	3.80	3.90	4.00
7	4.00	4.20	4.40	4.70	5.20	5.60	6.00	6.30	6.60	6.80	7.00					7.00	5.20	4.10	3.90	3.80	3.90	3.90	3.90	4.00	4.00	3.90
8	3.80	3.90	4.10	4.50	4.80	5.10	5.30	5.50	5.60	5.50	5.70	5.70	5.80	5.90	6.10	6.10	4.80	3.90	3.50	3.40	3.50	3.50	3.60	3.60	3.70	3.70
9	4.10	4.10	4.30	4.40	4.50	4.90	5.30	5.50	5.80	5.90	6.20					6.20	4.70	3.90	3.80	3.80	3.80	4.00	4.00	4.10	4.20	
10	3.70	3.70	3.70	4.10	4.00	4.60	4.80	5.10	5.30	5.70	5.80	6.30				6.30	5.00	4.00	3.60	3.30	3.30	3.50	3.50	3.50	3.60	3.60
n	10	10	10	10	10	10	10	10	9	9						10	10	10	10	10	10	10	10	10	10	9
Mean	3.93	3.94	4.12	4.55	4.81	5.23	5.59	5.86	6.09	6.31						6.63	4.98	3.93	3.60	3.52	3.62	3.74	3.77	3.80	3.88	3.88
SD	0.24	0.18	0.22	0.26	0.35	0.32	0.37	0.41	0.44	0.57						0.37	0.31	0.16	0.19	0.21	0.23	0.19	0.20	0.22	0.17	0.19

Table A 2.2 Peak increase in plasma Δ [K+]a (mM) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin Pre-exercise Exercise Recovery

Time (min)

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	0.00	0.10	0.30	0.90	1.10	1.70	2.10	2.60	2.90	3.10	3.30			3.30	1.50	0.20	0.00	-0.30	-0.30	-0.20	-0.10	-0.10	0.00	0.10
2	0.00	-0.10	0.20	0.80	0.90	1.10	1.50	1.80	2.22	2.48				2.48	0.90	-0.10	-0.20	-0.30	0.00	-0.20	-0.20	0.00	0.10	0.00
3	0.00	-0.10	-0.10	0.70	1.20	1.20	1.70	1.90	1.50	1.50				1.50	0.90	-0.20	-0.50	-0.60	-0.30	-0.20	-0.20	-0.10	-0.10	-0.10
4	0.00	0.10	0.40	0.60	1.00	1.50	1.80	2.00	2.40	2.70	2.70			2.70	0.70	-0.10	-0.30	-0.30	-0.20	-0.10	-0.10	-0.10	-0.10	0.00
5	0.00	-0.10	0.10	0.60	0.60	1.50	2.30	2.90	3.10	3.40				3.40	1.10	0.10	-0.20	-0.30	-0.40	-0.20	-0.10	-0.20	-0.20	-0.10
6	0.00	-0.10	0.20	0.70	1.20	1.20	0.90	1.60	2.00	2.80	3.10	2.60		2.60	1.20	0.10	-0.40	-0.60	-0.40	-0.30	-0.20	-0.20	-0.20	-0.10
7	0.00	0.10	0.50	0.90	1.20	1.50	2.00	2.40	2.60	2.90	2.90	2.90		2.90	1.00	0.00	-0.30	-0.40	-0.30	-0.30	-0.20	-0.50	-0.30	-0.40
8	0.00	-0.10	0.40	0.60	0.90	1.10	1.30	1.80	2.00	2.10	2.30	2.40	2.40	2.40	0.50	-0.20	-0.30	-0.40	-0.40	-0.20	-0.30	-0.20	-0.20	-0.10
9	0.00	0.10	0.30	0.50	0.80	1.30	1.40	1.70	2.00	2.00	2.30			2.30	0.80	0.00	-0.20	-0.20	-0.10	0.10	0.20	0.40	0.50	0.50
10	0.00	0.10	0.20	0.70	1.10	1.40	1.70	2.20	1.80	2.00	2.30	2.70		2.70	0.90	0.40	0.10	-0.10	0.00	0.10	0.10	0.10	0.20	0.20
n	10	10	10	10	10	10	10	10	10	10				10	10	10	10	10	10	10	10	10	10	10
Mean	0.00	0.00	0.25	0.70	1.00	1.35	1.67	2.09	2.25	2.50				2.63	0.95	0.02	-0.23	-0.35	-0.24	-0.15	-0.11	-0.09	-0.03	0.00
SD	0.00	0.11	0.17	0.13	0.20	0.20	0.41	0.43	0.50	0.59				0.54	0.28	0.19	0.18	0.16	0.16	0.14	0.15	0.23	0.24	0.24

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	0.00	0.00	0.10	0.50	1.00	1.30	1.70	2.10	2.30	2.50	2.70	3.00		3.00	1.10	-0.20	-0.30	-0.50	-0.50	-0.30	-0.30	-0.20	0.10	0.20
2	0.00	-0.20	0.10	0.70	0.90	1.40	1.60	2.20	2.30					2.60	0.50	-0.20	-0.50	-0.50	-0.40	-0.40	-0.40	-0.30	-0.40	-0.30
3	0.00	0.00	0.30	0.70	1.10	1.60	2.10	2.10	2.60	3.00				3.00	0.90	0.10	-0.40	-0.30	-0.20	0.00	-0.10	-0.10	0.10	0.00
4	0.00	-0.10	0.30	0.70	1.10	1.50	1.80	2.10	2.60	2.30	2.80			2.80	1.10	0.10	-0.40	-0.40	-0.30	-0.10	0.00	-0.10	-0.10	-0.10
5	0.00	0.30	0.40	1.10	1.30	1.60	2.20	2.40	2.70	3.60				3.60	1.40	0.40	0.00	-0.10	0.10	0.20	0.30	0.30	0.30	0.50
6	0.00	-0.20	-0.20	0.40	0.50	1.00	1.40	1.60	1.90	2.10	2.40			2.40	1.40	-0.50	-0.90	-1.00	-0.70	-0.60	-0.50	-0.50	-0.40	-0.30
7	0.00	0.20	0.40	0.70	1.20	1.60	2.00	2.30	2.60	2.80	3.00			3.00	1.20	0.10	-0.10	-0.20	-0.10	-0.10	-0.10	0.00	0.00	-0.10
8	0.00	0.10	0.30	0.70	1.00	1.30	1.50	1.70	1.80	1.90	1.90	2.00	2.10	2.30	1.00	0.10	-0.30	-0.40	-0.30	-0.30	-0.20	-0.20	-0.10	-0.10
9	0.00	0.00	0.20	0.30	0.40	0.80	1.20	1.40	1.70	1.80	2.10			2.10	0.60	-0.20	-0.30	-0.30	-0.30	-0.10	-0.10	0.00	0.10	-0.20
10	0.00	0.00	0.00	0.40	0.30	0.90	1.10	1.40	1.60	2.00	2.10	2.60		2.60	1.30	0.30	-0.10	-0.40	-0.40	-0.20	-0.20	-0.20	-0.10	-0.10
n	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	0.00	0.01	0.19	0.62	0.88	1.30	1.66	1.93	2.21					2.74	1.05	0.00	-0.33	-0.41	-0.31	-0.19	-0.16	-0.13	-0.05	-0.05
SD	0.00	0.16	0.19	0.23	0.35	0.30	0.37	0.37	0.42					0.44	0.31	0.27	0.25	0.24	0.22	0.22	0.22	0.21	0.22	0.24

Table A 2.3 Blood Hb_v ($g\text{-}dL^{-1}$) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin	Pre-exercise			Exercise										Recovery										
									Time (min)																
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	12.80	13.40	13.90	14.30	14.30	14.50	14.60	14.90	15.10	15.00	15.30				15.30	15.00	14.80	14.60	13.70	13.40	13.00	12.90	12.70	12.80	12.70
2	12.30	12.30	12.40	13.00	13.10	13.20	13.30	13.40	13.70	13.90					13.90	13.40	13.10	13.00	12.80	12.60	12.40	12.20	12.20	12.10	12.10
3	14.90	15.30	15.50	16.00	16.30	16.30	16.70	16.70	16.10	16.40					16.40	17.00	16.80	16.60	16.30	15.90	15.20	14.70	14.60	14.80	14.90
4	12.30	12.40	12.90	13.20	13.40	13.70	13.90	14.00	14.20	14.40	14.10				14.10	14.30	14.00	14.10	13.80	13.40	12.60	12.40	12.10	12.10	12.10
5	13.10	13.10	13.70	14.00	13.50	14.20	14.80	15.00	15.40	15.40					15.40	15.00	15.00	15.00	14.90	14.50	13.70	13.30	13.20	13.10	13.10
6	10.90	11.50	12.10	12.80	13.00	12.90	12.00	12.80	13.10	13.70	13.80	13.80			13.80	13.40	13.30	13.30	13.00	12.60	11.70	11.10	11.20	11.00	11.00
7	13.60	14.00	14.70	15.20	15.20	15.40	15.50	16.10	16.30	16.20	16.20	16.20			16.20	16.30	16.00	15.80	15.60	15.10	14.20	14.10	13.40	13.60	13.50
8	12.00	12.00	12.60	13.00	12.90	13.10	13.00	13.60	13.80	13.80	13.90	14.00	14.00	13.90	13.90	13.50	13.60	13.50	13.20	13.20	12.50	12.10	11.90	11.60	11.60
9	13.50	14.10	14.60	14.60	14.80	15.20	15.10	15.30	15.20	15.30	15.50				15.50	15.30	15.30	15.10	15.00	14.40	14.00	13.80	13.70	13.70	13.50
10	14.70	15.00	15.40	15.60	16.00	16.00	16.20	16.70	16.30	16.30	16.40	17.10			17.10	17.10	17.10	16.50	16.80	16.20	15.60	15.20	14.80	14.60	14.60
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	13.01	13.31	13.78	14.17	14.25	14.45	14.51	14.85	14.92	15.04					15.16	15.03	14.90	14.75	14.51	14.13	13.49	13.18	12.98	12.94	12.91
SD	1.23	1.28	1.25	1.17	1.27	1.23	1.47	1.38	1.16	1.06					1.19	1.42	1.42	1.29	1.42	1.30	1.27	1.28	1.18	1.26	1.26

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	13.60	13.80	14.20	14.60	15.00	15.00	15.30	15.30	15.30	15.40	15.60	15.70			15.70	15.40	14.70	15.00	14.50	14.20	13.60	13.10	13.10	12.80	13.00
2	12.50	12.60	12.80	13.50	13.50	13.80	13.70	14.20	14.20	14.30					14.30	14.00	13.70	13.80	13.60	13.20	12.90	12.60	12.70	12.20	12.30
3	14.10	14.50	15.30	15.40	15.50	15.80	15.90	15.90	16.30	16.50					16.50	16.20	15.80	15.50	15.40	15.00	14.50	14.00	13.80	14.00	13.90
4	12.40	12.60	13.40	13.60	13.80	13.90	14.10	14.30	14.50	13.90	14.40				14.40	14.70	14.40	14.40	14.00	13.90	13.20	13.00	12.70	12.30	12.50
5	13.00	12.70	13.10	13.90	13.90	14.10	14.40	14.30	14.60	15.20					15.20	14.90	14.70	14.60	14.50	14.00	13.20	12.90	12.70	12.50	12.40
6	12.30	12.30	13.20	13.80	13.80	13.90	14.10	14.20	14.40	14.80	14.80				14.80	14.50	14.20	14.20	13.90	13.60	12.70	12.30	12.00	12.00	11.90
7	14.30	14.70	15.20	15.70	16.00	16.10	16.40	16.60	16.50	16.60	17.00				17.00	16.70	16.80	16.10	16.10	15.60	14.90	14.40	14.30	14.20	13.90
8	12.80	13.00	13.30	13.90	14.10	14.10	14.30	14.50	14.50	14.70	14.80	14.70	14.90	14.90	14.90	14.80	14.70	14.80	14.40	14.30	13.60	13.20	12.90	12.70	12.60
9	13.40	14.10	14.30	14.60	14.50	14.80	14.90	15.00	15.20	15.20	15.40				15.40	15.30	15.10	15.00	14.70	14.50	13.80	13.50	13.40	13.30	13.00
10	14.40	14.80	15.20	15.30	15.10	15.70	15.60	15.90	15.90	16.30	16.40	16.70			16.70	16.60	16.40	16.60	16.30	16.10	15.40	15.00	14.60	14.50	14.60
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	13.28	13.51	14.00	14.43	14.52	14.72	14.87	15.02	15.14	15.29					15.49	15.31	15.05	15.00	14.74	14.44	13.78	13.40	13.22	13.05	13.01
SD	0.80	0.97	0.97	0.81	0.84	0.89	0.90	0.87	0.84	0.93					0.96	0.92	0.99	0.86	0.91	0.90	0.89	0.84	0.81	0.90	0.86

Table A 2.4 Blood Hct_a (%) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin	Pre-exercise			Exercise										Recovery										
										Time (min)															
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	39.30	41.10	42.50	43.90	43.80	44.30	44.60	45.80	46.40	46.00	47.00				47.00	46.10	45.40	44.80	42.20	41.20	40.00	39.60	39.00	39.30	39.00
2	38.00	38.00	38.30	39.80	40.10	40.50	40.80	41.10	41.40	41.70					41.70	41.20	40.30	39.90	39.40	38.60	38.20	37.40	37.40	37.30	37.20
3	45.60	47.00	47.40	49.10	50.00	49.90	51.00	51.20	49.40	51.00					51.00	52.00	51.40	50.90	49.80	46.60	48.60	45.20	44.90	45.30	45.70
4	37.80	38.20	39.70	40.60	41.30	41.90	42.80	42.90	43.60	44.10	43.20				43.20	43.90	43.10	43.40	42.40	41.30	38.90	38.20	37.30	37.30	37.40
5	40.10	40.30	41.90	42.80	41.50	43.60	45.40	46.10	47.30	47.20					47.20	46.10	45.90	46.00	45.60	44.60	41.90	41.00	40.60	40.10	40.20
6	33.50	35.40	37.20	39.50	39.90	39.60	37.00	39.50	40.20	42.10	42.50	42.30			42.30	41.10	40.80	40.80	40.00	38.70	36.10	34.30	34.50	33.80	34.00
7	41.70	43.10	45.20	46.50	46.60	47.10	47.60	49.30	49.90	49.60	49.70	49.50			49.50	49.80	48.80	48.40	47.80	46.40	43.70	43.20	41.20	41.80	41.50
8	36.80	37.00	38.70	40.10	39.80	40.30	40.00	41.80	42.50	42.30	42.70	43.00	42.60	42.60	42.60	41.40	41.60	41.50	40.70	40.50	38.40	37.30	36.60	35.90	35.80
9	41.60	43.30	44.70	44.80	45.40	46.40	46.10	46.80	46.60	46.70	47.60				47.60	47.00	46.90	46.30	46.10	44.20	43.10	42.40	42.10	42.10	41.60
10	45.10	46.10	47.00	47.90	49.10	49.10	49.50	51.10	49.80	50.00	50.20	52.30			52.30	52.20	52.40	50.40	51.40	49.50	47.70	46.50	45.50	44.80	44.90
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	39.95	40.95	42.26	43.50	43.75	44.27	44.48	45.56	45.71	46.07					46.44	46.08	45.66	45.24	44.54	43.16	41.66	40.51	39.91	39.77	39.73
SD	3.72	3.89	3.71	3.52	3.85	3.73	4.39	4.17	3.58	3.45					3.82	4.25	4.29	3.89	4.23	3.66	4.15	3.85	3.61	3.78	3.80

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	41.80	42.40	43.70	44.90	45.90	45.80	46.80	46.90	46.90	47.10	47.70	48.20			48.20	47.20	45.20	45.90	44.50	43.50	41.70	40.20	40.40	39.50	39.80
2	38.30	38.80	39.50	41.30	41.40	42.30	42.10	43.60	43.40	43.80					43.80	43.00	42.20	42.30	41.80	40.60	39.70	38.90	39.00	37.70	38.00
3	43.20	44.30	46.70	47.10	47.40	48.30	48.60	48.60	49.90	50.40					50.40	49.50	48.50	47.40	47.20	46.00	44.40	42.90	42.40	43.10	42.60
4	38.30	38.90	41.10	41.60	42.50	42.60	43.20	43.90	44.40	42.80	44.30				44.30	45.20	44.30	44.10	43.10	42.60	40.70	39.90	38.90	37.70	38.50
5	39.80	39.00	40.20	42.50	42.60	43.30	44.10	43.90	44.90	46.60					46.60	45.60	45.10	44.80	44.50	42.80	40.70	39.70	39.20	38.40	38.20
6	37.80	37.90	40.50	42.50	42.50	42.80	43.30	43.50	44.20	45.30	45.20				45.20	44.50	43.60	43.40	42.80	41.90	39.10	37.90	36.80	37.00	36.70
7	43.90	45.00	46.70	48.10	49.10	49.40	50.10	50.90	50.50	51.20	51.90				51.90	51.10	51.30	49.30	49.20	47.90	45.60	44.20	43.90	43.60	42.80
8	39.30	40.00	40.80	42.60	43.30	43.40	44.00	44.50	45.50	44.60	45.10	45.40	45.20	45.70	45.70	45.20	44.90	45.20	44.00	43.90	41.70	40.50	39.80	39.10	38.80
9	41.20	43.30	43.70	44.70	44.50	45.50	45.70	46.00	46.50	46.50	47.20				47.20	46.70	46.30	46.00	45.00	44.50	42.30	41.60	41.30	41.00	40.00
10	44.00	45.30	46.50	47.00	46.10	48.00	47.90	48.70	48.80	49.90	50.30	50.90			50.90	50.80	50.20	50.80	49.90	49.40	47.10	45.90	44.80	44.50	44.70
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	40.76	41.49	42.94	44.23	44.53	45.14	45.58	46.05	46.50	46.82					47.42	46.88	46.16	45.92	45.20	44.31	42.30	41.17	40.65	40.16	40.01
SD	2.39	2.87	2.89	2.49	2.51	2.65	2.67	2.62	2.49	2.87					2.85	2.75	2.94	2.62	2.71	2.73	2.61	2.49	2.47	2.72	2.55

Table A 2.5 Plasma [Na^+]a (mM) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin

	Pre-exercise			Exercise											Recovery										
	Time (min)																								
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	141.0	142.0	142.0	144.0	145.0	146.0	147.0	148.0	149.0	150.0	150.0				150.0	145.0	143.0	144.0	142.0	141.0	141.0	142.0	142.0	141.0	141.0
2	139.0	140.0	140.0	143.0	143.0	143.0	144.0	145.0	145.0	146.0					146.0	143.0	141.0	140.0	139.0	138.0	139.0	139.0	139.0	137.0	139.0
3	140.0	139.0	140.0	141.0	143.0	144.0	146.0	147.0	148.0	149.0					149.0	146.0	145.0	143.0	142.0	140.0	139.0	139.0	139.0	139.0	139.0
4	140.0	139.0	140.0	140.0	142.0	143.0	145.0	146.0	147.0	148.0	149.0				148.0	146.0	144.0	144.0	143.0	140.0	139.0	139.0	140.0	139.0	139.0
5	140.0	139.0	135.0	139.0	142.0	144.0	147.0	149.0	150.0	151.0					151.0	147.0	146.0	146.0	144.0	141.0	139.0	139.0	139.0	139.0	139.0
6	139.0	140.0	141.0	143.0	144.0	146.0	147.0	148.0	149.0	151.0	152.0	151.0			151.0	148.0	146.0	146.0	144.0	141.0	140.0	140.0	140.0	140.0	140.0
7	140.0	139.0	140.0	141.0	142.0	143.0	145.0	146.0	147.0	148.0	149.0	149.0			148.0	147.0	145.0	144.0	143.0	140.0	139.0	140.0	140.0	139.0	140.0
8	140.0	141.0	141.0	142.0	143.0	143.0	144.0	145.0	146.0	146.0	147.0	147.0	149.0	148.0	146.0	144.0	143.0	143.0	142.0	141.0	141.0	141.0	140.0	138.0	139.0
9	141.0	141.0	142.0	142.0	143.0	145.0	146.0	147.0	149.0	149.0	150.0				149.0	148.0	146.0	146.0	144.0	142.0	141.0	141.0	141.0	140.0	140.0
10	140.0	139.0	139.0	140.0	141.0	142.0	144.0	145.0	146.0	147.0	148.0	150.0			147.0	147.0	147.0	146.0	144.0	141.0	139.0	139.0	139.0	139.0	139.0
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	140.0	139.9	140.0	141.5	142.8	143.9	145.5	146.6	147.6	148.5					148.5	146.1	144.6	144.2	142.7	140.5	139.7	139.9	139.9	139.1	139.5
SD	0.7	1.1	2.0	1.6	1.1	1.4	1.3	1.4	1.6	1.8					1.8	1.7	1.8	1.9	1.6	1.1	0.9	1.1	1.0	1.1	0.7

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	141.0	141.0	142.0	143.0	144.0	145.0	147.0	148.0	148.0	149.0	149.0	150.0			149.0	147.0	146.0	144.0	143.0	141.0	140.0	142.0	141.0	141.0	141.0
2	139.0	140.0	139.0	141.0	142.0	143.0	144.0	146.0	146.0	147.0					147.0	143.0	142.0	141.0	139.0	138.0	138.0	138.0	138.0	138.0	138.0
3	139.0	139.0	139.0	140.0	142.0	143.0	144.0	146.0	147.0	149.0					149.0	146.0	144.0	142.0	142.0	140.0	139.0	139.0	139.0	139.0	139.0
4	139.0	138.0	139.0	139.0	141.0	142.0	144.0	145.0	146.0	147.0	148.0				147.0	146.0	145.0	144.0	142.0	140.0	138.0	138.0	138.0	138.0	138.0
5	142.0	141.0	140.0	143.0	144.0	145.0	147.0	149.0	150.0	152.0					152.0	147.0	146.0	145.0	145.0	142.0	141.0	140.0	140.0	141.0	141.0
6	140.0	141.0	141.0	144.0	145.0	146.0	148.0	149.0	150.0	151.0	152.0				151.0	150.0	146.0	145.0	144.0	142.0	140.0	139.0	139.0	139.0	140.0
7	138.0	139.0	139.0	139.0	140.0	142.0	143.0	145.0	146.0	146.0	147.0				147.0	145.0	143.0	142.0	141.0	139.0	138.0	138.0	137.0	136.0	136.0
8	142.0	141.0	141.0	142.0	142.0	143.0	144.0	145.0	146.0	147.0	147.0	148.0	148.0	150.0	147.0	147.0	146.0	145.0	144.0	142.0	141.0	141.0	141.0	140.0	140.0
9	142.0	142.0	142.0	142.0	143.0	144.0	146.0	147.0	148.0	149.0	150.0				149.0	148.0	148.0	147.0	146.0	143.0	142.0	142.0	142.0	142.0	142.0
10	141.0	141.0	141.0	142.0	143.0	143.0	145.0	146.0	147.0	148.0	149.0	150.0			148.0	149.0	149.0	147.0	146.0	143.0	140.0	140.0	140.0	140.0	140.0
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	140.3	140.3	140.3	141.5	142.6	143.6	145.2	146.6	147.4	148.5					148.6	146.8	145.5	144.2	143.2	141.0	139.7	139.7	139.5	139.4	139.5
SD	1.5	1.3	1.3	1.7	1.5	1.3	1.7	1.6	1.6	1.9					1.8	2.0	2.1	2.0	2.3	1.7	1.4	1.6	1.6	1.8	1.8

Table A 2.6 Plasma [Ca^{+}]a (mM) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin Pre-exercise Exercise Recovery

Time (min)

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	1.17	1.18	1.17	1.20	1.19	1.23	1.25	1.28	1.30	1.31	1.33				1.33	1.30	1.25	1.26	1.24	1.21	1.17	1.15	1.14	1.16	1.16
2	1.20	1.21	1.18	1.22	1.23	1.23	1.25	1.26	1.27	1.28					1.28	1.25	1.22	1.20	1.18	1.18	1.18	1.20	1.21	1.21	1.22
3	1.19	1.19	1.21	1.24	1.25	1.25	1.26	1.27	1.22	1.23					1.23	1.30	1.27	1.26	1.24	1.27	1.21	1.20	1.20	1.22	1.21
4	1.18	1.18	1.21	1.20	1.22	1.23	1.25	1.26	1.28	1.29	1.29				1.29	1.30	1.28	1.28	1.26	1.23	1.19	1.18	1.16	1.17	1.18
5	1.21	1.20	1.15	1.18	1.17	1.24	1.30	1.32	1.34	1.35					1.35	1.29	1.31	1.31	1.28	1.25	1.21	1.20	1.19	1.19	1.20
6	1.21	1.22	1.21	1.25	1.24	1.26	1.19	1.26	1.28	1.36	1.37	1.36			1.36	1.35	1.34	1.32	1.31	1.27	1.22	1.21	1.20	1.20	1.20
7	1.18	1.19	1.20	1.20	1.20	1.22	1.23	1.26	1.29	1.29	1.28	1.30			1.30	1.32	1.29	1.28	1.25	1.22	1.18	1.18	1.12	1.17	1.18
8	1.21	1.22	1.23	1.23	1.23	1.23	1.22	1.25	1.27	1.27	1.28	1.29	1.15	1.34	1.34	1.30	1.27	1.27	1.26	1.20	1.17	1.17	1.17	1.16	1.18
9	1.23	1.25	1.25	1.23	1.25	1.27	1.27	1.30	1.30	1.30	1.32				1.32	1.31	1.28	1.31	1.29	1.28	1.25	1.25	1.23	1.24	1.25
10	1.19	1.22	1.22	1.23	1.25	1.25	1.27	1.29	1.26	1.26	1.27	1.33			1.33	1.31	1.31	1.30	1.29	1.27	1.22	1.22	1.21	1.21	1.20
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	1.20	1.21	1.20	1.22	1.22	1.24	1.25	1.28	1.28	1.29					1.31	1.30	1.28	1.28	1.26	1.24	1.20	1.20	1.18	1.19	1.20
SD	0.02	0.02	0.03	0.02	0.03	0.02	0.03	0.02	0.03	0.04					0.04	0.02	0.03	0.04	0.04	0.03	0.03	0.03	0.03	0.03	0.03

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	1.18	1.18	1.15	1.18	1.21	1.21	1.24	1.26	1.27	1.28	1.29	1.32			1.32	1.30	1.24	1.27	1.23	1.26	1.17	1.17	1.15	1.16	1.15
2	1.25	1.26	1.26	1.29	1.30	1.31	1.31	1.34	1.35	1.36					1.36	1.33	1.30	1.29	1.26	1.22	1.22	1.21	1.22	1.21	1.23
3	1.14	1.17	1.18	1.20	1.21	1.22	1.23	1.24	1.27	1.29					1.29	1.27	1.25	1.21	1.26	1.19	1.18	1.15	1.16	1.16	1.15
4	1.18	1.19	1.22	1.18	1.21	1.22	1.22	1.24	1.27	1.23	1.29				1.29	1.32	1.34	1.31	1.30	1.26	1.22	1.19	1.17	1.15	1.17
5	1.23	1.24	1.21	1.25	1.26	1.27	1.31	1.31	1.33	1.39					1.39	1.34	1.33	1.30	1.32	1.31	1.25	1.24	1.23	1.25	1.25
6	1.20	1.22	1.17	1.24	1.25	1.28	1.31	1.32	1.35	1.37	1.38				1.38	1.38	1.35	1.32	1.30	1.27	1.19	1.18	1.17	1.17	1.19
7	1.14	1.16	1.16	1.15	1.17	1.19	1.21	1.23	1.24	1.24	1.25				1.25	1.25	1.22	1.21	1.21	1.18	1.15	1.13	1.14	1.14	1.14
8	1.23	1.24	1.24	1.24	1.26	1.25	1.27	1.29	1.28	1.29	1.29	1.29	1.32	1.33	1.35	1.32	1.30	1.28	1.28	1.23	1.19	1.18	1.18	1.19	1.19
9	1.22	1.23	1.23	1.23	1.24	1.25	1.27	1.28	1.29	1.29	1.31				1.31	1.29	1.30	1.28	1.28	1.25	1.22	1.22	1.21	1.23	1.22
10	1.23	1.24	1.25	1.25	1.20	1.26	1.26	1.27	1.27	1.29	1.29	1.31			1.31	1.33	1.32	1.32	1.29	1.29	1.25	1.23	1.22	1.22	1.23
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	1.20	1.21	1.21	1.22	1.23	1.25	1.26	1.28	1.29	1.30					1.33	1.31	1.30	1.28	1.27	1.25	1.20	1.19	1.19	1.19	1.19
SD	0.04	0.03	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.05					0.04	0.04	0.04	0.04	0.03	0.04	0.03	0.04	0.03	0.04	0.04

Table A 2.7 Plasma [Cl^-]a (mM) at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin

	Pre-exercise		Exercise												Recovery										
	Time (min)																								
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	109.0	109.0	110.0	112.0	113.0	115.0	116.0	117.0	117.0	118.0	118.0				118.0	114.0	112.0	111.0	109.0	110.0	110.0	110.0	110.0	109.0	110.0
2	106.0	108.0	109.0	111.0	111.0	111.0	113.0	114.0	115.0	115.0					115.0	112.0	109.0	109.0	109.0	108.0	107.0	107.0	107.0	107.0	106.0
3	105.0	105.0	105.0	106.0	108.0	109.0	112.0	113.0	117.0	118.0					118.0	111.0	109.0	109.0	108.0	104.0	105.0	104.0	105.0	104.0	104.0
4	107.0	108.0	108.0	109.0	111.0	113.0	114.0	115.0	116.0	118.0	119.0				119.0	114.0	112.0	110.0	109.0	108.0	107.0	107.0	109.0	108.0	107.0
5	106.0	106.0	109.0	109.0	113.0	112.0	114.0	116.0	117.0	118.0					118.0	114.0	111.0	109.0	109.0	107.0	107.0	107.0	107.0	107.0	107.0
6	108.0	109.0	109.0	111.0	112.0	114.0	119.0	118.0	119.0	118.0	119.0	120.0			120.0	116.0	113.0	111.0	110.0	109.0	109.0	109.0	109.0	109.0	109.0
7	104.0	104.0	104.0	106.0	107.0	109.0	110.0	111.0	112.0	113.0	115.0	115.0			115.0	109.0	107.0	106.0	106.0	105.0	105.0	104.0	106.0	104.0	104.0
8	106.0	108.0	107.0	108.0	110.0	111.0	113.0	113.0	114.0	115.0	115.0	116.0	113.0	113.0	113.0	110.0	109.0	108.0	108.0	109.0	108.0	108.0	107.0	107.0	105.0
9	107.0	108.0	108.0	110.0	111.0	113.0	114.0	115.0	117.0	118.0	118.0				118.0	116.0	114.0	111.0	110.0	108.0	108.0	108.0	108.0	108.0	107.0
10	107.0	106.0	106.0	107.0	108.0	110.0	111.0	113.0	114.0	116.0	117.0	117.0			117.0	113.0	111.0	110.0	108.0	107.0	107.0	106.0	106.0	107.0	107.0
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	106.5	107.1	107.5	108.9	110.4	111.7	113.6	114.5	115.8	116.7					112.9	112.9	110.7	109.4	108.6	107.5	107.3	107.0	107.4	107.0	106.6
SD	1.4	1.7	2.0	2.1	2.1	2.1	2.5	2.1	2.0	1.8					2.4	2.4	2.2	1.6	1.2	1.8	1.6	1.9	1.6	1.8	2.0

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	108.0	110.0	112.0	112.0	113.0	114.0	115.0	116.0	117.0	117.0	118.0	118.0			118.0	113.0	113.0	110.0	111.0	112.0	110.0	110.0	108.0	109.0	110.0
2	104.0	105.0	105.0	106.0	109.0	110.0	112.0	112.0	113.0	114.0					114.0	109.0	108.0	107.0	107.0	105.0	104.0	105.0	105.0	105.0	104.0
3	108.0	105.0	104.0	106.0	108.0	110.0	110.0	113.0	113.0	115.0					115.0	110.0	109.0	108.0	105.0	106.0	106.0	106.0	105.0	106.0	106.0
4	105.0	105.0	104.0	106.0	108.0	110.0	112.0	113.0	114.0	116.0	116.0				116.0	111.0	108.0	107.0	106.0	106.0	105.0	104.0	105.0	106.0	105.0
5	106.0	107.0	108.0	110.0	112.0	113.0	114.0	117.0	117.0	118.0					118.0	114.0	112.0	112.0	109.0	108.0	108.0	107.0	108.0	107.0	107.0
6	109.0	109.0	108.0	110.0	111.0	113.0	114.0	115.0	117.0	117.0	117.0				117.0	116.0	113.0	112.0	111.0	109.0	109.0	109.0	109.0	109.0	108.0
7	108.0	107.0	107.0	109.0	110.0	111.0	113.0	114.0	115.0	116.0	117.0				117.0	113.0	111.0	110.0	108.0	108.0	107.0	108.0	107.0	106.0	107.0
8	106.0	106.0	107.0	108.0	109.0	111.0	112.0	113.0	114.0	114.0	115.0	115.0	115.0	114.0	114.0	111.0	110.0	109.0	109.0	108.0	108.0	107.0	107.0	106.0	107.0
9	109.0	110.0	111.0	112.0	113.0	115.0	116.0	117.0	118.0	119.0	121.0				121.0	118.0	114.0	113.0	113.0	111.0	110.0	111.0	111.0	110.0	110.0
10	105.0	105.0	105.0	106.0	109.0	108.0	111.0	112.0	114.0	114.0	115.0	116.0			116.0	114.0	111.0	110.0	109.0	107.0	106.0	105.0	106.0	106.0	106.0
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	106.8	106.9	107.1	108.5	110.2	111.5	112.9	114.2	115.2	116.0					116.6	112.9	110.9	109.8	108.8	108.0	107.3	107.2	107.1	107.0	107.0
SD	1.8	2.1	2.8	2.5	1.9	2.2	1.9	1.9	1.9	1.8					2.1	2.8	2.1	2.1	2.4	2.2	2.1	2.3	2.0	1.7	1.9

Table A 2.8 Plasma pH_a at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin

	Pre-exercise			Exercise											Recovery										
	Time (min)																								
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	7.43	7.44	7.48	7.45	7.43	7.40	7.36	7.31	7.27	7.21	7.19				7.19	7.21	7.22	7.18	7.19	7.25	7.35	7.40	7.42	7.42	7.43
2	7.41	7.39	7.40	7.38	7.37	7.38	7.36	7.36	7.27	7.24					7.24	7.31	7.29	7.29	7.29	7.32	7.35	7.37	7.38	7.40	7.39
3	7.41	7.45	7.41	7.39	7.37	7.36	7.33	7.31	7.31	7.37					7.37	7.23	7.21	7.21	7.18	7.20	7.31	7.40	7.41	7.39	7.42
4	7.40	7.40	7.38	7.40	7.36	7.36	7.33	7.32	7.29	7.26	7.23				7.23	7.15	7.13	7.12	7.11	7.16	7.26	7.33	7.37	7.38	7.39
5	7.40	7.41	7.47	7.44	7.37	7.33	7.29	7.25	7.23	7.19					7.19	7.22	7.20	7.17	7.14	7.13	7.20	7.27	7.30	7.33	7.34
6	7.43	7.42	7.46	7.41	7.39	7.35	7.32	7.28	7.24	7.19	7.15	7.13			7.13	7.15	7.16	7.16	7.13	7.15	7.26	7.33	7.38	7.41	7.41
7	7.39	7.42	7.41	7.42	7.39	7.37	7.34	7.31	7.29	7.27	7.26	7.23			7.23	7.22	7.19	7.17	7.16	7.19	7.28	7.33	7.38	7.37	7.38
8	7.40	7.41	7.41	7.41	7.39	7.39	7.37	7.36	7.33	7.31	7.28	7.27	7.34	7.20	7.20	7.21	7.21	7.19	7.19	7.24	7.34	7.37	7.38	7.40	7.39
9	7.41	7.42	7.41	7.42	7.41	7.38	7.36	7.34	7.33	7.31	7.30				7.30	7.26	7.25	7.23	7.23	7.22	7.31	7.35	7.40	7.40	7.40
10	7.41	7.41	7.42	7.41	7.39	7.38	7.35	7.32	7.32	7.31	7.31	7.27			7.27	7.25	7.24	7.22	7.20	7.19	7.26	7.31	7.37	7.40	7.41
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	7.41	7.42	7.43	7.41	7.39	7.37	7.34	7.32	7.29	7.27					7.24	7.22	7.21	7.19	7.18	7.20	7.29	7.35	7.38	7.39	7.40
SD	0.01	0.02	0.03	0.02	0.02	0.02	0.02	0.03	0.04	0.06					0.07	0.05	0.05	0.05	0.05	0.06	0.05	0.04	0.03	0.03	0.02

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	7.42	7.44	7.45	7.45	7.40	7.40	7.34	7.30	7.26	7.23	7.19	7.16			7.16	7.18	7.17	7.15	7.15	7.20	7.30	7.36	7.41	7.42	7.44
2	7.40	7.41	7.42	7.40	7.38	7.38	7.37	7.36	7.34	7.38					7.38	7.28	7.26	7.24	7.25	7.26	7.33	7.37	7.38	7.39	7.40
3	7.45	7.43	7.42	7.41	7.37	7.36	7.35	7.31	7.29	7.26					7.26	7.22	7.19	7.16	7.16	7.20	7.31	7.38	7.40	7.40	7.42
4	7.43	7.42	7.38	7.42	7.39	7.38	7.37	7.33	7.30	7.28	7.25				7.25	7.17	7.15	7.14	7.12	7.16	7.28	7.36	7.40	7.40	7.42
5	7.39	7.38	7.44	7.42	7.37	7.36	7.31	7.28	7.25	7.20					7.20	7.21	7.16	7.15	7.12	7.12	7.22	7.29	7.33	7.35	7.35
6	7.43	7.43	7.49	7.40	7.39	7.34	7.31	7.27	7.23	7.20	7.14				7.14	7.10	7.12	7.12	7.10	7.08	7.19	7.28	7.33	7.36	7.38
7	7.39	7.40	7.40	7.42	7.39	7.37	7.34	7.32	7.29	7.28	7.28				7.28	7.23	7.22	7.20	7.17	7.20	7.29	7.35	7.36	7.38	7.39
8	7.40	7.40	7.41	7.41	7.39	7.39	7.37	7.34	7.32	7.30	7.28	7.26	7.24	7.22	7.20	7.17	7.18	7.14	7.15	7.18	7.28	7.33	7.36	7.37	7.39
9	7.40	7.42	7.43	7.43	7.39	7.38	7.36	7.34	7.32	7.31	7.29				7.29	7.28	7.24	7.22	7.22	7.24	7.34	7.39	7.42	7.40	7.40
10	7.42	7.45	7.41	7.41	7.40	7.38	7.37	7.35	7.34	7.33	7.32	7.32			7.32	7.26	7.24	7.22	7.21	7.18	7.25	7.31	7.37	7.41	7.43
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	7.41	7.42	7.43	7.42	7.39	7.37	7.35	7.32	7.29	7.28					7.25	7.21	7.19	7.18	7.16	7.18	7.28	7.34	7.38	7.39	7.40
SD	0.02	0.02	0.03	0.01	0.01	0.02	0.02	0.03	0.04	0.06					0.07	0.06	0.04	0.04	0.05	0.05	0.05	0.04	0.03	0.02	0.03

Table A 2.9 Blood $[Lac^-]_a$ at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin

	Pre-exercise			Exercise											Recovery										
	Time (min)																								
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	0.40	0.50	0.80	1.40	3.00	5.00	7.60	11.00	13.40	17.00	19.00				19.00	17.00	16.00	17.00	16.00	12.50	8.00	5.10	3.60	2.70	2.00
2	0.60	0.60	0.70	2.10	2.60	3.30	4.20	5.60	8.00	9.40					9.40	7.70	8.50	8.80	8.90	7.10	5.70	3.30	2.30	1.30	1.10
3	0.90	1.30	1.30	2.10	4.50	5.30	8.50	10.70	10.80	12.10					12.10	17.00	16.00	17.00	17.00	16.00	10.20	6.30	4.00	2.90	2.10
4	0.50	0.50	0.90	1.10	3.10	4.90	7.40	9.80	12.90	16.00	17.00				17.00	20.00	20.00	20.00	20.00	17.00	11.00	6.80	4.40	3.00	2.30
5	0.50	0.50	0.40	1.10	2.40	4.50	7.90	11.40	13.60	17.00					17.00	16.00	17.00	17.00	17.00	16.00	12.00	8.90	6.70	5.20	3.90
6	0.90	0.60	1.00	3.10	4.70	6.10	7.50	10.60	12.90	18.00	20.00	21.00			21.00	19.00	17.00	17.00	18.00	16.00	12.30	8.50	6.20	4.70	3.40
7	0.70	0.50	0.70	1.30	2.70	4.10	5.80	8.30	9.90	12.00	13.10	15.00			15.00	16.00	16.00	16.00	16.00	14.00	9.90	6.70	4.60	3.50	2.70
8	1.10	0.90	0.90	1.00	2.30	3.20	5.00	8.20	11.00	12.90	15.00	16.00	17.00	18.00	18.00	17.00	17.00	17.00	15.00	12.30	8.30	5.40	3.70	2.80	2.20
9	1.10	0.90	1.60	1.90	3.50	5.70	7.00	9.20	11.40	12.90	14.50				14.50	16.00	16.00	17.00	16.00	15.00	10.00	6.20	4.60	3.50	2.60
10	0.80	0.70	1.10	1.20	2.30	3.20	5.30	8.30	8.30	10.30	12.00	16.00			16.00	16.00	17.00	17.00	17.00	15.00	12.50	8.40	5.50	3.90	2.90
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	0.75	0.70	0.94	1.63	3.11	4.53	6.62	9.31	11.22	13.76					15.90	16.17	16.05	16.38	16.09	14.09	9.99	6.56	4.56	3.35	2.52
SD	0.25	0.26	0.34	0.67	0.87	1.06	1.44	1.77	2.03	3.02					3.37	3.28	2.91	2.86	2.87	2.90	2.16	1.73	1.30	1.10	0.78

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fatigue	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	0.70	0.60	1.00	1.60	3.40	4.20	6.60	9.00	11.20	13.80	14.70	17.00			17.00	16.00	14.60	15.00	14.50	12.60	8.50	6.10	4.60	3.40	2.70
2	0.90	0.40	0.50	1.20	2.80	4.40	5.80	8.30	8.90	10.20					10.20	10.10	10.40	10.30	10.30	9.70	6.50	4.20	2.70	1.70	1.20
3	0.70	0.60	0.60	1.60	3.80	5.90	7.50	11.00	13.40	17.00					17.00	18.00	18.00	18.00	19.00	17.00	10.40	6.30	4.30	3.10	2.30
4	0.80	0.50	1.00	1.20	3.00	4.80	7.60	10.70	14.10	14.90	17.00				17.00	21.00	22.00	22.00	21.00	18.00	12.20	7.90	5.40	3.60	2.80
5	1.60	1.00	0.90	1.80	3.20	4.40	7.10	9.20	10.60	14.70					14.70	14.70	14.60	14.60	14.90	13.90	10.80	8.50	6.20	4.80	4.00
6	0.80	0.70	1.60	3.90	4.70	7.60	10.30	12.70	15.00	18.00	21.00				21.00	22.00	18.00	18.00	18.00	17.00	12.60	8.60	6.50	4.30	3.30
7	1.10	0.90	1.00	1.20	2.80	4.20	6.20	8.70	11.00	12.80	14.80				14.80	17.00	16.00	17.00	17.00	14.60	9.90	6.30	4.40	3.30	2.40
8	0.90	0.80	1.10	1.60	3.00	4.30	6.00	8.80	11.20	12.80	14.60	17.00	18.00	20.00	21.00	21.00	20.00	19.00	19.00	17.00	12.10	7.90	5.20	3.80	2.70
9	1.80	1.70	2.10	2.40	3.60	5.30	7.30	9.70	12.00	14.10	17.00				17.00	17.00	18.00	18.00	17.00	15.00	9.60	5.80	4.20	2.90	2.60
10	1.00	1.10	1.30	1.40	2.10	3.50	5.00	7.40	9.50	11.60	13.60	16.00			16.00	17.00	18.00	18.00	18.00	17.00	13.90	10.30	6.90	4.80	3.60
n	10	10	10	10	10	10	10	10	10	10					10	10	10	10	10	10	10	10	10	10	10
Mean	1.03	0.83	1.11	1.79	3.24	4.86	6.94	9.55	11.69	13.99					16.57	17.38	16.96	16.99	16.87	15.18	10.65	7.19	5.04	3.57	2.76
SD	0.38	0.38	0.47	0.83	0.70	1.17	1.45	1.54	1.96	2.34					3.12	3.50	3.23	3.12	3.01	2.58	2.17	1.76	1.27	0.94	0.77

Table A 2.10 Plasma $[Glu^-]_a$ at pre-exercise, during and following high-intensity cycling with and without digoxin

Digoxin	Pre-exercise			Exercise											Recovery									
												Time (min)												
Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	5.10	5.00	4.90	5.00	5.00	5.10	5.10	5.20	5.20	5.20	5.30					6.50	7.60	7.80	7.80	7.20	6.20	5.20	4.60	4.50	4.60
2	5.20	4.80	5.30	5.90	6.00	6.10	6.20	6.20	6.02	6.02						6.10	5.90	5.90	5.80	5.70	5.80	5.20	5.00	4.40	4.90
3	5.70	6.00	6.30	6.40	6.50	6.50	6.60	6.50	6.10	6.30	6.40					6.90	7.00	7.00	7.10	7.00	6.40	5.80	5.10	5.10	5.00
4	4.70	4.80	5.00	5.00	5.00	5.10	5.20	5.20	5.20	5.30	5.10					6.40	6.70	6.90	6.70	6.10	5.90	5.40	4.70	4.20	4.20
5	5.20	5.30	5.30	5.70	5.40	5.80	6.00	6.00	6.00	6.20	6.20					6.90	7.40	7.60	7.80	7.40	6.70	6.40	5.90	5.40	5.10
6	5.40	5.30	5.50	5.90	5.90	5.90	5.50	5.90	5.90	6.30	6.40	6.30				7.30	8.30	8.40	8.40	7.70	7.10	6.00	5.20	4.80	4.80
7	5.40	5.10	5.40	5.80	5.80	5.90	5.90	6.00	6.10	6.10	5.90	6.00				6.70	7.20	7.30	7.00	6.50	6.10	5.70	5.10	5.00	5.10
8	5.20	6.10	5.10	5.10	5.10	5.10	5.00	5.10	5.10	5.00	4.90	4.80	4.30	5.10		5.80	6.00	6.00	5.80	5.30	5.00	4.70	4.70	5.00	5.10
9	6.70	5.90	6.10	6.10	6.20	6.20	6.20	6.30	6.40	6.30	6.50					6.60	6.90	7.30	7.20	6.80	6.50	6.00	5.70	5.60	5.70
10	5.20	5.30	5.50	5.70	5.70	5.80	5.80	5.90	5.70	5.70	5.70	5.80				6.10	6.50	6.60	6.90	6.50	6.10	5.70	5.40	5.00	5.00
n	10	10	10	10	10	10	10	10	10	10						10	10	10	10	10	10	10	10	10	10
Mean	5.38	5.36	5.44	5.66	5.66	5.75	5.75	5.83	5.77	5.84						6.53	6.95	7.08	7.05	6.62	6.18	5.61	5.14	4.90	4.95
SD	0.53	0.48	0.45	0.48	0.52	0.49	0.53	0.49	0.45	0.50						0.45	0.73	0.78	0.83	0.76	0.57	0.49	0.43	0.44	0.39
delta	0.00	-0.02	0.06	0.28	0.28	0.37	0.37	0.45	0.39	0.46						1.15	1.57	1.70	1.67	1.24	0.80	0.23	-0.24	-0.48	-0.43

Placebo

Subject	-60	-10	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	Fat	+1	+2	+3	+5	+10	+20	+30	+40	+50	+60
1	5.20	5.20	5.50	5.70	5.80	5.80	5.90	5.90	6.10	6.10	6.10	6.20				8.00	8.40	9.00	8.80	8.50	8.00	7.30	6.40	6.00	5.50
2	4.90	5.10	5.10	5.20	5.30	5.40	5.30	5.50	5.40	5.75	5.65					5.40	5.30	5.20	5.30	5.20	5.10	4.70	4.60	4.70	4.80
3	5.70	5.70	6.10	6.40	6.50	6.60	6.70	6.60	6.80	6.80						7.40	7.60	7.60	7.80	7.30	7.00	6.30	5.80	5.50	5.50
4	4.80	4.80	5.00	5.00	5.10	5.10	5.20	5.20	5.30	5.00	5.10					6.40	7.10	7.30	7.10	6.40	6.10	5.70	5.10	4.40	4.10
5	5.00	5.00	5.00	5.20	5.20	5.20	5.40	5.20	5.20	5.40						6.10	6.20	6.20	6.50	6.10	5.40	5.10	5.10	5.00	5.00
6	5.60	5.60	6.20	6.60	6.50	6.80	6.80	6.80	6.90	7.00	7.00					7.40	9.40	9.60	9.90	9.50	8.90	8.10	7.30	6.50	6.20
7	5.70	5.20	5.70	5.80	5.90	6.00	6.00	6.10	6.10	6.00	5.90					6.30	6.80	6.90	6.80	6.20	5.90	5.60	6.00	6.00	5.80
8	5.60	5.70	5.10	5.10	5.20	5.20	5.20	5.20	5.10	5.20	5.00	5.00	4.90	4.90	5.60	5.10	6.10	6.30	6.30	5.90	5.40	5.10	4.90	5.10	5.40
9	6.90	6.40	7.30	7.40	7.60	7.70	7.80	7.80	7.90	7.90	7.80					7.80	7.70	7.70	7.60	7.40	7.00	6.30	5.80	5.50	5.10
10	5.50	5.30	5.70	5.90	5.70	6.00	5.90	6.00	6.00	6.10	6.10	6.10				6.50	6.90	7.20	7.50	7.30	6.90	6.70	6.30	6.00	5.60
n	10	10	10	10	10	10	10	10	10	10						10	10	10	10	10	10	10	10	10	10
Mean	5.49	5.40	5.67	5.83	5.88	5.98	6.02	6.03	6.08	6.13						6.64	7.15	7.30	7.36	6.98	6.57	6.09	5.73	5.47	5.30
SD	0.60	0.46	0.72	0.78	0.79	0.84	0.85	0.84	0.90	0.89						0.99	1.19	1.30	1.30	1.30	1.23	1.07	0.82	0.67	0.58
delta	0.00	-0.09	0.18	0.34	0.39	0.49	0.53	0.54	0.59	0.64						1.15	1.66	1.81	1.87	1.49	1.08	0.60	0.24	-0.02	-0.19

Table A 2.11 MVC (Nm) at pre-exercise, following high-intensity cycling, during recovery and expressed as a percentage of pre-exercise with and without digoxin

						Expressed as a % of pre-exercise			
Digoxin		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	MVC (Nm)				MVC (%)			
1	0.32	81.7	72.9	75.7	76.4	100	89.2	92.6	93.4
2	0.32	47.6	37.6	32.3	42.2	100	79.0	67.9	88.5
3	0.32	46.4	30.3	35.3	34.9	100	65.4	76.0	75.2
4	0.33	129.4	96.2	94.1	98.6	100	74.3	72.7	76.2
5	0.32	88.1	60.4	60.0	71.8	100	68.6	68.1	81.5
6	0.32	95.0	56.5	74.3	77.0	100	59.5	78.2	81.0
7	0.32	142.4	90.9	86.9	107.0	100	63.8	61.0	75.2
8	0.37	61.1	44.8	51.6	67.2	100	73.3	84.5	110.1
9	0.32	88.1	41.3	41.0	47.2	100	46.8	46.5	53.6
10	0.32	89.0	39.8	33.2	26.9	100	44.7	37.3	30.3
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**86.9**	**57.1**	**58.4**	**64.9**	**100**	**66.5**	**68.5**	**76.5**
SD	**0.0**	**29.7**	**21.7**	**22.0**	**25.3**		**13.0**	**15.9**	**20.7**

Placebo		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	MVC (Nm)				MVC (%)			
1	0.32	89.2	79.9	72.9	70.7	100	89.7	81.8	79.3
2	0.32	64.1	46.6	47.1	64.3	100	72.7	73.5	100.4
3	0.32	58.6	38.0	49.5	37.9	100	64.9	84.5	64.7
4	0.33	119.6	80.7	78.2	80.3	100	67.5	65.4	67.2
5	0.32	93.5	78.6	78.1	77.7	100	84.1	83.5	83.1
6	0.32	96.9	53.6	52.1	52.1	100	55.3	53.8	53.8
7	0.32	118.1	87.1	92.5	90.1	100	73.8	78.3	76.3
8	0.37	47.5	25.8	36.5	37.9	100	57.7	81.4	84.5
9	0.32	66.5	40.2	35.1	43.0	100	60.5	52.8	64.7
10	0.32	86.5	32.3	30.1	38.7	100	37.4	34.8	44.7
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**84.0**	**56.3**	**57.2**	**59.3**	**100**	**66.3**	**69.0**	**71.9**
SD	**0.0**	**23.2**	**21.9**	**20.5**	**18.8**		**14.2**	**16.0**	**15.4**

Table A 2.12 Q_{twpot} force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

						Expressed as a % of pre-exercise			
Digoxin		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	Twitch (Nm)				Twitch (%)			
1	0.32	23.8	19.0	19.2	20.4	100	80.0	80.9	85.7
2	0.32	20.1	9.5	10.1	18.3	100	47.1	50.0	91.0
3	0.32	17.8	8.1	7.5	7.8	100	45.2	41.8	43.7
4	0.33	26.0	5.8	5.3	5.9	100	22.4	20.4	22.6
5	0.32	23.3	9.4	6.5	5.3	100	40.2	27.9	22.9
6	0.32	15.0	11.9	11.2	12.7	100	79.5	74.7	84.9
7	0.32	26.2	11.5	11.8	12.9	100	43.7	45.2	49.3
8	0.37	19.6	4.8	5.3	8.5	100	24.5	27.1	43.2
9	0.32	15.7	6.2	5.6	6.8	100	39.2	35.9	43.2
10	0.32	14.7	11.6	10.2	12.9	100	78.7	69.0	87.9
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**20.2**	**8.7**	**8.2**	**10.1**	**100**	**50.06**	**47.28**	**57.44**
SD	**0.0**	**4.2**	**2.5**	**2.5**	**4.1**		**20.71**	**20.07**	**25.84**

Placebo		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	Twitch (Nm)				Twitch (%)			
1	0.32	26.4	17.6	16.4	16.0	100	66.8	62.1	60.5
2	0.32	22.2	15.0	16.0	15.7	100	67.5	71.9	70.8
3	0.32	27.2	11.8	12.2	13.0	100	43.3	45.0	47.8
4	0.33	18.9	3.1	4.1	5.2	100	16.6	21.7	27.7
5	0.32	15.6	4.1	3.5	3.8	100	26.1	22.7	24.0
6	0.32	13.6	11.2	11.9	11.1	100	82.2	87.4	81.4
7	0.32	22.8	12.1	12.8	13.7	100	52.8	55.9	60.2
8	0.37	11.5	2.9	2.5	2.7	100	25.7	21.9	23.6
9	0.32	28.2	12.2	13.0	12.6	100	43.4	46.2	44.7
10	0.32	31.4	10.5	7.8	8.9	100	33.3	24.7	28.4
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**21.8**	**10.1**	**10.0**	**10.3**	**100**	**45.8**	**45.9**	**46.9**
SD	**0.0**	**6.4**	**4.8**	**4.9**	**4.6**		**20.3**	**22.2**	**19.8**

Table A 2.13 Doublet force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

						Expressed as a % of pre-exercise			
Digoxin		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	**Doublet (Nm)**				**Doublet (%)**			
1	0.32	45.7	43.9	43.4	32.2	100	96.0	94.9	70.4
2	0.32	36.0	26.7	31.9	33.8	100	74.0	88.6	93.8
3	0.32	28.6	14.7	14.0	26.7	100	51.3	48.9	93.5
4	0.33	36.5	14.1	21.6	25.0	100	38.7	59.1	68.6
5	0.32	47.4	8.3	8.8	16.7	100	17.6	18.6	35.3
6	0.32	36.7	23.8	42.7	42.9	100	65.0	116.4	117.1
7	0.32	52.0	24.6	11.6	21.9	100	47.3	22.3	42.2
8	0.37	23.6	13.2	15.3	19.6	100	55.8	64.7	83.2
9	0.32	19.6	12.4	9.1	15.2	100	63.0	46.1	77.5
10	0.32	45.5	20.2	21.3	24.6	100	44.3	46.7	54.0
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**37.2**	**20.2**	**21.9**	**25.9**	**100**	**55.3**	**60.6**	**73.6**
SD	**0.0**	**10.2**	**9.8**	**12.4**	**8.1**		**20.1**	**29.8**	**23.8**

Placebo		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	**Doublet (Nm)**				**Doublet (%)**			
1	0.32	50.5	29.8	43.4	44.7	100	59.1	85.8	88.4
2	0.32	40.5	28.2	43.4	44.9	100	69.7	107.1	110.9
3	0.32	48.5	26.7	36.6	40.1	100	54.9	75.4	82.7
4	0.33	28.1	18.5	17.7	34.4	100	65.7	62.9	122.3
5	0.32	19.9	19.3	26.7	42.8	100	97.1	134.3	215.3
6	0.32	35.1	23.8	21.9	34.0	100	67.9	62.6	96.9
7	0.32	31.8	24.5	26.3	30.4	100	76.8	82.7	95.4
8	0.37	22.3	7.7	15.3	23.6	100	34.6	68.5	105.8
9	0.32	41.2	27.5	27.3	40.1	100	66.9	66.3	97.5
10	0.32	52.8	19.9	18.6	36.7	100	37.6	35.3	69.5
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**37.1**	**22.6**	**27.7**	**37.2**	**100**	**63.0**	**78.1**	**108.5**
SD	**0.0**	**11.0**	**6.2**	**9.7**	**6.4**		**17.3**	**25.7**	**38.3**

Table A 2.14 20 Hz Tetani (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

						Expressed as a % of pre-exercise			
Digoxin		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	**Tetani (Nm)**				**Tetani (%)**			
1	0.32	67.7	65.3	66.4	66.4	100	96.5	98.1	98.1
2	0.32	57.1	49.4	53.4	55.4	100	86.5	93.6	97.1
3	0.32	40.7	39.7	39.7	40.2	100	97.6	97.6	98.8
4	0.33	47.3	41.9	44.6	46.6	100	88.6	94.3	98.6
5	0.32	31.1	26.4	26.5	26.4	100	56.6	78.1	93.0
6	0.32	69.4	43.3	45.2	49.7	100	62.5	65.2	71.6
7	0.32	60.6	46.9	50.3	55.6	100	77.4	83.1	91.9
8	0.37	40.7	37.7	38.7	39.2	100	92.6	95.0	96.3
9	0.32	25.7	25.5	25.1	25.5	100	99.2	97.9	99.4
10	0.32	75.2	42.8	49.2	59.3	100	53.2	61.2	73.7
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**51.5**	**41.9**	**43.9**	**46.4**	**100**	**81.1**	**86.4**	**91.9**
SD	**0.0**	**16.1**	**10.8**	**11.7**	**12.9**		**16.7**	**13.2**	**9.9**

Placebo		**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**	**100%**	**Fatigue**	**+10 min**	**+60 min**
Subject	leg length (cm)	**Tetani (Nm)**				**Tetani (%)**			
1	0.32	74.2	68.8	71.1	70.0	100	92.7	95.9	94.3
2	0.32	69.5	62.3	63.2	65.0	100	89.6	90.9	93.5
3	0.32	87.3	63.0	67.6	75.7	100	72.2	77.4	86.7
4	0.33	57.9	52.2	53.2	55.1	100	90.1	91.9	95.1
5	0.32	64.5	36.5	50.4	60.0	100	56.6	78.1	93.0
6	0.32	67.7	43.3	43.7	59.1	100	64.0	64.5	87.2
7	0.32	64.2	46.2	55.2	62.4	100	72.0	86.1	97.2
8	0.37	62.7	39.6	53.2	58.4	100	63.1	84.8	93.1
9	0.32	55.8	53.9	54.2	54.3	100	96.6	97.2	97.4
10	0.32	80.4	51.5	61.2	72.3	100	64.0	76.1	89.8
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**0.3**	**68.4**	**51.7**	**57.3**	**63.2**	**100**	**76.1**	**84.3**	**92.7**
SD	**0.0**	**9.3**	**10.1**	**7.9**	**7.0**		**14.0**	**9.8**	**3.5**

Table A 2.15 Pre-exercise 1 Hz stimulations separated by 3 s at 50, 60, 70, 80, 90 and 100% of magnetic stimulator output

Digoxin

	Percentage (%) of Magnetic Stimulator Output																									
	50%			60%			70%			80%						90%						100%					
Stimulation	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV
Subject	Twitch (Nm)															Twitch (Nm)						Twitch (Nm)					
1	4.9			9.1	8.6	8.6	15.5	16.0	16.1	17.7	17.8	17.3	17.6	0.3	1.5	18.4	18.9	18.8	18.7	0.3	1.6	19.4	19.3	19.3	19.3	0.0	0.1
2	2.8	2.7	2.6	4.5	4.6	4.3	6.5	6.4	6.5	8.0	8.6	8.3	8.3	0.3	3.9	10.7	10.4	10.4	10.5	0.2	1.6	12.5	12.4	12.5	12.5	0.1	0.5
3	2.2	2.3	2.8	11.0	11.0	10.9	12.3	11.8	12.5	14.8	13.8	11.5	13.4	1.7	12.7	19.8	19.4	19.0	19.4	0.4	2.1	18.6	20.7	21.2	20.2	1.3	6.7
4	4.1	4.6	4.9	9.8	13.3	12.5	17.7	15.4	17.5	23.1	21.6	23.2	22.6	0.9	3.9	22.5	24.0	22.7	23.1	0.8	3.5	24.0	24.1	25.1	24.4	0.6	2.6
5	2.2	4.0		7.1	7.1	7.3	12.7	12.9	10.9	16.5	15.7	16.1	16.1	0.4	2.4	17.8	17.3	17.0	17.3	0.4	2.2	18.6	18.6	18.7	18.6	0.1	0.3
6	1.3	1.2	1.1	2.1	2.5	2.6	4.0	4.4	4.3	6.8	6.4	6.3	6.5	0.2	3.8	9.3	9.4	8.9	9.2	0.2	2.7	11.4	10.9	11.0	11.0	0.1	0.8
7	1.8	2.4	1.5	4.3	4.2	4.1	5.9	5.9	5.6	14.0	14.9	12.9	13.9	1.0	7.0	17.7	16.8	18.3	17.6	0.7	4.1	19.7	20.2	19.0	19.6	0.6	3.1
8	1.8	1.9	1.7	1.7	2.5	2.1	2.8	2.5	3.3	3.9	4.4	4.5	4.3	0.3	6.7	6.8	7.8	8.2	7.6	0.7	9.1	12.2	11.4	11.2	11.6	0.6	4.8
9	1.7	1.2	1.2	3.3	3.3	3.9	5.1	5.8	6.3	6.7	6.6	6.4	6.6	0.1	2.1	8.4	8.6	8.6	8.6	0.1	1.5	12.1	11.8	11.7	11.9	0.2	1.8
10	2.6	2.4	1.7	2.6	3.4	2.6	3.2	5.9	5.6	9.7	10.7	10.9	10.4	0.7	6.5	12.1	13.9	13.1	13.1	0.9	6.9	12.9	13.1	13.1	13.0	0.1	0.8
n	10	9	8	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
mean	2.5	2.5	2.2	5.6	6.1	5.9	8.6	8.7	8.9	12.1	12.0	11.7	12.0	0.6	5.1	14.4	14.7	14.5	14.5	0.5	3.5	16.2	16.2	16.3	16.2	0.4	2.2
SD	1.1	1.1	1.2	3.4	3.8	3.7	5.5	4.8	5.1	6.1	5.6	5.8	5.8	0.5	5.8	5.5	5.5	5.3	6.4	6.1	5.4	4.4	4.8	5.0	6.3	6.2	4.7

Placebo

Stimulation	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV
Subject	Twitch (Nm)															Twitch (Nm)						Twitch (Nm)					
1	12.98	12.58	12.19	18.09	18.79	17.03	19.12	20.13	19.97	20.76	21.28	21.04	21.03	0.26	1.23	20.25	20.37	20.63	20.42	0.20	0.97	20.59	20.92	20.50	20.71	0.22	1.08
2	1.58	1.41	1.47	3.92	4.21	5.04	6.66	6.60	6.49	10.65	9.81	9.10	9.86	0.78	7.88	11.80	13.53	12.78	12.70	0.87	6.86	12.09	12.39	12.53	12.34	0.23	1.83
3	9.89	10.18	9.24	14.01	14.01	13.52	16.16	16.21	16.10	18.72	18.87	18.59	18.72	0.14	0.74	20.00	19.63	19.88	19.84	0.19	0.93	20.95	21.11	21.10	21.06	0.09	0.44
4	1.25	1.04	0.99	1.91	1.79	1.64	3.78	3.81	3.87	5.88	6.12	6.14	6.05	0.14	2.37	8.41	8.67	7.81	8.30	0.44	5.29	11.90	11.38	11.28	11.52	0.33	2.89
5	2.40	1.63		4.25	3.56	3.77	4.16	4.65	4.39	6.52	6.63	6.40	6.52	0.11	1.76	8.23	8.12	9.89	8.75	0.99	11.30	12.68	11.21	10.26	11.38	1.22	10.68
6	1.35	-0.22	1.14	2.65	2.42	2.35	3.55	3.46	3.54	5.95	5.80	5.79	5.85	0.09	1.56	8.10	7.71	8.00	7.94	0.20	2.53	10.80	10.18	10.28	10.42	0.33	3.20
7	0.65	1.64	2.04	4.19	4.11	4.18	5.70	4.91	6.17	9.78	8.35	10.18	9.44	0.96	10.19	16.20	17.23	17.20	16.88	0.59	3.47	21.79	19.96	19.89	20.55	1.08	5.24
8	1.87	0.81	0.96	1.28	1.28	1.29	1.17	2.40	1.71	2.80	4.31	3.84	3.16	1.16	36.56	4.23	4.96	4.72	4.64	0.37	8.04	6.08	6.71	6.46	5.25	2.29	43.56
9	5.68	5.68	5.39	8.30	8.71	8.69	12.90	13.32	13.82	17.54	17.47	17.37	17.46	0.08	0.46	20.63	20.72	20.71	20.69	0.05	0.23	20.91	20.73	20.58	20.74	0.17	0.81
10	3.02	3.25	3.02	7.47	6.96	7.78	14.20	13.88	13.97	18.29	16.46	16.87	17.20	0.96	5.58	18.26	17.87	17.66	17.93	0.30	1.68	18.21	18.07	17.90	18.06	0.16	0.88
n	10	10	9	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	9	10	10	10	10	10
mean	4.07	3.80	4.05	6.61	6.58	6.53	8.74	8.94	9.00	10.96	11.51	11.53	11.53	0.47	6.83	13.61	13.88	13.93	13.81	0.42	4.13	15.31	15.27	15.08	15.20	0.61	7.06
SD	4.19	4.34	4.10	5.53	5.76	5.26	6.27	6.33	6.36	6.55	6.32	6.31	6.45	0.44	10.96	6.15	6.03	6.02	6.05	0.31	3.65	5.53	5.42	5.46	5.68	0.71	13.19

Table A 2.16 Q_{twpot} vastus medialis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.33	3.67	4.67	4.33	100	85	108	100
2	4.80	4.70	4.80	4.30	100	98	100	90
3	4.67	5.33	4.33	3.67	100	114	93	79
4	4.67	4.67	4.67	4.00	100	100	100	86
5	5.00	4.33	4.33	4.33	100	87	87	87
6	4.80	4.70	4.30	4.40	100	98	90	92
7	6.33	6.67	5.33	5.00	100	105	84	79
8	5.67	5.00	5.67	5.00	100	88	100	88
9	3.67	3.67	3.67	3.67	100	100	100	100
10	4.33	4.33	4.00	4.00	100	100	92	92
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.83**	**4.71**	**4.58**	**4.27**	**100**	**97.49**	**95.33**	**89.17**
SD	**0.74**	**0.87**	**0.59**	**0.47**		**9.01**	**7.36**	**7.35**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.53	5.07	4.53	4.53	100	112	100	100
2	4.33	4.00	3.00	3.67	100	92	69	85
3	1.20	1.27	1.07	1.13	100	106	89	94
4	5.00	5.00	5.00	5.33	100	100	100	107
5	4.80	4.60	3.87	4.00	100	87	87	87
6	4.33	4.33	5.33	5.00	100	100	123	115
7	6.00	5.00	5.33	5.33	100	83	89	89
8	5.33	5.67	5.00	5.33	100	106	94	100
9	4.00	4.00	5.00	4.67	100	100	125	117
10	4.33	4.33	4.33	4.33	100	100	100	100
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.39**	**4.33**	**4.25**	**4.33**	**100**	**98.59**	**97.55**	**99.33**
SD	**1.26**	**1.20**	**1.33**	**1.26**		**8.85**	**16.69**	**11.17**

Table A 2.17 Q_{twpot} vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				**(%)**			
1	1.66	5.20	1.90	1.32	100	313	114	80
2	1.71	2.36	3.65	3.68	100	138	213	215
3	9.50	7.09	2.60	5.43	100	75	27	57
4	1.24	2.13	1.52	5.48	100	172	123	443
5	2.27	2.74	2.55	2.54	100	121	112	112
6	3.16	2.53	2.18	3.63	100	80	69	115
7	1.09	1.24	1.70	2.08	100	114	156	191
8	1.19	3.47	1.28	2.93	100	291	108	246
9	2.36	1.94	2.08	3.54	100	82	88	150
10	2.03	2.36	6.43	5.15	100	116	316	254
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**2.62**	**3.11**	**2.59**	**3.58**	**100**	**150.12**	**132.74**	**186.22**
SD	**2.50**	**1.76**	**1.51**	**1.43**		**85.34**	**81.23**	**113.02**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				**(%)**			
1	1.25	1.51	2.87	1.48	100	121	229	118
2	3.61	5.03	5.69	6.99	100	139	158	193
3	3.70	3.58	1.28	5.16	100	97	34	139
4	2.19	4.39	1.43	1.95	100	201	65	89
5	1.37	2.37	1.57	1.59	100	173	115	116
6	3.59	2.27	2.08	2.36	100	63	58	66
7	1.61	1.65	1.32	1.23	100	102	82	76
8	2.28	2.28	1.66	1.47	100	100	73	64
9	6.09	5.04	3.89	3.83	100	83	64	63
10	5.58	8.32	8.32	9.92	100	149	149	178
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.13**	**3.64**	**3.01**	**3.60**	**100**	**122.80**	**102.66**	**110.30**
SD	**1.70**	**2.11**	**2.34**	**2.92**		**42.60**	**59.84**	**47.61**

Table A 2.18 Q_{twpot} vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	13	35	3	9	100	269	23	69
2	15	24	29	61	100	160	193	407
3	52	42	26	30	100	81	50	58
4	11	21	3	45	100	191	27	409
5	13	17	2	19	100	131	15	146
6	21	14	17	25	100	67	81	119
7	7	1	18	21	100	14	257	300
8	13	41	3	32	100	315	23	246
9	15	15	15	34	100	100	100	227
10	15	16	35	35	100	107	233	233
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**17.50**	**22.60**	**15.10**	**31.10**	**100**	**143.47**	**100.36**	**221.40**
SD	**12.62**	**13.11**	**12.16**	**14.48**		**92.99**	**93.29**	**125.88**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	10	10	8	13	100	100	80	130
2	15	19	49	71	100	127	327	473
3	79	95	63	79	100	120	80	100
4	13	30	3	5	100	231	23	38
5	7	3	4	5	100	43	57	71
6	25	8	14	19	100	32	56	76
7	4	10	9	10	100	250	225	250
8	3	2	7	4	100	67	233	133
9	54	10	23	32	100	19	43	59
10	35	47	52	29	100	134	149	83
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**24.50**	**23.40**	**23.20**	**26.70**	**100**	**112.20**	**127.21**	**141.47**
SD	**24.88**	**28.67**	**22.70**	**27.31**		**78.92**	**101.94**	**130.74**

Table A 2.19 Q_{twpot} vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	20.33	33.00	31.33	36.33	100	162	154	179
2	32.40	37.84	35.12	39.52	100	117	108	122
3	32.00	42.00	45.67	33.00	100	131	143	103
4	19.33	42.67	29.33	50.67	100	221	152	262
5	34.00	47.67	39.67	47.33	100	140	117	139
6	37.52	30.21	31.27	39.87	100	81	83	106
7	18.00	25.67	53.33	49.67	100	143	296	276
8	56.33	61.00	38.67	64.33	100	108	69	114
9	35.00	28.67	28.00	64.33	100	82	80	184
10	47.00	32.00	28.67	37.33	100	68	61	79
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**33.19**	**38.07**	**36.11**	**46.24**	**100**	**125.26**	**126.29**	**156.47**
SD	**12.20**	**10.65**	**8.31**	**11.18**		**45.40**	**68.78**	**67.69**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	17.33	15.00	19.60	17.93	100	87	113	103
2	40.00	55.67	54.33	65.33	100	139	136	163
3	18.93	18.73	19.00	19.07	100	99	100	101
4	18.67	37.33	22.00	33.33	100	200	118	179
5	14.47	14.93	11.33	15.53	100	103	78	107
6	39.00	26.33	26.00	26.33	100	68	67	68
7	32.00	37.00	36.67	48.33	100	116	115	151
8	37.00	33.00	42.00	43.00	100	89	114	116
9	48.00	48.33	55.67	54.33	100	101	116	113
10	52.67	48.33	51.67	75.67	100	92	98	144
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**31.81**	**33.47**	**33.83**	**39.89**	**100**	**109.27**	**105.43**	**124.51**
SD	**13.71**	**14.59**	**16.40**	**20.96**		**37.05**	**20.31**	**33.74**

Table A 2.20 Q_{twpot} vastus lateralis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.00	3.00	3.67	3.33	100	75	92	83
2	3.33	3.67	3.67	3.67	100	110	110	110
3	4.33	5.33	4.67	4.00	100	123	108	92
4	4.33	3.67	3.67	4.00	100	85	85	92
5	4.00	4.00	3.67	3.67	100	100	92	92
6	3.33	3.67	3.67	4.33	100	110	110	130
7	3.33	3.33	3.33	3.33	100	100	100	100
8	3.67	3.33	3.33	3.33	100	91	91	91
9	3.33	3.33	3.67	3.67	100	100	110	110
10	3.33	3.67	3.33	3.67	100	110	100	110
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.94**	**3.61**	**3.67**	**3.70**	**100**	**100.37**	**99.66**	**101.06**
SD	**0.55**	**0.33**	**0.39**	**0.33**		**14.05**	**9.53**	**13.90**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.53	4.53	3.67	5.07	100	100	81	112
2	3.33	3.67	3.67	3.67	100	110	110	110
3	4.33	4.20	4.07	3.47	100	97	94	80
4	5.33	4.00	4.67	4.67	100	75	88	88
5	3.33	3.47	3.53	3.87	100	104	106	116
6	3.33	3.67	3.67	4.33	100	110	110	130
7	4.67	4.00	3.67	3.33	100	86	79	71
8	4.00	3.67	3.67	3.67	100	92	92	92
9	3.67	3.67	3.33	3.67	100	100	91	100
10	4.00	3.67	4.00	3.67	100	92	100	92
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.05**	**3.85**	**3.79**	**3.94**	**100**	**96.51**	**94.95**	**99.01**
SD	**0.67**	**0.32**	**0.37**	**0.56**		**10.9**	**11.3**	**17.9**

Table A 2.21 Q_{twpot} vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	1.43	3.02	0.76	1.98	100	212	53	139
2	0.63	1.53	2.45	3.21	100	245	392	514
3	2.13	5.81	2.74	3.31	100	273	129	156
4	0.61	2.79	2.79	5.01	100	454	454	816
5	4.25	6.24	5.67	6.05	100	147	133	142
6	1.06	3.02	3.33	3.10	100	285	314	292
7	2.50	2.17	1.56	1.37	100	87	62	55
8	1.91	1.39	0.22	0.31	100	73	12	16
9	1.70	1.13	1.42	1.89	100	67	83	111
10	2.69	2.84	4.02	4.16	100	105	149	154
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**1.89**	**2.99**	**2.49**	**3.04**	**100**	**194.75**	**178.17**	**239.47**
SD	**1.10**	**1.74**	**1.61**	**1.73**		**123.62**	**153.23**	**245.90**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**		**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	2.09	1.24	1.42	2.09	100	59	68	100
2	0.57	1.42	2.42	3.07	100	250	427	542
3	4.06	3.87	3.78	4.91	100	95	93	121
4	0.99	1.75	1.14	1.47	100	176	115	148
5	4.82	3.47	7.18	3.40	100	72	149	71
6	1.09	3.02	3.73	4.91	100	278	343	452
7	0.71	1.89	2.65	2.08	100	267	373	293
8	1.37	0.19	0.95	0.24	100	14	69	17
9	1.42	1.98	2.41	2.65	100	140	170	187
10	8.32	8.08	8.55	6.99	100	97	103	84
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**2.54**	**2.69**	**3.42**	**3.18**	**100**	**144.82**	**191.00**	**201.45**
SD	**2.48**	**2.19**	**2.55**	**1.97**		**93.77**	**136.44**	**173.71**

Table A 2.22 Q_{twpot} vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	5	16	5	9	100	320	100	180
2	19	25	11	21	100	132	58	111
3	19	25	11	41	100	132	58	216
4	14	37	16	21	100	264	114	150
5	25	44	49	52	100	176	196	208
6	11	34	9	36	100	309	82	327
7	13	22	16	11	100	169	123	85
8	19	14	1	4	100	74	5	21
9	15	1	9	12	100	7	60	80
10	23	23	34	38	100	100	148	165
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**16.30**	**24.10**	**16.10**	**24.50**	**100**	**168.21**	**94.41**	**154.25**
SD	**5.93**	**12.33**	**14.56**	**16.22**		**102.50**	**54.14**	**86.56**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	16	9	12	19	100	56	75	119
2	4	12	2	27	100	300	50	675
3	18	15	17	11	100	83	94	61
4	3	16	3	3	100	533	100	100
5	27	18	44	2	100	67	163	7
6	9	22	33	37	100	244	367	411
7	5	13	14	22	100	260	280	440
8	5	1	4	5	100	20	80	100
9	10	13	17	19	100	130	170	190
10	33	33	55	57	100	100	167	173
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**13.00**	**15.20**	**20.10**	**20.20**	**100**	**179.40**	**154.57**	**227.61**
SD	**10.35**	**8.38**	**18.13**	**17.10**		**156.98**	**100.33**	**211.87**

Table A 2.23 Q_{twpot} vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	19.67	38.00	26.00	37.00	100	193	132	188
2	29.66	38.22	40.32	42.53	100	129	136	143
3	44.67	30.67	19.33	72.00	100	69	43	161
4	30.67	64.33	37.00	33.33	100	210	121	109
5	37.00	34.67	51.67	52.67	100	94	140	142
6	35.66	40.11	36.42	37.11	100	112	102	104
7	31.33	46.67	43.67	25.33	100	149	139	81
8	49.00	48.33	25.00	44.00	100	99	51	90
9	38.00	30.33	38.33	27.67	100	80	101	73
10	32.00	31.67	35.33	38.00	100	99	110	119
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**34.77**	**40.30**	**35.31**	**40.96**	**100**	**123.30**	**107.55**	**121.00**
SD	**8.21**	**10.49**	**9.57**	**13.46**	**0.0**	**47.3**	**35.0**	**37.2**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	19.27	15.47	19.00	17.87	100	80	99	93
2	27.67	39.00	41.00	44.00	100	141	148	159
3	17.87	15.33	18.67	19.47	100	86	104	109
4	20.00	32.67	20.67	28.00	100	163	103	140
5	36.67	16.07	16.00	15.67	100	44	44	43
6	25.67	32.00	43.33	38.33	100	125	169	149
7	34.00	31.00	26.33	52.00	100	91	77	153
8	25.67	18.00	26.33	26.00	100	70	103	101
9	29.67	23.33	23.33	25.00	100	79	79	84
10	30.00	30.00	56.33	62.67	100	100	188	209
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**26.65**	**25.29**	**29.10**	**32.90**	**100**	**97.88**	**111.36**	**124.02**
SD	**6.27**	**8.69**	**13.28**	**15.78**		**35.63**	**44.29**	**47.23**

Table A 2.24 Doublet vastus medialis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.67	4.00	4.33	4.64	100	86	93	99
2	4.70	4.50	4.50	4.20	100	96	96	89
3	4.33	5.33	4.33	4.33	100	123	100	100
4	4.67	4.00	4.33	4.00	100	86	93	86
5	4.67	4.00	4.33	5.33	100	86	93	114
6	4.37	4.00	4.63	4.33	100	92	106	99
7	6.00	6.33	7.00	4.67	100	106	117	78
8	5.00	5.00	5.00	5.33	100	100	100	107
9	4.00	3.67	3.67	4.00	100	92	92	100
10	4.00	3.33	5.00	5.00	100	83	125	125
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.64**	**4.42**	**4.71**	**4.58**	**100**	**94.81**	**101.37**	**99.74**
SD	**0.57**	**0.90**	**0.89**	**0.50**		**12.22**	**11.36**	**13.68**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.67	4.53	4.67	4.67	100	97	100	100
2	4.00	4.00	3.67	3.67	100	100	92	92
3	5.33	6.00	5.33	5.00	100	113	100	94
4	5.00	5.33	4.33	4.67	100	107	87	93
5	4.60	4.33	4.53	4.00	100	94	99	87
6	4.33	5.00	5.00	5.33	100	115	115	123
7	5.33	6.00	5.33	3.67	100	113	100	69
8	5.67	6.00	6.67	5.33	100	106	118	94
9	4.00	4.00	4.00	4.00	100	100	100	100
10	4.33	4.33	5.33	5.00	100	100	123	115
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.73**	**4.95**	**4.89**	**4.53**	**100**	**104.43**	**103.30**	**96.71**
SD	**0.58**	**0.83**	**0.85**	**0.65**		**7.26**	**11.65**	**14.89**

Table A 2.25 Doublet: Vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	4.11	2.50	5.76	4.10	100	61	140	100
2	3.45	5.39	3.12	3.69	100	156	90	107
3	8.84	2.84	8.84	2.60	100	32	100	29
4	3.45	5.39	3.12	3.69	100	156	90	107
5	4.21	2.79	3.50	4.35	100	66	83	103
6	4.11	2.50	5.76	4.10	100	61	140	100
7	1.57	3.72	1.47	1.84	100	237	94	118
8	4.37	2.95	3.09	4.35	100	68	71	99
9	7.56	2.93	3.73	2.65	100	39	49	35
10	7.56	7.70	3.35	7.94	100	102	44	105
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.92**	**3.87**	**4.17**	**3.93**	**100**	**97.79**	**90.29**	**90.30**
SD	**2.28**	**1.73**	**2.08**	**1.65**		**65.57**	**32.17**	**31.11**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	1.51	1.48	1.51	1.48	100	98	100	98
2	5.98	7.42	5.98	5.93	100	124	100	99
3	8.84	10.28	8.84	8.50	100	116	100	96
4	4.11	4.11	4.39	4.58	100	100	107	112
5	1.37	1.91	1.82	1.59	100	140	133	116
6	2.27	3.64	2.60	2.79	100	160	115	123
7	2.37	3.97	1.94	1.18	100	167	82	50
8	3.78	3.95	2.76	2.74	100	104	73	72
9	6.05	6.00	5.34	6.28	100	99	88	104
10	7.94	8.55	8.50	5.20	100	108	107	65
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.42**	**5.13**	**4.37**	**4.03**	**100**	**121.69**	**100.43**	**93.55**
SD	**2.67**	**2.87**	**2.73**	**2.45**		**25.82**	**16.96**	**23.59**

Table A 2.26 Doublet vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	16	11	32	17	100	69	200	106
2	24	41	22	23	100	171	92	96
3	47	18	47	26	100	38	100	55
4	24	41	22	23	100	171	92	96
5	19	17	15	25	100	89	79	132
6	16	11	32	17	100	69	200	106
7	13	30	12	17	100	231	92	131
8	36	29	33	25	100	81	92	69
9	44	15	21	17	100	34	48	39
10	44	58	2	6	100	132	5	14
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**28.30**	**27.10**	**23.80**	**19.60**	**100**	**108.42**	**99.85**	**84.36**
SD	**13.17**	**15.65**	**12.75**	**6.10**		**65.01**	**60.14**	**39.11**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	11	13	11	17	100	118	100	155
2	55	63	54	54	100	115	98	98
3	47	18	47	26	100	38	100	55
4	29	22	21	20	100	76	72	69
5	7	10	7	5	100	143	100	71
6	13	18	12	14	100	138	92	108
7	12	18	7	7	100	150	58	58
8	35	9	7	20	100	26	20	57
9	30	47	33	31	100	157	110	103
10	45	90	71	21	100	200	158	47
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**28.40**	**30.80**	**27.00**	**21.50**	**100**	**116.06**	**90.90**	**82.16**
SD	**17.13**	**27.08**	**23.14**	**13.87**		**54.67**	**35.85**	**33.43**

Table A 2.27 Doublet vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	25.00	22.00	24.33	25.33	100	88	97	101
2	25.00	23.33	24.00	29.00	100	93	96	116
3	28.67	27.67	28.67	45.67	100	97	100	159
4	43.67	28.00	39.33	31.67	100	64	90	73
5	33.67	34.00	28.00	31.33	100	101	83	93
6	27.67	22.00	26.67	29.00	100	80	96	105
7	25.00	23.33	24.00	29.00	100	93	96	116
8	45.33	45.00	45.00	35.00	100	99	99	77
9	27.67	22.00	26.67	29.00	100	80	96	105
10	27.67	44.67	29.00	44.33	100	161	105	160
n	**8**	**8**	**8**	**8**	**10**	**10**	**10**	**10**
Mean	**30.93**	**29.20**	**29.57**	**32.93**	**100**	**95.60**	**95.94**	**110.53**
SD	**7.60**	**9.07**	**7.02**	**6.83**		**25.7**	**5.8**	**29.7**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	15.33	17.93	15.33	15.33	100	117	100	100
2	59.67	46.00	49.00	46.67	100	77	82	78
3	15.33	19.00	25.33	29.33	100	124	165	191
4	40.67	32.67	32.33	23.33	100	80	80	57
5	14.93	15.20	15.00	15.53	100	102	100	104
6	26.33	31.67	25.33	29.33	100	120	96	111
7	37.33	23.67	18.67	25.67	100	63	50	69
8	43.00	40.33	37.00	37.00	100	94	86	86
9	32.67	44.33	37.00	33.33	100	136	113	102
10	45.67	45.67	44.00	29.33	100	100	96	64
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**33.09**	**31.65**	**29.90**	**28.49**	**100**	**101.32**	**96.92**	**96.34**
SD	**15.07**	**12.12**	**11.89**	**9.45**		**23.14**	**29.43**	**38.14**

Table A 2.28 Doublet vastus lateralis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	3.67	3.67	3.33	2.67	100	100	91	73
2	3.00	3.00	4.33	4.00	100	100	144	133
3	5.33	4.00	4.67	5.33	100	75	88	100
4	4.00	3.67	3.67	4.00	100	92	92	100
5	4.00	3.67	4.33	3.67	100	92	108	92
6	4.67	4.67	4.00	4.33	100	104	93	96
7	3.00	3.00	4.33	4.00	100	100	144	133
8	4.00	3.33	3.33	3.00	100	100	109	127
9	3.67	4.00	3.67	4.00	100	85	92	108
10	3.33	3.33	3.33	3.33	100	100	110	110
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.87**	**3.63**	**3.90**	**3.83**	**100**	**94.66**	**107.16**	**107.25**
SD	**0.72**	**0.51**	**0.50**	**0.74**		**8.99**	**21.36**	**19.51**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.67	4.67	4.20	4.33	100	100	90	93
2	3.67	3.00	3.67	3.67	100	82	100	100
3	3.91	3.90	3.99	4.23	100	100	102	108
4	4.00	4.00	4.00	4.33	100	100	100	108
5	3.73	3.87	3.47	3.60	100	104	93	96
6	3.67	4.33	3.67	4.33	100	118	100	118
7	3.67	3.67	4.00	4.67	100	100	109	127
8	4.33	3.67	4.00	4.67	100	85	92	108
9	3.33	3.33	3.67	3.67	100	100	110	110
10	4.00	4.00	4.33	4.33	100	100	108	108
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.90**	**3.84**	**3.90**	**4.18**	**100**	**98.79**	**100.45**	**107.73**
SD	**0.38**	**0.47**	**0.27**	**0.40**		**9.97**	**7.18**	**10.03**

Table A 2.29 Doublet vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	2.36	3.17	4.02	4.58	100	134	170	194
2	4.11	5.91	4.84	2.73	100	144	118	66
3	5.81	6.43	2.74	5.81	100	111	47	100
4	8.32	5.72	9.12	9.31	100	69	110	112
5	9.17	5.91	8.79	7.89	100	64	96	86
6	5.81	6.43	3.74	5.72	100	111	64	98
7	1.42	2.17	2.32	1.47	100	153	163	103
8	4.11	4.96	4.84	2.73	100	121	118	66
9	5.86	1.65	1.51	1.09	100	28	26	19
10	3.73	5.86	5.29	5.06	100	157	142	135
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**5.07**	**4.82**	**4.72**	**4.64**	**100**	**109.13**	**105.37**	**98.06**
SD	**2.43**	**1.80**	**2.53**	**2.69**		**42.64**	**47.95**	**46.31**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	1.51	1.70	2.10	2.15	100	113	139	142
2	3.69	3.87	2.17	2.13	100	105	59	58
3	3.00	3.33	2.97	3.17	100	111	99	106
4	1.75	1.80	1.18	1.28	100	103	68	73
5	2.13	3.40	3.47	2.29	100	160	163	108
6	3.02	5.34	3.73	4.91	100	177	123	162
7	1.84	1.84	1.89	1.84	100	100	103	100
8	3.33	1.28	1.18	3.73	100	38	35	112
9	2.41	3.02	3.26	2.65	100	126	135	110
10	7.37	7.18	7.09	6.71	100	97	96	91
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.00**	**3.28**	**2.90**	**3.09**	**100**	**112.90**	**102.06**	**106.18**
SD	**1.70**	**1.85**	**1.72**	**1.64**		**37.37**	**39.73**	**30.25**

Table A 2.30 Doublet vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	16	13	17	22	100	81	106	138
2	28	33	31	19	100	118	111	68
3	25	47	11	25	100	188	44	100
4	42	58	45	43	100	138	107	102
5	49	46	58	42	100	94	118	86
6	25	47	11	25	100	143	129	93
7	7	17	15	7	100	243	214	100
8	28	33	31	19	100	109	136	118
9	30	21	17	10	100	25	14	57
10	29	30	39	39	100	106	129	112
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**27.90**	**34.50**	**27.50**	**25.10**	**100**	**124.48**	**110.94**	**97.34**
SD	**11.76**	**14.80**	**16.04**	**12.64**	**0.0**	**59.53**	**53.64**	**23.42**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	11	14	16	15	100	127	145	136
2	23	21	25	21	100	91	109	91
3	19	19	18	19	100	100	95	100
4	16	16	5	5	100	100	31	31
5	14	20	18	13	100	143	129	93
6	22	34	33	37	100	155	150	168
7	11	12	15	13	100	109	136	118
8	28	7	4	16	100	25	14	57
9	17	18	22	19	100	106	129	112
10	28	26	23	25	100	93	82	89
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**18.90**	**18.70**	**17.90**	**18.30**	**100**	**104.88**	**102.09**	**99.63**
SD	**6.26**	**7.50**	**8.77**	**8.51**	**0.0**	**35.26**	**47.17**	**38.36**

Table A 2.31 Doublet vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise with and without digoxin

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	36.67	26.33	22.00	33.33	100	72	60	91
2	30.67	31.00	29.33	35.33	100	101	96	115
3	30.67	31.00	19.33	38.33	100	101	63	125
4	34.67	46.67	32.33	28.33	100	135	93	82
5	26.67	43.67	31.67	21.67	100	164	119	81
6	30.67	33.00	29.33	32.33	100	108	96	105
7	28.67	37.67	35.00	18.33	100	131	122	64
8	37.33	38.00	38.00	29.00	100	102	102	78
9	28.00	44.67	45.33	35.00	100	160	162	125
10	36.00	18.33	46.33	46.33	100	51	129	129
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**32.00**	**35.03**	**32.87**	**31.80**	**100**	**112.36**	**104.08**	**99.49**
SD	**3.86**	**8.88**	**8.79**	**8.05**	**0.0**	**35.79**	**30.52**	**23.33**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	19.20	19.27	15.87	17.40	100	100	83	91
2	31.00	29.33	30.00	43.67	100	95	97	141
3	28.37	30.41	28.74	27.03	100	107	101	95
4	32.00	32.00	15.67	15.67	100	100	49	49
5	15.80	15.67	16.07	16.00	100	99	102	101
6	32.00	29.00	43.33	38.33	100	91	135	120
7	24.67	29.00	39.00	37.00	100	118	158	150
8	44.67	35.33	21.00	25.33	100	79	47	57
9	33.33	46.67	41.00	25.00	100	140	123	75
10	31.67	37.33	36.00	24.33	100	118	114	77
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**29.27**	**30.40**	**28.67**	**26.98**	**100**	**104.65**	**100.86**	**95.54**
SD	**8.04**	**8.73**	**10.95**	**9.78**	**0.0**	**17.06**	**35.07**	**33.52**

Table A 2.32 20Hz Tetani vastus medialis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.33	4.67	5.33	6.67	100	108	123	154
2	3.67	4.33	4.00	3.33	100	79	65	54
3	3.67	6.33	6.67	3.33	100	173	182	91
4	4.33	4.67	5.33	4.33	100	108	123	100
5	5.00	4.67	5.00	5.00	100	93	100	100
6	4.67	5.33	5.33	6.67	100	78	94	105
7	5.67	6.00	6.33	5.00	100	106	112	88
8	5.33	4.67	5.00	6.33	100	100	125	108
9	4.00	3.33	3.00	3.67	100	79	84	116
10	4.33	4.00	4.67	4.00	100	100	100	100
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.50**	**4.80**	**5.07**	**4.83**	**100**	**102.38**	**110.79**	**101.61**
SD	**0.67**	**0.89**	**1.05**	**1.33**	**0.0**	**27.44**	**31.37**	**24.77**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	6.13	4.87	5.33	6.67	100	79	87	109
2	3.67	3.33	3.00	3.33	100	91	82	91
3	4.20	4.13	4.00	3.33	100	98	95	79
4	4.67	4.67	4.00	6.33	100	100	86	136
5	4.27	3.33	4.00	4.47	100	93	100	100
6	4.67	5.33	4.67	4.67	100	114	100	100
7	5.33	5.33	6.67	5.78	100	100	125	108
8	6.33	5.00	5.33	7.33	100	79	84	116
9	4.00	4.00	4.00	4.00	100	100	100	100
10	5.00	4.33	5.33	5.33	100	87	107	107
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.83**	**4.43**	**4.63**	**5.12**	**100**	**94.19**	**96.56**	**104.54**
SD	**0.88**	**0.74**	**1.05**	**1.39**	**0.0**	**10.76**	**13.03**	**14.97**

Table A 2.33 20Hz Tetani vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	3.50	6.00	5.00	4.00	100	172	143	114
2	4.00	5.20	5.00	4.00	100	130	125	100
3	5.43	4.13	3.54	5.39	100	76	65	99
4	5.62	9.12	9.26	8.08	100	162	165	144
5	4.02	2.55	2.84	3.35	100	64	71	84
6	3.45	2.79	3.83	2.79	100	81	111	81
7	2.09	3.69	5.72	1.65	100	177	274	79
8	4.35	4.11	3.59	3.05	100	95	83	70
9	2.65	1.94	1.80	2.50	100	73	68	95
10	5.58	7.28	4.72	3.64	100	131	85	65
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.14**	**5.42**	**5.19**	**4.11**	**100**	**115.91**	**118.86**	**93.08**
SD	**1.53**	**2.85**	**2.99**	**2.04**	**0.0**	**43.69**	**64.22**	**23.19**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+30 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	2.58	1.94	1.80	2.50	100	75	70	97
2	3.17	5.34	5.39	5.10	100	169	170	161
3	4.69	5.16	5.10	4.89	100	110	109	104
4	2.69	2.22	3.73	3.35	100	82	139	125
5	1.68	1.58	1.59	1.52	100	94	95	91
6	3.45	2.79	3.83	2.79	100	81	111	81
7	1.94	1.71	1.24	1.63	100	88	64	84
8	1.66	2.22	2.74	0.76	100	134	165	46
9	6.09	5.06	5.20	5.95	100	83	85	98
10	5.01	9.97	10.02	5.20	100	199	200	104
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.29**	**3.80**	**4.06**	**3.37**	**100**	**111.55**	**120.74**	**98.98**
SD	**1.52**	**2.64**	**2.60**	**1.82**	**0.0**	**42.40**	**45.95**	**29.93**

Table A 2.34 20Hz Tetani vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Digoxin					**Expressed as a % of pre-exercise**			
Subject	**Pre-exercise Area (uV.s)**	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue (%)**	**+10 min**	**+60 min**
1	22	27	29	22	100	123	132	100
2	22	29	28	22	100	132	127	100
3	30	27	18	28	100	90	60	93
4	52	70	69	42	100	135	133	81
5	15	17	20	14	100	113	133	93
6	21	27	28	22	100	129	133	105
7	18	19	30	11	100	106	167	61
8	25	28	24	15	100	112	96	60
9	17	8	7	8	100	47	41	47
10	27	43	23	46	100	159	85	170
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**24.90**	**29.50**	**27.60**	**23.00**	**100**	**114.49**	**110.75**	**91.07**
SD	**10.57**	**16.91**	**16.09**	**12.61**	**0.0**	**30.20**	**38.92**	**34.24**

Placebo								
Subject	**Pre-exercise Area (uV.s)**	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue (%)**	**+10 min**	**+60 min**
1	11	12	13	14	100	109	118	127
2	26	28	28	27	100	108	108	104
3	19	17	22	12	100	89	116	63
4	12	18	13	14	100	150	108	117
5	12	6	5	2	100	50	42	17
6	17	14	19	30	100	82	112	176
7	7	2	1	3	100	29	14	43
8	9	14	12	6	100	156	133	67
9	37	23	25	33	100	62	68	89
10	57	73	74	22	100	128	130	39
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**20.70**	**20.70**	**21.20**	**16.30**	**100**	**96.30**	**94.84**	**84.14**
SD	**15.63**	**19.85**	**20.39**	**11.21**	**0.0**	**41.95**	**39.98**	**48.23**

Table A 2.35 20Hz Tetani vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	44.67	19.67	32.33	33.67	100	44	72	75
2	31.00	33.38	31.67	31.70	100	108	102	102
3	33.00	33.33	25.00	31.67	100	101	76	96
4	34.67	42.00	40.33	30.67	100	121	116	88
5	27.33	32.33	34.00	23.67	100	118	124	87
6	32.33	34.00	37.67	35.33	100	105	116	109
7	33.67	33.67	23.33	37.00	100	100	69	110
8	35.00	41.00	37.67	28.00	100	117	108	80
9	29.00	20.33	20.00	19.33	100	70	69	67
10	26.00	39.33	24.67	51.33	100	151	95	197
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**31.15**	**33.78**	**31.00**	**31.54**	**100**	**103.59**	**94.83**	**101.19**
SD	**7.63**	**8.70**	**8.79**	**9.61**	**0.0**	**29.23**	**21.63**	**36.69**

Placebo

	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	15.93	15.13	14.47	15.53	100	95	91	97
2	27.00	18.67	31.67	29.33	100	69	117	109
3	16.47	19.07	18.67	19.00	100	116	113	115
4	28.33	38.67	24.33	30.00	100	136	86	106
5	15.27	14.47	15.53	18.07	100	95	102	118
6	24.67	29.33	25.33	24.67	100	119	103	100
7	18.67	12.67	25.67	19.00	100	68	137	102
8	36.00	32.33	37.00	35.00	100	90	103	97
9	35.00	22.33	22.67	32.67	100	64	65	93
10	27.00	42.33	43.00	30.67	100	157	159	114
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**24.43**	**24.50**	**25.83**	**25.39**	**100**	**100.83**	**107.61**	**105.17**
SD	**7.65**	**10.54**	**9.14**	**7.02**	**0.0**	**30.93**	**26.58**	**8.57**

Table A 2.36 20Hz Tetani vastus lateralis muscle M-wave latency evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	3.00	3.33	3.67	3.33	100	111	122	111
2	3.00	4.00	3.27	3.47	100	133	109	116
3	3.67	4.00	3.33	3.00	100	109	91	82
4	3.67	4.00	4.33	3.33	100	109	118	91
5	3.67	4.00	4.33	4.00	100	109	118	109
6	3.00	4.67	4.33	3.33	100	156	144	111
7	3.00	4.00	3.00	4.33	100	133	100	144
8	4.00	3.33	3.33	3.33	100	83	83	83
9	3.33	3.67	3.33	4.00	100	110	100	120
10	3.67	3.33	3.67	3.33	100	91	100	91
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.40**	**3.83**	**3.66**	**3.55**	**100**	**114.48**	**108.61**	**105.82**
SD	**0.38**	**0.42**	**0.50**	**0.42**	**0.0**	**21.20**	**17.72**	**19.38**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Latency (ms)				**(%)**			
1	4.53	3.67	4.00	4.00	100	81	88	88
2	3.33	3.00	2.67	3.33	100	90	80	100
3	3.27	3.47	3.33	3.33	100	106	102	102
4	4.00	5.00	4.00	4.00	100	125	100	100
5	3.53	3.87	3.13	3.13	100	109	89	89
6	4.00	3.67	4.00	4.33	100	92	100	108
7	3.67	4.33	4.33	4.11	100	118	118	112
8	4.67	4.33	4.00	4.00	100	93	86	86
9	3.67	3.33	3.67	3.67	100	91	100	100
10	4.33	4.00	4.33	4.67	100	92	100	108
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**3.90**	**3.87**	**3.75**	**3.86**	**100**	**99.74**	**96.28**	**99.28**
SD	**0.49**	**0.58**	**0.54**	**0.49**	**0.0**	**14.17**	**10.88**	**9.10**

Table A 2.37 20Hz Tetani vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	3.89	5.95	5.48	3.93	100	153	141	101
2	5.46	6.45	5.87	4.97	100	118	108	91
3	6.43	5.67	5.76	6.47	100	88	90	101
4	5.43	6.38	5.39	2.69	100	117	99	50
5	9.64	8.60	6.61	4.30	100	89	69	45
6	5.21	5.29	4.88	3.92	100	101	94	75
7	1.42	1.47	2.17	2.32	100	103	153	163
8	7.89	4.96	4.84	2.81	100	63	61	36
9	1.70	1.51	1.42	1.09	100	89	83	64
10	6.19	5.67	5.20	6.28	100	92	84	102
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**5.33**	**5.19**	**4.76**	**3.88**	**100**	**101.44**	**98.15**	**82.66**
SD	**2.53**	**2.19**	**1.66**	**1.72**	**0.0**	**24.20**	**29.25**	**37.66**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	Amplitude (mV)				(%)			
1	2.99	2.97	2.46	2.41	100	99	82	81
2	5.46	6.43	5.69	5.48	100	118	104	100
3	5.84	4.91	5.75	3.93	100	84	99	67
4	5.72	3.57	3.54	3.21	100	62	62	56
5	2.74	3.40	4.70	2.74	100	124	172	100
6	3.45	5.76	5.48	2.93	100	167	159	85
7	1.84	1.89	1.47	1.74	100	103	80	94
8	3.73	1.70	1.89	4.82	100	46	51	129
9	2.41	2.46	2.41	1.61	100	102	100	67
10	6.95	7.18	7.09	6.99	100	103	102	101
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**4.11**	**4.03**	**4.05**	**3.59**	**100**	**100.84**	**101.00**	**88.01**
SD	**1.74**	**1.93**	**1.95**	**1.73**	**0.0**	**33.41**	**38.31**	**21.46**

Table A 2.38 20Hz Tetani vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	22	28	24	21	100	127	109	95
2	29	33	36	25	100	114	124	86
3	33	30	58	33	100	91	176	100
4	42	42	34	18	100	100	81	43
5	52	60	50	27	100	115	96	52
6	28	31	34	26	100	111	121	93
7	7	7	14	15	100	100	200	214
8	42	33	31	21	100	79	74	50
9	17	9	10	10	100	53	59	59
10	32	60	59	34	100	188	184	106
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**30.40**	**33.30**	**35.00**	**23.00**	**100**	**107.71**	**122.45**	**89.87**
SD	**13.13**	**17.73**	**16.79**	**7.57**	**0.0**	**35.13**	**49.10**	**49.56**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Area (uV.s)**				**(%)**			
1	18	18	23	22	100	100	128	122
2	24	33	26	22	100	138	108	92
3	20	21	26	25	100	105	130	125
4	39	23	22	22	100	59	56	56
5	18	20	24	13	100	111	133	72
6	26	38	35	15	100	146	135	58
7	12	12	5	9	100	100	42	75
8	16	6	8	25	100	38	50	156
9	18	14	13	12	100	78	72	67
10	23	26	23	22	100	113	100	96
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**21.40**	**21.10**	**20.50**	**18.70**	**100**	**98.71**	**95.44**	**91.88**
SD	**7.41**	**9.59**	**9.13**	**5.85**	**0.0**	**33.20**	**37.14**	**33.18**

Table A 2.39 20Hz Tetani vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Digoxin					**Expressed as a % of pre-exercise**			
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	37.33	21.67	27.33	26.67	100	58	73	71
2	31.34	33.62	36.12	30.46	100	107	115	97
3	29.00	34.33	29.67	29.67	100	118	102	102
4	49.00	33.33	29.67	25.67	100	68	61	52
5	27.00	37.33	41.33	33.00	100	138	153	122
6	30.10	31.48	31.00	30.43	100	105	103	101
7	28.67	28.33	37.67	35.00	100	99	131	122
8	31.67	38.00	38.00	30.67	100	120	120	97
9	46.67	24.67	27.00	35.00	100	53	58	75
10	29.00	30.12	33.33	29.33	100	104	115	101
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**33.98**	**31.29**	**33.11**	**30.59**	**100**	**97.01**	**103.16**	**94.17**
SD	**7.83**	**5.24**	**4.95**	**3.11**	**0.0**	**28.30**	**30.96**	**22.05**

Placebo								
	Pre-exercise	**Fatigue**	**+10 min**	**+60 min**	**Pre-exercise**	**Fatigue**	**+10 min**	**+60 min**
Subject	**Duration (ms)**				**(%)**			
1	16.47	16.60	16.75	16.67	100	101	102	101
2	26.67	29.33	27.33	25.33	100	110	102	95
3	15.13	19.47	16.00	15.67	100	129	106	104
4	43.00	21.33	26.67	26.67	100	50	62	62
5	16.00	15.67	16.40	16.40	100	98	103	103
6	26.67	29.33	32.33	30.33	100	110	121	114
7	29.00	29.67	23.00	27.22	100	102	79	94
8	25.33	21.67	29.33	28.33	100	86	116	112
9	28.67	26.00	24.33	26.00	100	91	85	91
10	21.00	37.33	36.00	19.67	100	178	171	94
n	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mean	**24.79**	**24.64**	**24.81**	**23.23**	**100**	**105.33**	**104.71**	**96.81**
SD	**8.34**	**6.86**	**6.90**	**5.54**	**0.0**	**32.71**	**29.30**	**14.45**

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

Appendix K

INFORMATION TO PARTICIPANTS INVOLVED IN RESEARCH
Chapter 5

You are invited to participate

You are invited to participate in a research project entitled: **The effects of high intensity interval training on potassium concentration, muscle excitability and fatigue**.

This project is being conducted by a student researcher Trevor Farr ***as part of a PhD study*** at Victoria University, under the supervision of Professor Michael McKenna from Institute of Sport, Exercise and Active Living (ISEAL).

Project explanation

This project aims to investigate the effects of a seven week sprint training regime on arterial and venous [K^+], muscle excitability and fatigue.
Exhaustive exercise is well known to impair muscle excitability and alter muscle properties as a result of muscle electrical activity (action potential), in particular changes in ions and metabolites. Short term high intensity exercise is typical of many team sports, which are played worldwide. Furthermore, little is known about the physiological effects of muscle following repeat sprint training, specifically a seven week protocol, has on potassium concentration, muscle excitability and fatigue. Recent studies have investigated short term high intensity exercise and shown large increases in the arterial blood plasma potassium concentration and an accumulation of potassium inside and outside the contracting muscles. This has been linked with muscle fatigue during intense exercise in humans, via muscle activity. Here we will focus on the effects of the regulation of potassium concentrations, which are integral in sustaining muscle contractions. Muscle contractile properties and excitability will also be accessed via muscle force and relaxation and the muscle activity (M-wave) characteristics, respectively as they are perturbed with fatigue. Understanding the effects of this type of activity on skeletal muscle will make an important contribution to knowledge. This knowledge is especially relevant to understanding processes of muscle excitability and muscle fatigue.
The following inclusion/exclusion criteria provide guidelines to your means of participating in this research project.

Inclusion criteria-:	Exclusion criteria-:
ages 18-35	ages under 18 or over 35
free from injury, skin or anaesthetic allergies	suffering skeletal muscle injury,
free from bleeding disorders	or bleeding disorder
skin or anaesthetic allergies	neuromuscular or
no known neuromuscular or cardiovascular diseases	cardiovascular diseases

What will I be asked to do?

You will be required to complete a total of 25 **visits in the laboratory**

Perform the following:

Graded exercise test ($\dot{V}O_{2peak}$): A graded exercise tests (GXT) (two leg) will be performed followed by four 30 s sprints, interspersed with 4 min of passive recovery between bouts with 30min separating the GXT and Sprints. These tests will determine the maximal work rate which you can complete for a sustained period, and determine oxygen uptake via measurement of expired gases. The cycle ergometer will be set up according to your individual physical characteristics. You will be fitted with a Polar heart rate strap (which is not restrictive to movement, and is commonly used by athletes) and with an adult-size mouthpiece to breathe through to collect expired gas. You will then be requested to undertake the test, which consists of an increasing incremental exercise on an electronically-braked cycle ergometer. At the conclusion of the test, you will be given a drink and perform a self-paced cool down. All testing will be performed under the Exercise Physiology Laboratory's (College of Sport and Exercise Science, VU) guidelines for maximal exercise testing.

Maximal Sprint Exercise

Four 30 s sprints interspersed with 4 min of passive recovery. Sprints will be initiated with the right leg, with the crank arm located 45° forward to the vertical axis. You will be asked to remain seated during every sprint and during the recovery periods. The cycle ergometer will be equipped with toe-clips to prevent your feet from slipping. The high intensity efforts, each lasting only 30 seconds, and with a short recovery, are designed to replicate the type of efforts involved in intermittent team sports. Maximal Sprint Exercise protocols are extensively used in the VU Exercise Physiology Laboratory and across the world.

Power output will be determined from pedalling velocity samples Blood (venous & arterial) samples (see procedure details below) will be drawn from antecubital vein and radial artery respectively, before and after each sprint bout.

Sprint Training

Sprint training will be conducted in a laboratory under supervision 3 times per week over 7 weeks on a Velotron cycle. The sprint training protocol consists of twenty-one sessions spread over 7 weeks, with 2-3 days recovery between training sessions. Sprint training consists of repeated 30 s **maximal cycling efforts**, interspersed with 4 min of recovery. Training progression will be implemented by increasing the number of repeats from four bouts during week 1, six bouts during week 2, eight bouts during week 3 and finally to ten bouts during weeks 4-7.

Peripheral Magnetic Stimulation

While lying on a bench with the knee flexed at 90°, a series of magnetic stimulations of the quadriceps will be used at rest and following Maximal Voluntary Contractions (MVC) to measure muscle function properties. Magnetic stimulation is relatively painless however you may experience a slight discomfort during stimulation. A thorough preliminary session to familiarise you with the stimulation will be performed.

Electromyography (EMG) recording

EMG signals of the quadriceps muscles (*vastus lateralis and*, *vastus medialis,)*, will be recorded via skin surface electrodes to estimate muscle activation. Recording electrodes will be fixed (attached to the skin) longitudinally over the area of greatest muscle bulk. The reference electrode will be fixed over an electrically-neutral site (epicondyle of femur). Electrode site preparation will be thoroughly performed before the beginning of every test by careful preparation of the skin (shaving, light abrasion and cleaning with alcohol swab). The position of the EMG electrodes will be marked with indelible ink to ensure that they are placed in the same location at subsequent visits. To ensure low levels of movement artefact, electrode cables will be fastened to the subjects' body with medical adhesive tape and wrapped in net. There is no discomfort associated with the application, wearing, or removal of the EMG electrodes.

Maximal voluntary contraction (MVC) test

This test will determine the maximal isometric strength of your quadriceps muscle. You will be lying on a bench with the knee flexed at 90° (0° = knee fully extended). Your leg will be placed in a mould to ensure the knee is flexed at 90° and to ensure movement is in a transverse direction. The upper body and hips will be strapped to the bench to reduce body movement and the recruitment of ancillary muscles. You will be asked to perform a couple of short maximal knee extensions of 4 s before and immediately after the sprint exercise.

Venous Catheterisation

Blood samples will be taken during rest, exercise and recovery via a catheter placed in the arm. The catheter consists of a needle and teflon tubing. The tubing is fed over the top of the needle on entering the vein. The needle is then withdrawn, leaving only the teflon tubing in your vein for the remainder of the experiment. A tap (stopcock) is placed into the tubing so the flow of blood along the tubing can be altered at will. This procedure allows the taking of multiple blood samples without the need for multiple venepuncture (puncturing of the vein). Each time a blood sample is taken, a small volume of fluid will be injected to keep the catheter from clotting. Catheterisation is slightly uncomfortable, with minimal possibility of bruising and infection. The use of sterile, disposable catheters, syringes, single dose vials and aseptic techniques will markedly reduce the possibility of infection. Only staff qualified and experienced in venepuncture will be used in order to prevent complications. Although the possibility of infection, bleeding, local blood clots, local swelling and redness, and bruising are remote, should any one of these conditions eventuate, please inform us immediately and then consult your doctor.

Arterial Catheterisation

A similar catheter will be used as above and inserted into the radial artery (wrist). Pain is minimised by use of a local anaesthetic. Infection is unlikely as an experienced medical practitioner will perform all arterial catheterisations.

Muscle Biopsy

The muscle biopsy procedure will be performed by a qualified, experienced medical doctor, and using aseptic techniques. In this procedure needle biopsies will be taken from the vastus lateralis muscle with suction, between 12 and 24 cm above the knee. There are no large blood vessels or nerves in the region that will be biopsied. Prior to the biopsy, the skin around the area of investigation will be cleaned with surgical spirit, and the skin and subcutaneous tissue will be anaesthetised with 1% Xylocaine. Using aseptic techniques, the skin and muscle fascia will be punctured with a sterile scalpel blade. The tip of the biopsy needle with the inner cylinder will be introduced into the muscle to a depth of 2-5 cm. The inner cylinder will then be drawn back a few cm without moving the needle, and pushed back to cut a small piece of muscle bulging into the cylinder. This can be repeated a number of times to increase the mass of muscle taken. The procedure takes on average 5-10 seconds, and the weight of tissue can range from 0.01-0.4 g.

What will I gain from participating?

Potential benefits to you include the opportunity to be involved in human research and gaining valuable research experience, furthering your knowledge, networking and exploring opportunities for the future. Furthermore, you will have the opportunity to access your current fitness (Vo2peak, usual cost is ~$200) improve your fitness levels and discuss your results, training strategies and lifestyle strategies with researchers.

How will the information I give be used?

No persons other than the investigators (Professor Mike McKenna, Dr Aaron Petersen, Mr Trevor Farr)

will be privy to any information that may identify you. The purpose of these persons having access is to review and discuss information provided.

What are the potential risks of participating in this project?

The **physical risks** associated with the performance testing will not be greater than that experienced by you during one of your standard training sessions. However, the cycle exercise involves a highly unlikely risk of sudden death due to heart failure or fainting episode. Fainting **episode** risks or precipitating factors include; high intensity exercise on a cycle ergometer, particularly if followed immediately by passive recovery on the ergometer, high intensity exercise if you suffer with low exercise tolerance; previous fainting or light-headedness during procedures or associated with exercise. Signs and symptoms may include; precipitous drop in heart rate during recovery (common) or exercise (rare); drop in blood pressure; facial pallor; fixed facial expression; pupils constricted; you become uncommunicative or slurring of words; restless and irritability; sweating; fatigue (if exercising). While fainting episodes are not uncommon, they are reversed quickly when employing a first aid management plan, and long-term risks are minimal. Furthermore, the cycle exercises and the knee extensor exercise carry the risk of muscle soreness, stiffness and the potential for soft tissue injury.

In session 3 you will requested to lie-down on a bed where resting blood sample and resting muscle biopsy will be taken.
What is muscle biopsy: The muscle biopsy procedure is used to obtain small samples of your muscle tissue for analysis of proteins, genes and energy sources. Before the test we will ask you to wear shorts in order for the doctor to have access to your thigh muscles. An injection of a local anaesthetic is made in the skin overlying the muscle in your thigh, and then a small incision (approx. 0.6 cm long) is made in the skin. The biopsy needle is then inserted into your muscle and a small piece of tissue removed from the muscle. During this part of the procedure you will feel pressure and this will be quite uncomfortable and you may also experience some pain, but will last for only few seconds. When the small piece of muscle is removed you may also experience a mild muscle cramp, but this only persists for a few seconds. The size of muscle removed by the biopsy needle is similar to 3-4 grains of rice. This poses no long-term effects for your muscle and will not be noticeable to others apart from a small scar on the skin for a few months. Following the biopsy the incision will be closed using a steri-strip and covered by a transparent waterproof dressing. Then a pressure bandage will be applied which should be maintained for 24-48 hours. Steri-strip closure should be maintained for a few days. It is common for participants to experience some soreness in the muscle over the next 2-3 days, however this passes and does not restrict movement. The soreness is due to slight bleeding within the muscle and is best treated by “ice, compression and elevation”. An ice pack will be applied over the biopsy site after the biopsy procedure to minimise any bleeding and therefore soreness. In some rare cases mild haematomas have been reported, but these symptoms disappear within a week. A medical practitioner will perform the whole procedure under sterile conditions. On very rare occasions, some people have reported altered sensation (numbness or tingling) in the skin near the site of the biopsy. This is due to a very small nerve being cut, but this sensation disappears over a period of a few weeks-to-months. Although the possibility of infection, significant bruising and altered sensation is quite small, if by chance it does eventuate, please inform us immediately and we will immediately consult the doctor who performed the biopsy to review the reported problems and recommend appropriate action.

If you have any concerns regarding your participation Dr. Harriet Speed (registered psychologist) is available for counselling. Her contact details are: (03) 99195412 or at harriet.speed@vu.edu.au.

How will this project be conducted?

Methodology

Research design:

You will be required to complete a total of 25 **visits in the laboratory**.
Please note you will be asked to provide personal health information.

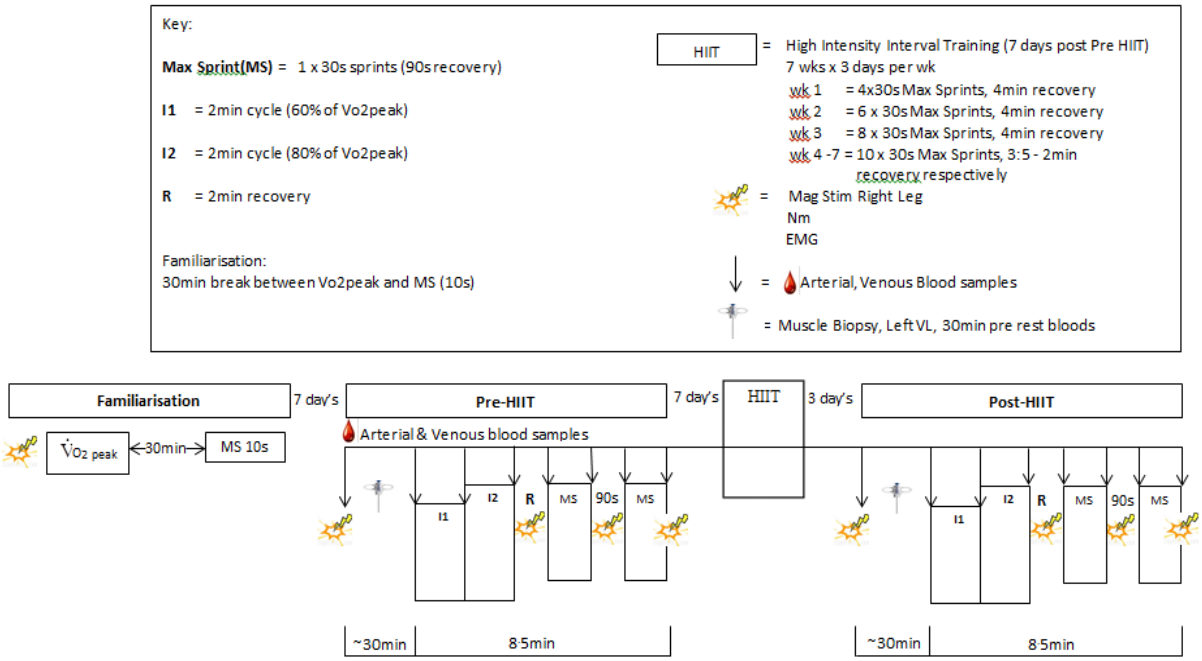

Figure 1. Schematic diagram of the project

Visit 1: **Preliminary Screening and Pre-Test Procedures**
Preliminary screening, you will be requested to complete the Cardiovascular Risk Questionnaire. To proceed with the study, you must be healthy, free from injury and known neuromuscular or cardiovascular diseases (as assessed via questionnaires). You will be given the opportunity to ask any questions about the study. The principal investigator will then assess your suitability for participation in the study.

Following clearance, you will then be requested to perform a Vo2max (GXT) followed by ***familiarisation*** session involving the Two Leg Cycle Exercise that will be similar to the ones used in the Sprint Training Sessions.

Electromyography (EMG) signals of two thigh muscles (vastus medialis and vastus lateralis) will be record via skin surface electrodes to estimate muscle activation. There is no discomfort associated with the application, wearing, or removal of the EMG electrodes. Measurement of magnetic activity of muscles during exercise is a routine procedure in most Physiology and Biomechanics laboratories world-wide.
Peripheral Muscle Fatigue Assessment (PMFA) will include stimulations at 50, 60, 70, 80, 90 & 100% of stimulator output to gain a levelling off in amplitude. Magnetic Stimulation of the quadriceps will be performed immediately following each sprint bout during PMFA for the duration of the exercise test to determine whether changes can be detected with fatigue.

Visit 2: **Pre-Test Procedures**

The familiarisation procedures are exactly the same as Visit 1, except there is no GXT.

Visit 3: **Experimental Exercise Performance and Muscle Function Assessment**
Medical Dr will confirm informed consent sighted. Upon arriving to the lab, you will be asked to lie down on a bench where arterial and venous access will be achieved via the cannulation of the radial artery and antecubital vein for blood sampling. A muscle biopsy will then be taken from your left vastus lateralus by a qualified medical doctor. Skin surface electrodes will then be positioned on the right vatus medialis and vastus lateralis (quadriceps) muscles. ECG electrodes will also be attached to record electrical activity of the heart. Twenty minutes after the arterial/venous cannulation a resting blood sample will then be taken.

Peripheral Magnetic Stimulation will then be performed whilst lying on a bench with the knee flexed at 90°, a series of magnetic stimulations, three single twitches every 4 s at 50, 60, 70, 80, 85, 90, 95, and 100% of maximal power output of the stimulator, of the quadriceps at rest to determine whether quadriceps stimulation is supramaximal. A maximal voluntary contraction (MVC) followed by three single twitches at 1 Hz followed by another MVC and three paired twitches at 20Hz will then be performed to asses potentiated twitch force (Figure 2). We will also request you to perform Maximal Voluntary Contractions (MVC) followed by two single twitches at 1 Hz followed by another MVC and two paired twitches at 20Hz to measure muscle function properties between each Maximal Sprint.

Electromyography (EMG) recording of the quadriceps muscles (*vastus lateralis and vastus medialis)* will be recorded via standard skin preparation and electrode placement to estimate muscle activation. The EMG signals will also be used to analyse M-wave.
You will then be requested to move to the exercise cycle where gas exchange measures will be collected for two minutes followed by a two-leg graded exercise test (GXT) on a cycle ergometer to determine aerobic fitness.

The Cycle Exercise will then be initiated on an electrically-braked cycle-ergometer (Excalibur sport, Lode®, Netherlands). Immediately after each Maximal Sprint exercise bout blood samples (venous & arterial) will be drawn from antecubital vein and radial artery respectively, and before the next sprint, whilst two single 1Hz stimulation and two paired stimulation at 20Hz will be performed to asses muscle force and EMG signals (see section 9 for details of these procedures). Blood samples are performed at the end of exercise, 1, 2, 5, 10, 20 & 30 min and magnetic stimulations at end of exercise, 10 and 30min post exercise to measure fatigue and recovery. Following the experimental exercise, all instrumentation will be removed and a self-paced cool down will be performed. During the recovery period, you will be monitored, and allowed to leave following recovery.

Maximal Sprint Exercise
Maximal Sprint Exercise will be assessed 2min after the Two Leg Exercise to measure maximal sprint performance by performing two maximal 30 s sprints exercise bouts on a Velotron cycle ergometer (Dynafit Pro – RacerMate Cycle, Seattle, Washington). You will be familiarised with Maximal Sprint Exercise during Visit 2. You will perform each sprint bout at a comfortable saddle height, with feet secured to the pedals by toe clips. The participants will be verbally encouraged to produce their maximum effort during each bout. Power output will be determined from pedalling velocity samples at 83 Hz, with the peak power, cumulative work output, and fatigue index each calculated by a microcomputer. The fatigue index is defined as the relative decline in power output from the peak power attained in the first few pedal strokes to the final power at the end of the test and presented as a percentage. Blood (venous & arterial) samples will be drawn from the antecubital vein and radial artery respectively, before and after each exercise bout.

Visits 4-24: **Sprint Training Program**
Sprint training will be conducted in a laboratory under supervision 3 times per week over 7 weeks (Figure 3) and performed on a Velotron cycle ergometer (Dynafit Pro – RacerMate Cycle, Seattle, Washington). The sprint training protocol will commence 4 days after the Maximal Sprint Exercise and consists of twenty-one sessions spread over 7 weeks, with 2-3 days recovery between training sessions. You will be required to perform training on Mondays, Wednesdays and Fridays for 7 weeks. Sprint training consists of repeated 30 s **maximal cycling efforts**, interspersed with 4 min of recovery (rest or light cycling at 30 W). Training progression will be implemented by increasing the number of repeats from four bouts during week 1, six bouts during week 2, eight bouts during week 3 and finally to ten bouts during weeks 4-7.

Visit 25: **Two Leg Exercise**
Two Leg Cycle Exercise comprising the same methods and protocols previously described in Visit 3 will be performed.

Who is conducting the study?

Victoria University, College of Sport and Exercise Science, Institute of Sport, Exercise and Active Living

Professor Michael McKenna: (w) 9919 4499 (email) michael.mckenna@vu.edu.au
Dr Aaron Petersen: (w) 9919 9452 (email) aaron.petersen@vu.edu.au
Trevor Farr: (w) 9919 4066 (email) trevor.farr@vu.edu.au

Any queries about your participation in this project may be directed to the Principal Researcher listed above.
If you have any queries or complaints about the way you have been treated, you may contact the Ethics and Biosafety Coordinator, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 phone (03) 9919 4148.

Appendix L

CONSENT FORM FOR PARTICIPANTS INVOLVED IN RESEARCH
Chapter 5

INFORMATION TO PARTICIPANTS:

We would like to invite you to be a part of a **PhD project** into:

"**The effects of high intensity interval training on potassium concentration, muscle excitability and fatigue**".

As part of the informed consent process, participants have been provided with ***'Information to Participants Involved in Research Letter'*** *prior to obtaining consent.*

CERTIFICATION BY SUBJECT

I, ... of .....(suburb)

certify that I am at least 18 years old* and that I am voluntarily giving my consent to participate in the study:

The effects of potassium on muscle excitability and fatigue during high intensity exercise being conducted at Victoria University by: Prof Mike McKenna and Trevor Farr.

I certify that the objectives of the study, together with any risks and safeguards associated with the procedures listed hereunder to be carried out in the research, have been fully explained to me by: Trevor Farr and that I freely consent to participation involving the below mentioned procedures:

- **Graded exercise test ($\dot{V}O_{2peak}$)**
- ***Two Leg Cycle***
- ***Maximal Sprint Cycle & 21 training sessions over 7 weeks (3 times per week)***
- ***Maximal Voluntary Contraction***
- **Electromyography (EMG) recording**
- **Peripheral Magnetic Stimulation**
- **Maximal Voluntary Contraction**
- **Blood Sampling**
- **Muscle Biopsy**

I certify that I have had the opportunity to have any questions answered and that I understand that I can withdraw from this study at any time and that this withdrawal will not jeopardise me in any way. I also understand that I will be required to provide information regarding my personal health.

I have been informed that the information I provide will be kept confidential.

Signed: Date:

Any queries about your participation in this project may be directed to a researcher:

Professor Michael McKenna: (w) 9919 4499 (email) michael.mckenna@vu.edu.au

Dr Aaron Petersen: (w) 9919 9452 (email) aaron.petersen@vu.edu.au

Trevor Farr: (w) 9919 4066 (email) trevor.farr@vu.edu.au

If you have any queries or complaints about the way you have been treated, you may contact the Ethics & Biosafety Coordinator, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 phone (03) 9919

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

Appendix M
Individual Raw Data
Chapter 5

Table A 3.1 Pre-training plasma $[K^+]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group		Exercise							Recovery					
							Time (min)							
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	3.90	4.30	5.20	5.40	4.40	5.60	4.80	4.70	5.80	3.90	4.10	4.40	4.50	3.80
2	3.90	4.30	5.40	5.70	4.20	4.90	4.40	5.10	5.10	4.30	4.00	4.00	4.10	4.10
3	4.10	4.60	5.30	5.50	5.40	4.30	4.30	4.70	5.40	4.10	3.60	3.90	4.00	4.00
4	3.80	4.10	4.90	5.50	4.10	4.10	4.30	4.50	4.80	4.00	3.60	3.80	3.90	4.00
5	4.00	4.40	5.40	5.60	4.70	5.60	4.80		4.20	3.90	3.50	4.20	4.30	4.20
6	3.40	3.60	4.80	5.80	4.10	4.90		5.30	4.60	4.40	4.10	4.50	3.90	3.90
7	4.30	4.20	5.10	5.70	4.50	4.90	5.20		4.50	4.30	4.30	4.30	4.30	4.20
8	3.60	4.00	5.10	5.90	4.20	5.60	4.50	6.00	4.60	4.10	4.00	4.00	4.00	4.00
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	3.88	4.19	5.15	5.64	4.45	4.99	4.61	5.05	4.88	4.13	3.90	4.14	4.13	4.03
SD	0.28	0.30	0.22	0.17	0.44	0.59	0.33	0.55	0.53	0.19	0.29	0.25	0.22	0.14
Control Group														
1	3.90	4.10	3.90	6.30	5.00	6.10	5.40	5.00	4.80	4.80	4.80	4.90	4.90	4.80
2	3.90	4.10	5.40	5.30		4.50		4.50						
3	3.90	4.80	5.40	5.70	4.20	4.30	4.20	4.40	4.70	4.10	3.80	4.20	4.30	4.30
4	4.10	4.20	5.20	5.70	3.90	5.10	4.20	5.60	5.00	3.90	3.40	3.90	4.00	3.90
5	3.90	4.60	5.70	6.00	4.40	5.70		5.20	5.00	4.20	4.00	4.20	4.20	4.30
6	3.60	3.90	4.80	5.10	4.00	4.90	4.40	4.80	4.30	3.90	3.70	4.10	4.20	4.20
7	3.90	4.20	5.10	5.40	3.90	4.00	4.00	4.30	3.80	3.60	3.50	3.70	3.90	3.80
8	3.50	3.70	4.60	4.90	3.80	4.80	3.90	4.30	4.10	3.50	3.60	3.80	4.00	4.10
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	3.84	4.20	5.01	5.55	4.17	4.93	4.35	4.76	4.53	4.00	3.83	4.11	4.21	4.20
SD	0.19	0.35	0.57	0.47	0.42	0.70	0.54	0.47	0.47	0.43	0.47	0.40	0.33	0.33

Table A 3.2 Post-training plasma $[K^+]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group		Exercise						Recovery					
		Time (min)											
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	3.70	3.90	5.00	4.90	4.30	6.10	4.30	5.00	4.00	4.10	4.20	4.10	4.10	4.10
2	3.50	3.80	4.70	4.90	3.70	4.70	3.90	4.70	4.50	3.70	3.40	3.80	3.80	4.00
3	3.80	4.10	5.10	5.40	3.90	4.70	4.30	4.90	4.50	4.10	3.90	4.20	4.20	4.30
4	4.10	4.20	5.10	5.30	4.00	5.50	4.20	5.60	4.40	3.90	3.80	4.10	4.20	4.60
5	3.80	3.90	4.90	4.90	4.20	5.80	4.20	5.70	3.80	3.60	3.60	3.80	3.80	3.90
6	3.60	3.80	5.20	4.90	4.30	5.20	4.80	5.20	4.60	4.10	3.80	4.50	4.20	4.20
7	4.00	4.30	5.00	5.20	4.60	5.50	4.80	5.20	5.30	4.30	4.00	4.20	4.30	4.10
8	4.10	4.40	5.40	5.90	4.70	4.90	5.20	5.10	4.70	4.50	4.10	4.30	4.40	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	3.83	4.05	5.05	5.18	4.21	5.30	4.46	5.18	4.48	4.04	3.85	4.13	4.13	4.17
SD	0.23	0.23	0.21	0.36	0.34	0.52	0.43	0.34	0.45	0.30	0.26	0.24	0.22	0.23
Control Group														
1	3.80	4.00	4.90	5.50	4.20	4.80	4.80	5.20	5.10	4.20	4.00	4.00	4.30	4.20
2	3.90	4.20	5.10	5.70	1.60		4.50	4.30	3.30	3.40	3.40	3.80	3.50	3.80
3	4.20	4.30	5.10	5.30	3.80	5.40	3.70	4.70	4.10	3.80	3.40	3.70	3.70	3.40
4	3.90	3.80	4.70	5.40	3.70	4.70	5.60	5.10	5.10	4.00	3.50	4.20	4.10	4.10
5	4.10	4.10	5.40	5.70	4.10	5.40	4.30	5.70	4.80	4.10	3.80	4.30	4.10	4.40
6	3.90	4.20	5.40	5.30	4.30	5.00	4.60	4.70	4.80	4.30	4.20	4.30	4.30	4.30
7	4.20	4.40	4.50	4.30	4.20	5.50	4.20	5.70	4.30	3.70	3.40	4.20	4.30	4.30
8	3.80	4.30	4.90	5.10	4.00	5.20	4.20	4.50	4.40	3.90	4.00	4.60	4.60	4.50
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	3.98	4.16	5.00	5.29	3.74	5.14	4.49	4.99	4.49	3.93	3.71	4.14	4.11	4.13
SD	0.17	0.19	0.32	0.45	0.89	0.32	0.56	0.53	0.60	0.29	0.33	0.29	0.36	0.36

Table A 3.3 Pre-training plasma $[K^+]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Venous K^+ (mM)

Pre-Training

Training Group		Exercise							Recovery					
						Time (min)								
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	4.60	4.50	4.40	4.50	4.50	4.70	4.40	5.00	4.90	4.70	4.20	4.00	4.90	
2	3.80	4.30	4.60	4.90	4.20	4.30	4.90	4.60	4.40	4.10	4.00	4.00	4.20	4.30
3	3.90	3.60	4.10	4.40	3.50	4.60	3.80	4.50	4.30	3.90	3.50	3.70	4.00	3.90
4	3.90	3.70	3.90	4.10	3.70	4.20	3.90	4.10	4.40	3.70	3.50	3.90	4.00	4.00
5	3.90	4.20	4.50	4.60	4.40	4.60	4.70		4.30	4.10	4.00	4.10	4.20	4.20
6	3.40	3.50	4.00	4.60	3.80	4.20	4.10	4.20	4.40	4.20	3.80	3.90	3.60	3.90
7	4.00	4.20	4.70	4.70	5.30	6.30	8.30		6.90	6.50	5.50	4.40	4.90	4.40
8	3.50	3.80	4.30	4.90	4.00	4.70	4.30	4.80	4.40	4.00	4.10	4.10	4.10	4.00
n	8	8	8	8	8	8	8	6	8	8	8	8	8	7
Mean	3.88	3.98	4.31	4.59	4.18	4.70	4.80	4.53	4.75	4.40	4.08	4.01	4.24	4.10
SD	0.36	0.37	0.29	0.26	0.57	0.68	1.46	0.34	0.89	0.90	0.63	0.20	0.45	0.20

Control Group

1	3.60	4.30	4.70	4.60	4.00	6.00	3.80	4.20	3.60	3.60	4.30	4.50	4.40	4.30
2	4.00	4.50	5.40	4.40		4.50	5.00	4.20	4.10	3.70				
3	4.10	4.60	4.40	4.40	4.40	4.30		5.10	4.80	4.30	3.60	4.00	4.10	4.10
4	4.20	4.30	4.10	4.00	4.20	4.30	4.00	4.20	4.10	4.00	3.50	3.90	4.00	4.10
5	4.20	4.40	4.70	5.00	4.20	4.80		4.80	4.50	4.10	3.70	4.20	4.40	4.40
6	3.50	3.90	4.50	4.80	4.20	4.80	4.40	5.00	4.50	4.20	3.90	4.20	4.20	4.20
7	3.70	4.20	4.70	4.40	4.20	4.10	4.30	4.10	3.50	3.80	3.60	3.70	3.80	4.20
8	3.60	4.00	4.30	4.80	3.90	4.10	4.20	4.10	3.40	3.50	3.70	4.00	4.10	4.20
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	3.86	4.28	4.60	4.55	4.16	4.61	4.28	4.46	4.06	3.90	3.76	4.07	4.14	4.21
SD	0.29	0.24	0.39	0.32	0.16	0.62	0.41	0.43	0.52	0.29	0.27	0.26	0.21	0.11

Table A 3.4 Post-training plasma $[K^+]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group		Exercise						Recovery						
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	3.70	3.60	4.20	4.20	4.40	4.70	4.40	4.80	4.40	4.30	4.20	4.30	4.30	4.10
2	3.40	3.50	3.60	4.20	3.70	4.10	4.00	5.90	4.30	3.80	3.50	3.80	3.80	3.90
3	3.90	4.60	4.80	5.20	4.20	4.40	4.40	4.50	4.40	4.30	4.30	4.40	4.50	4.40
4	4.10	4.30	4.60	4.80	4.00	4.80	4.30	4.30	4.40	4.10	4.00	4.30	4.20	4.50
5	3.90	3.90	3.70	4.10	3.00	3.50	4.50	4.30	3.90	3.80	3.80	4.00	3.90	3.90
6	3.30	4.50	6.00	4.30	4.10	4.70	5.20	5.20	5.20	4.80	4.50	4.00	4.40	4.30
7	3.80	3.90	4.20	4.20	4.00	5.00	4.00	4.60	4.50	4.20	3.90	4.20	4.30	4.10
8	3.90	4.00	5.10	5.10	4.00	5.40	4.70	5.10	4.60	4.20	4.00	4.20	4.30	4.30
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	3.75	4.04	4.53	4.51	3.93	4.58	4.44	4.84	4.46	4.19	4.03	4.15	4.21	4.19
SD	0.27	0.40	0.79	0.45	0.42	0.58	0.39	0.54	0.36	0.32	0.31	0.20	0.24	0.22
Control Group														
1	3.90	3.80	4.20	4.40	4.20	4.40	4.50	4.40	4.80	4.20	4.10	4.10	4.30	4.20
2	4.20	4.60	4.60	5.10	4.10	4.30	4.30	4.20		3.90				
3	4.00	3.60	3.70	4.30	3.80	4.20	3.80	4.30	4.40	4.00	3.00	3.40	3.70	3.60
4	4.10	4.00	4.40	4.20	4.00	4.20	4.40	5.20	4.70	4.20	3.80	4.10	4.10	4.10
5	4.00	4.60	4.30	4.50	4.50	5.40	4.70	5.30	4.60	4.20	3.90	4.10	4.20	4.20
6	3.80	4.00	4.20	4.20	4.00	4.20	4.20	4.40	4.60	4.10	4.00	4.20	4.10	4.40
7	4.10	4.50	4.90	4.90	4.20	5.10	4.30	4.50	4.30	4.20	4.00	4.10	4.40	4.30
8	3.70	4.10	4.20	4.40	4.30	4.30	4.20	4.30	4.60	4.00	4.00	4.30	4.40	4.50
n	8	8	8	8	8	8	8	8	7	8	7	7	7	7
Mean	3.98	4.15	4.31	4.50	4.14	4.51	4.30	4.58	4.57	4.10	3.83	4.04	4.17	4.19
SD	0.17	0.38	0.35	0.33	0.21	0.47	0.26	0.43	0.17	0.12	0.38	0.29	0.24	0.29

Table A 3.5 Pre-training plasma $[K^+]_{a-v}$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group		Exercise							Recovery					
								Time (min)						
Subject	Rest	1	2	3	4	5	6	7	+1	+2	+5	+10	+20	+30
1	-0.70	-0.20	0.80	0.90	-0.10	0.90	0.40		0.90	-0.80	-0.10	0.40	-0.40	3.80
2	0.10	0.00	0.80	0.80	0.00	0.60	-0.50		0.70	0.20	0.00	0.00	-0.10	-0.20
3	0.20	1.00	1.20	1.10	1.90	-0.30	0.50		1.10	0.20	0.10	0.20	0.00	0.10
4	-0.10	0.40	1.00	1.40	0.40	-0.10	0.40		0.40	0.30	0.10	-0.10	-0.10	0.00
5	0.10	0.20	0.90	1.00	0.30	1.00	0.10		-0.10	-0.20	-0.50	0.10	0.10	0.00
6	0.00	0.10	0.80	1.20	0.30	0.70	-4.10		0.20	0.20	0.30	0.60	0.30	0.00
7	0.30	0.00	0.40	1.00	-0.80	-1.40	-3.10		-2.40	-2.20	-1.20	-0.10	-0.60	-0.20
8	0.10	0.20	0.80	1.00	0.20	0.90	0.20		0.20	0.10	-0.10	-0.10	-0.10	0.00
n	8	8	8	8	8	8	8		8	8	8	8	8	8
Mean	0.00	0.21	0.84	1.05	0.28	0.29	-0.76		0.13	-0.28	-0.18	0.13	-0.11	0.44
SD	0.31	0.36	0.23	0.19	0.76	0.83	1.80		1.10	0.86	0.47	0.26	0.28	1.36
	0.11	0.13	0.08	0.07	0.27	0.29	0.64		0.39	0.30	0.17	0.09	0.10	0.48
Control Group														
1	0.30	-0.20	-0.80	1.70	1.00	0.10	1.60			1.20	0.50	0.40	0.50	0.50
2	-0.10	-0.40	0.00	0.90	0.00	0.00	-5.00			-3.70	0.00	0.00	0.00	0.00
3	-0.20	0.20	1.00	1.30	-0.20	0.00	4.20			-0.20	0.20	0.20	0.20	0.20
4	-0.10	-0.10	1.10	1.70	-0.30	0.80	0.20			-0.10	-0.10	0.00	0.00	-0.20
5	-0.30	0.20	1.00	1.00	0.20	0.90	0.00			0.10	0.30	0.00	-0.20	-0.10
6	0.10	0.00	0.30	0.30	-0.20	0.10	0.00			-0.30	-0.20	-0.10	0.00	0.00
7	0.20	0.00	0.40	1.00	-0.30	-0.10	-0.30			-0.20	-0.10	0.00	0.10	-0.40
8	-0.10	-0.30	0.30	0.10	-0.10	0.70	-0.30			0.00	-0.10	-0.20	-0.10	-0.10
n	8	8	8	8	8	8	8		0	8	8	8	8	8
Mean	-0.03	-0.08	0.41	1.00	0.01	0.31	0.05		-0.49	-0.41	-0.32	-0.37	0.00	0.00
SD	0.21	0.22	0.64	0.58	0.43	0.41	2.55		1.34	1.14	1.18	1.22	1.83	1.83

Table A 3.6 Post-training plasma $[K^+]_{a-v}$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group		Exercise							Recovery					
						Time (min)								
Subject	**Rest**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.00	0.30	0.80	0.70	-0.10	1.40	-0.10		-0.40	-0.20	0.00	-0.20	-0.20	0.00
2	0.10	0.30	1.10	0.70	0.00	0.60	-0.10		0.20	-0.10	-0.10	0.00	0.00	0.10
3	-0.10	-0.50	0.30	0.20	-0.30	0.30	-0.10		0.10	-0.20	-0.40	-0.20	-0.30	-0.10
4	0.00	-0.10	0.50	0.50	0.00	0.70	-0.10		0.00	-0.20	-0.20	-0.20	0.00	0.10
5	-0.10	0.00	1.20	0.80	1.20	2.30	-0.30		-0.10	-0.20	-0.20	-0.20	-0.10	0.00
6	0.30	-0.70	-0.80	0.60	0.20	0.50	-0.40		-0.60	-0.70	-0.70	0.50	-0.20	-0.10
7	0.20	0.40	0.80	1.00	0.60	0.50	0.80		0.80	0.10	0.10	0.00	0.00	0.00
8	0.20	0.40	0.30	0.80	0.70	-0.50	0.50		0.10	0.30	0.10	0.10	0.10	-4.30
n	8	8	8	8	8	8	8		8	8	8	8	8	8
Mean	0.08	0.01	0.53	0.66	0.29	0.73	0.02		0.01	-0.15	-0.18	-0.03	-0.09	-0.54
SD	0.15	0.42	0.63	0.24	0.50	0.82	0.41		0.42	0.29	0.27	0.24	0.14	1.52
Control Group														
1	-0.10	0.20	0.70	1.10	0.00	0.40	0.30		0.30	0.00	-0.10	-0.10	0.00	0.00
2	-0.30	-0.40	0.50	0.60	-2.50	-4.30	0.20		3.30	-0.50	3.40	3.80	3.50	3.80
3	0.20	0.70	1.40	1.00	0.00	1.20	-0.10		-0.30	-0.20	0.40	0.30	0.00	-0.20
4	-0.20	-0.20	0.30	1.20	-0.30	0.50	1.20		0.40	-0.20	-0.30	0.10	0.00	0.00
5	0.10	-0.50	1.10	1.20	-0.40	0.00	-0.40		0.20	-0.10	-0.10	0.20	-0.10	0.20
6	0.10	0.20	1.20	1.10	0.30	0.80	0.40		0.20	0.20	0.20	0.10	0.20	-0.10
7	0.10	-0.10	-0.40	-0.60	0.00	0.40	-0.10		0.00	-0.50	-0.60	0.10	-0.10	0.00
8	0.10	0.20	0.70	0.70	-0.30	0.90	0.00		-0.20	-0.10	0.00	0.30	0.20	0.00
n	8	8	8	8	8	8	8		8	8	8	8	8	8
Mean	0.00	0.01	0.69	0.79	-0.40	-0.01	0.19		-0.49	-0.41	-0.32	-0.37	0.00	0.00
SD	0.18	0.39	0.57	0.60	0.88	1.77	0.48		1.34	1.14	1.18	1.22	1.83	1.83

Table A 3.7 Pre-training blood Hb_a ($g\text{-}dL^{-1}$) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	15.10	15.70	16.40	17.00	15.90	16.80	17.00	16.90	17.30	17.40	16.80	16.60	16.40	15.80
2	14.40	14.90	15.70	16.00	15.60	15.80	15.90	16.30	16.40	16.20	16.10	15.50	15.40	14.80
3	12.20	12.30	13.00	13.20	12.90	12.80	13.40	13.60	13.50	13.40	13.80	13.00	12.50	12.20
4	14.10	14.50	15.40	15.80	15.40	15.50	16.00	15.80	16.00	15.90	15.60	15.30	14.90	14.00
5	13.90	14.50	15.00	15.40	15.20	15.10	15.40		15.70	14.20	14.30	14.30	13.90	14.70
6	12.70	12.60	13.10	13.80	13.50	13.50		13.60	13.90	13.90	13.50	12.70	12.30	12.30
7	12.10	13.50	13.10	14.00	13.50	13.40	14.20		14.00	14.20	13.80	13.80	12.50	12.80
8	12.80	13.10	13.30	14.20	13.90	14.70	13.60	14.40	13.50	13.30	14.20	13.30	12.60	12.70
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	13.41	13.89	14.38	14.93	14.49	14.70	15.07	15.10	15.04	14.81	14.76	14.31	13.81	13.66
SD	1.11	1.20	1.39	1.31	1.16	1.37	1.36	1.43	1.49	1.50	1.23	1.37	1.59	1.35
Control Group														
1	14.40	14.60	14.30	15.60	15.70	15.70	15.30	15.40	15.70	14.80	15.20	14.90	14.30	14.20
2	13.60	14.00	14.80	14.80		14.90		14.80						
3	14.10	15.50	15.70	16.20	15.80	16.10	16.50	16.30	16.40	16.30	15.70	15.40	15.10	14.40
4	10.90	12.00	12.50	12.80	12.40	12.50	12.50	12.80	12.80	12.80	12.10	11.70	10.90	11.10
5	13.90	15.00	15.70	16.20	15.70	15.90		16.00	16.50	16.20	15.60	15.30	15.00	15.00
6	13.70	14.00	14.50	15.00	14.60	15.10	15.20	15.40	15.60	15.50	15.00	14.60	14.70	13.90
7	14.60	15.00	15.90	16.10	15.90	16.00	16.50	16.40	16.00	16.30	16.00	15.50	15.30	14.50
8	15.60	15.50	16.30	16.40	16.10	16.50	16.50	16.80	17.00	16.70	16.50	15.80	15.70	15.50
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	13.85	14.45	14.96	15.39	15.17	15.34	15.42	15.49	15.71	15.51	15.16	14.74	14.43	14.09
SD	1.35	1.15	1.22	1.20	1.31	1.26	1.55	1.26	1.37	1.35	1.44	1.40	1.62	1.42

Table A 3.8 Post-training blood Hb_a ($g\text{-}dL^{-1}$) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	15.70	16.20	16.40	15.80	16.30	17.20	16.60	17.20	17.00	16.80	16.40	15.90	15.30	15.90
2	13.90	14.30	14.90	15.10	14.70	15.20	14.90	15.50	15.50	15.30	14.90	14.60	14.40	14.40
3	11.80	12.30	12.70	13.10	12.70	12.90	13.10	13.40	13.20	13.20	12.80	12.10	11.60	11.70
4	14.30	14.80	15.40	15.60	15.50	16.00	15.40	16.20	15.70	15.60	15.10	15.20	14.00	13.80
5	14.40	14.40	15.40	15.30	15.40	15.70	15.80	16.30	16.10	15.90	15.50	15.20	14.30	14.30
6	12.70	12.60	13.40	13.30	12.90	13.50	14.00	14.00	13.90	13.80	13.20	13.30	12.50	12.40
7	14.30	14.80	15.60	15.90	15.70	15.70	16.20	16.40	16.50	16.00	16.20	15.40	14.80	14.60
8	11.90	12.60	13.10	13.20	13.10	13.10	13.10	13.30	13.50	14.70	13.70	12.80	11.80	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	13.63	14.00	14.61	14.66	14.54	14.91	14.89	15.29	15.18	15.16	14.73	14.31	13.59	13.87
SD	1.37	1.37	1.36	1.24	1.43	1.56	1.36	1.51	1.45	1.20	1.35	1.39	1.42	1.41

Control Group

1	15.80	16.10	16.70	17.10	17.00	17.30	17.30	17.90	17.70	17.90	17.50	16.80	16.30	16.20
2	13.00	13.50	13.90	14.50	13.30		13.30	14.30	14.50	14.10	14.00	14.00	13.40	12.40
3	14.10	15.50	15.70	16.20	15.80	16.10	16.50	16.30	16.40	16.30	15.70	15.40	15.10	14.40
4	11.60	12.10	12.60	12.80	13.10	13.70	12.60	13.20	13.50	13.10	13.90	12.90	11.60	11.90
5	14.50	14.10	15.20	15.60	15.20	15.70	15.70	16.10	16.10	16.00	14.90	15.30	14.10	14.50
6	13.90	14.20	14.70	15.00	14.60	14.90	14.90	15.10	15.30	15.00	14.80	14.70	14.00	13.80
7	14.60	15.30	15.50	15.50	15.50	15.70	16.10	16.60	16.60	16.40	15.70	15.60	15.00	14.40
8	15.60	16.30	17.00	17.30	16.80	16.60	16.70	17.00	17.50	17.00	17.10	16.40	16.60	16.50
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	14.14	14.64	15.16	15.50	15.16	15.71	15.39	15.81	15.95	15.73	15.45	15.14	14.51	14.26
SD	1.36	1.43	1.44	1.46	1.45	1.17	1.67	1.53	1.45	1.57	1.32	1.26	1.62	1.61

Table A 3.9 Pre-training blood Hb_v (g-dL^{-1}) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

	Rest	Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	15.30	15.70	15.70	16.30	15.60	16.20	15.60	16.60	16.50	16.70	16.00		16.20	
2	14.30	15.20	15.30	15.90	15.80	15.50	16.10	16.20	15.60	15.90	15.90	15.20	14.50	14.80
3	11.60	11.40	12.10	12.50	12.50	12.60	12.40	13.20	13.20	13.00	12.80	12.80	12.20	11.70
4	14.30	14.20	14.50	15.00	14.30	14.90	14.40	15.40	15.10	14.80	15.00	15.10	15.00	14.10
5	13.90	15.00	14.90	14.80	14.90	14.30	15.60		15.70	15.20	14.90	14.20	14.40	15.50
6	12.50	12.50	12.90	13.20	13.00	13.90	13.30	13.60	13.50	13.90	13.00	12.80	11.90	12.10
7	12.50	12.40	13.50	13.10	14.60	14.60	13.30		14.60	14.50	13.90	13.70	13.50	13.30
8	11.90	12.70	13.30	13.70	13.70	14.40	14.30	14.30	13.60	13.40	13.20	12.50	13.00	12.90
n	8	8	8	8	8	8	8	6	8	8	8	7	8	7
Mean	13.29	13.64	14.03	14.31	14.30	14.55	14.38	14.88	14.73	14.68	14.34	13.76	13.84	13.49
SD	1.34	1.58	1.26	1.39	1.18	1.07	1.32	1.40	1.20	1.25	1.29	1.12	1.46	1.39

Control Group

1	13.60	15.10	15.30	15.60	15.60	16.30	15.80	15.80	15.80	15.50	15.00	15.00	14.40	14.20
2	13.50	14.20	14.30	14.10		15.00	15.10	14.60	14.70	14.90				
3	14.40	15.30	14.80	14.90	15.10	14.50		15.80	16.20	15.90	14.60	15.10	14.80	14.50
4	10.90	12.10	11.60	11.60	12.30	12.00	12.30	11.90	13.00	12.40	12.40	11.80	10.80	11.60
5	14.10	14.30	14.80	15.30	15.10	15.00		15.80	15.10	14.90	14.40	15.20	14.90	15.00
6	13.60	14.40	14.60	14.80	15.00	15.10	15.00	15.20	15.20	15.30	15.00	14.30	13.90	13.30
7	13.80	15.10	15.30	15.40	15.70	15.30	15.80	15.20	14.40	15.30	15.70	15.30	15.00	14.80
8	15.80	15.90	16.00	15.80	16.00	15.70	16.40	16.40	15.50	15.80	16.60	16.50	15.80	15.80
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	13.71	14.55	14.59	14.69	14.97	14.86	15.07	15.09	14.99	15.00	14.81	14.74	14.23	14.17
SD	1.36	1.15	1.32	1.36	1.24	1.27	1.45	1.40	0.99	1.11	1.30	1.45	1.62	1.37

Table A 3.10 Post-training blood Hb_v ($g\text{-}dL^{-1}$) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	15.60	15.90	16.10	16.00	16.30	16.50	16.70	16.80	16.30	16.10	16.40	16.20	15.70	14.90
2	13.50	14.40	13.90	15.10	15.30	15.10	15.40	15.70	15.60	15.50	14.90	14.60	14.40	14.60
3	11.90	12.60	12.50	12.80	12.90	12.90	12.90	13.10	13.30	13.00	12.60	12.30	11.70	11.20
4	14.00	14.80	15.20	15.70	15.10	15.70	15.40	15.50	16.00	15.80	15.60	15.30	14.30	13.10
5	14.50	14.50	14.30	14.50	12.80	13.70	15.80	15.80	16.10	16.00	15.70	14.40	14.40	14.40
6	12.40	12.40	13.10	13.70	13.10	12.90	13.50	13.60	12.50	13.50	13.30	13.10	12.80	13.40
7	14.50	14.80	15.00	15.20	15.10	15.50	15.20	15.90	15.10	15.30	15.00	15.50	14.90	14.50
8	11.80	12.60	12.70	13.00	12.40	13.10	13.00	13.00	13.10	15.00	13.00	12.50	12.20	11.60
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	13.53	14.00	14.10	14.50	14.13	14.43	14.74	14.93	14.75	15.03	14.56	14.24	13.80	13.46
SD	1.38	1.30	1.29	1.21	1.48	1.44	1.41	1.46	1.54	1.16	1.41	1.45	1.40	1.42

Control Group

1	16.10	16.20	16.20	16.40	16.70	16.40	17.40	17.10	17.60	17.60	17.50	17.10	16.60	16.00
2	13.90	13.50	13.50	14.30	13.80	14.10	14.10	14.30		14.20				
3	11.10	10.90	11.70	12.10	12.80	12.80	12.80	12.50	12.50	12.40	12.80	12.50	12.00	10.90
4	12.00	12.80	12.40	13.10	13.20	12.70	12.70	13.30	13.50	12.70	12.10	11.80	11.20	12.10
5	14.40	14.80	15.00	15.20	15.70	15.60	15.80	16.00	15.90	15.90	15.30	14.80	14.60	14.10
6	14.00	14.50	13.90	13.80	13.90	14.80	14.10	14.70	14.70	14.70	13.70	14.00	13.80	14.10
7	14.70	16.00	15.80	15.70	14.80	15.80	15.50	15.90	16.20	16.00	15.30	15.20	14.60	14.70
8	15.60	16.30	16.00	16.60	16.50	16.60		16.30	16.70	17.10	16.90	16.40	16.20	16.20
n	8	8	8	8	8	8	7	8	7	8	7	7	7	7
Mean	13.98	14.38	14.31	14.65	14.68	14.85	14.63	15.01	15.30	15.08	14.80	14.54	14.14	14.01
SD	1.69	1.90	1.71	1.60	1.49	1.53	1.70	1.59	1.82	1.92	2.03	1.94	2.00	1.94

Table A 3.11 Pre-training blood Hct_a (%) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	46.40	48.10	50.30	52.00	48.60	51.50	52.00	51.70	52.80	53.10	51.50	50.70	50.30	48.40
2	44.30	45.80	48.20	49.00	47.70	48.30	48.60	49.90	50.20	49.50	49.40	47.50	47.10	45.20
3	37.60	38.00	39.90	40.70	39.60	39.50	41.30	41.60	41.50	41.30	42.30	40.10	38.40	37.50
4	43.20	44.40	47.20	48.40	47.10	47.40	48.90	48.50	48.80	48.80	47.70	46.70	45.70	42.90
5	42.60	44.50	46.00	47.20	46.50	46.40	47.20		47.90	43.50	44.00	44.00	42.80	45.00
6	39.00	38.70	40.10	42.40	41.60	41.50		41.70	42.80	42.70	41.40	39.00	37.80	37.90
7	37.20	41.50	40.30	43.10	41.40	41.30	43.40		43.00	43.70	42.30	42.40	38.40	39.50
8	39.40	40.30	40.80	43.60	42.70	45.10	41.90	44.20	41.50	41.00	43.50	40.90	38.70	39.10
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	41.21	42.66	44.10	45.80	44.40	45.13	46.19	46.27	46.06	45.45	45.26	43.91	42.40	41.94
SD	3.37	3.59	4.27	3.91	3.44	4.09	4.04	4.35	4.39	4.43	3.76	4.08	4.82	4.01

Control Group

1	44.10	44.80	43.90	47.80	48.10	48.00	46.90	47.00	48.20	45.50	46.60	45.60	43.90	43.70
2	41.80	43.10	45.50	45.20		45.60		45.40						
3	43.10	47.50	48.20	49.70	48.50	49.40	50.40	49.80	50.20	50.00	48.00	47.10	46.20	44.00
4	33.70	37.00	38.40	39.30	38.20	38.40	38.30	39.40	39.30	39.50	37.20	35.90	33.50	34.10
5	42.80	45.90	48.00	49.50	48.10	48.80		49.00	50.50	49.60	47.90	46.90	45.90	46.00
6	41.90	42.80	44.50	45.80	44.70	46.20	46.70	47.30	47.80	47.40	45.90	44.70	45.00	42.60
7	44.90	46.00	48.50	49.30	48.80	48.90	50.50	50.30	48.90	50.00	48.90	47.50	47.00	44.50
8	47.70	47.40	49.90	50.30	49.30	50.60	50.40	51.50	52.00	51.00	50.60	48.50	48.20	47.60
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	42.50	44.31	45.86	47.11	46.53	46.99	47.20	47.46	48.13	47.57	46.44	45.17	44.24	43.21
SD	4.04	3.43	3.68	3.67	3.97	3.84	4.71	3.81	4.15	4.02	4.35	4.27	4.93	4.34

Table A 3.12 Post-training blood Hct_a (%) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	48.20	49.60	50.30	48.50	50.00	52.50	50.70	52.70	51.80	51.40	50.30	48.60	46.80	48.80
2	42.60	43.80	45.70	46.40	45.10	46.60	45.70	47.40	47.50	46.90	45.60	44.80	44.00	44.10
3	36.40	37.80	39.10	40.20	39.20	39.80	40.20	41.10	40.60	40.70	39.40	37.20	35.80	36.20
4	43.90	45.40	47.20	47.90	47.40	49.10	47.30	49.70	48.10	47.80	46.40	46.50	42.80	42.40
5	44.00	44.10	47.10	47.00	47.20	48.00	48.50	49.70	49.20	48.80	47.30	46.60	43.80	43.90
6	38.90	38.80	41.10	40.80	39.60	41.50	42.90	43.00	42.80	42.30	40.70	40.90	38.60	38.10
7	43.80	45.40	47.90	48.60	48.00	48.20	49.60	50.20	50.60	49.00	49.50	47.10	45.50	44.90
8	36.70	38.70	40.20	40.60	40.20	40.30	40.40	40.70	41.60	45.00	42.10	39.50	36.20	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	41.81	42.95	44.83	45.00	44.59	45.75	45.66	46.81	46.53	46.49	45.16	43.90	41.69	42.63
SD	4.11	4.14	4.12	3.77	4.29	4.66	4.08	4.59	4.28	3.60	4.04	4.15	4.24	4.26

Control Group

1	48.50	49.30	51.00	52.30	52.00	52.90	52.80	54.70	54.00	54.80	53.40	51.40	50.00	49.50
2	40.00	41.50	42.70	44.60	40.10		40.80	43.90	44.50	43.30	42.80	42.90		38.00
3	45.20	46.50	48.50	49.00	46.50	49.10	48.70	50.50	49.70	49.60	45.60	49.90	46.20	44.60
4	35.60	37.20	38.80	39.40	40.20	41.90	38.80	40.60	41.60	40.40	42.60	39.70	35.80	36.60
5	44.50	43.10	46.50	47.90	46.70	48.20	48.10	49.30	49.40	48.90	45.80	46.80	43.40	44.30
6	42.70	43.50	45.10	46.00	44.80	45.70	45.60	46.40	46.80	45.90	45.30	45.00	42.90	42.30
7	44.80	46.80	47.60	47.40	47.40	48.10	49.20	50.70	50.90	50.30	48.20	47.80	46.00	44.30
8	47.60	49.90	51.80	52.80	51.50	50.90	51.20	52.10	53.50	52.00	52.20	50.30	50.60	50.60
n	8	8	8	8	8	7	8	8	8	8	8	8	7	8
Mean	43.61	44.73	46.50	47.43	46.15	48.11	46.90	48.53	48.80	48.15	46.99	46.73	44.99	43.78
SD	4.18	4.25	4.30	4.31	4.45	3.56	4.90	4.61	4.29	4.71	4.01	4.01	5.01	4.89

Table A 3.13 Pre-training blood Hct_v (%) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	46.80	48.10	48.20	49.90	47.80	49.50	47.80	50.70	50.30	51.00	49.00		49.60	
2	43.70	46.60	46.90	48.60	48.30	47.50	49.30	49.50	47.80	48.80	48.70	46.70	44.50	45.50
3	35.80	35.00	37.20	38.40	38.50	38.90	38.20	40.60	40.50	40.00	39.40	39.30	37.60	36.10
4	43.90	43.50	44.40	46.00	44.00	45.80	44.10	47.10	46.20	45.30	46.00	46.10	45.90	43.30
5	42.80	45.90	45.70	45.40	45.80	44.00	47.90		48.10	46.50	45.80	43.70	44.20	47.60
6	38.30	38.40	39.60	40.60	40.00	42.60	40.80	41.70	41.40	42.60	39.90	39.30	36.60	37.40
7	38.40	38.10	41.50	40.20	44.70	44.80	41.00		44.60	44.60	42.60	42.20	41.30	41.00
8	36.70	39.20	41.00	41.90	42.10	44.10	44.00	43.80	41.80	41.30	40.50	38.30	40.00	39.60
n	8	8	8	8	8	8	8	6	8	8	8	7	8	7
Mean	40.80	41.85	43.06	43.88	43.90	44.65	44.14	45.57	45.09	45.01	43.99	42.23	42.46	41.50
SD	4.00	4.79	3.83	4.20	3.51	3.18	3.97	4.17	3.60	3.73	3.90	3.41	4.40	4.21

Control Group

1	41.70	46.30	47.00	47.90	47.70	49.90	48.30	48.40	48.30	47.40	45.90	45.90	44.20	43.70
2	41.3	43.5	43.8	43.2		45.9	46.3	44.8	45.2	45.7				
3	44.2	46.7	45.3	45.6	46.4	44.6		48.2	49.5	48.6	44.6	46.1	45.3	44.3
4	33.5	37.2	35.8	35.7	37.9	36.9	37.8	36.6	39.9	38.2	38	36.3	33.4	35.8
5	43.2	43.8	45.3	47	46.2	45.9		48.4	46.2	45.8	44.1	46.7	45.7	45.9
6	41.6	44.2	44.8	45.3	46	46.2	46.1	46.5	46.6	46.8	45.9	44	42.6	40.7
7	42.5	46.2	46.8	47.1	47.9	47	48.4	46.6	44.3	46.9	48.1	46.8	46.1	45.4
8	48.3	48.8	48.8	48.5	49.1	48.2	50.2	50.1	47.3	48.4	50.9	50.4	48.3	48.3
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	42.04	44.59	44.70	45.04	45.89	45.58	46.18	46.20	45.91	45.98	45.36	45.17	43.66	43.44
SD	4.13	3.47	3.91	4.13	3.69	3.86	4.38	4.20	2.94	3.31	3.98	4.35	4.85	4.09

Table A 3.14 Post-training blood Hct_v (%) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	47.80	48.80	49.30	48.90	49.90	50.60	51.10	51.30	50.00	49.30	50.10	49.60	48.00	45.70
2	41.40	44.10	42.50	46.10	47.00	46.40	47.20	48.10	47.90	47.30	45.60	44.80	44.10	44.70
3	36.60	38.80	38.50	39.40	39.60	39.80	39.80	40.30	40.70	40.00	38.70	37.90	36.00	34.70
4	42.90	45.30	46.70	48.10	46.20	48.10	47.30	47.30	48.80	48.30	47.80	46.70	43.90	40.40
5	44.30	44.50	43.80	44.40	39.30	42.10	48.40	48.50	49.20	49.00	48.10	44.20	44.30	44.20
6	38.20	38.20	40.30	42.00	40.30	39.80	41.50	41.80	38.40	41.50	41.00	40.10	39.40	41.00
7	44.30	45.30	46.00	46.60	46.30	47.60	46.50	48.70	46.30	46.90	45.80	47.50	45.70	44.40
8	36.20	38.70	39.20	39.90	38.00	40.10	39.90	40.00	40.30	45.90	39.90	38.30	37.70	35.70
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	41.46	42.96	43.29	44.43	43.33	44.31	45.21	45.75	45.20	46.03	44.63	43.64	42.39	41.35
SD	4.15	3.91	3.87	3.64	4.49	4.35	4.24	4.36	4.64	3.46	4.23	4.40	4.19	4.22

Control Group

1	49.40	49.60	49.60	50.30	51.20	50.30	53.10	52.30	53.80	53.80	53.40	52.20	50.70	49.10
2	42.70	41.30	41.50	43.80	42.40	43.30	43.20	43.80		43.70				
3	44.90	44.30	44.50	47.80	45.10	48.00	45.60	48.70	49.50	50.10	44.00	47.10	45.50	44.80
4	36.90	39.30	38.20	40.30	40.60	39.10	39.00	40.70	41.40	39.00	37.40	36.50	34.50	37.10
5	44.10	45.50	46.10	46.60	48.00	47.80	48.50	49.00	48.70	48.70	46.90	45.50	44.80	43.30
6	43.00	44.40	42.80	42.40	42.70	45.40	43.30	45.00	45.10	45.00	42.20	42.90	42.50	43.30
7	45.00	49.10	48.40	48.00	45.20	48.30	47.50	48.80	49.60	48.90	47.00	46.60	44.80	45.20
8	47.90	50.00	48.90	50.80	50.40	50.90		49.80	51.00	52.20	51.70	50.30	49.50	49.50
n	8	8	8	8	8	8	7	8	7	8	7	7	7	7
Mean	44.24	45.44	45.00	46.25	45.70	46.64	45.74	47.26	48.44	47.68	46.09	45.87	44.61	44.61
SD	3.76	3.94	4.01	3.76	3.86	3.91	4.52	3.77	4.05	4.85	5.50	5.14	5.30	4.17

Table A 3.15 Pre-training plasma $[Na^+]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	140.0	138.0	140.0	141.0	138.0	141.0	143.0	142.0	146.0	143.0	143.0	141.0	139.0	116.0
2	142.0	142.0	145.0	146.0	141.0	143.0	145.0	146.0	149.0	147.0	144.0	143.0	142.0	142.0
3	141.0	138.0	141.0	143.0	137.0	139.0	144.0	146.0	149.0	146.0	144.0	143.0	140.0	140.0
4	139.0	139.0	142.0	143.0	139.0	140.0	145.0	144.0	146.0	144.0	142.0	140.0	139.0	140.0
5	137.0	139.0	142.0	141.0	138.0	141.0	141.0		142.0	141.0	139.0	138.0	138.0	138.0
6	140.0	139.0	144.0	146.0	140.0	142.0		143.0	142.0	140.0	139.0	137.0	139.0	139.0
7	138.0	138.0	139.0	141.0	138.0	140.0	140.0		144.0	142.0	139.0	136.0	137.0	136.0
8	141.0	140.0	145.0	147.0	143.0	148.0	146.0	149.0	146.0	145.0	143.0	140.0	141.0	140.0
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	139.75	139.13	142.25	143.50	139.25	141.75	143.43	145.00	145.50	143.50	141.63	139.75	139.38	136.38
SD	1.67	1.36	2.25	2.51	1.98	2.82	2.23	2.53	2.73	2.45	2.26	2.60	1.60	8.42

Control Group

1	146.0	139.0	142.0	142.0	142.0	143.0	142.0	140.0	141.0	140.0	139.0	138.0	137.0	137.0
2	138.0	138.0	141.0	143.0		141.0		142.0						
3	141.0	141.0	143.0	144.0	140.0	139.0	143.0	143.0	146.0	144.0	142.0	140.0	139.0	139.0
4	140.0	141.0	144.0	146.0	141.0	143.0	144.0	149.0	148.0	146.0	143.0	141.0	140.0	140.0
5	141.0	140.0	144.0	145.0	141.0	143.0		145.0	147.0	145.0	143.0	141.0	141.0	141.0
6	138.0	138.0	140.0	141.0	138.0	140.0	144.0	143.0	145.0	144.0	143.0	140.0	139.0	138.0
7	142.0	141.0	143.0	145.0	142.0	142.0	146.0	146.0	145.0	145.0	143.0	141.0	140.0	140.0
8	136.0	136.0	139.0	141.0	138.0	140.0	142.0	142.0	144.0	142.0	139.0	138.0	137.0	137.0
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	140.25	139.25	142.00	143.38	140.29	141.38	143.50	143.75	145.14	143.71	141.71	139.86	139.00	138.86
SD	3.06	1.83	1.85	1.92	1.70	1.60	1.52	2.82	2.27	2.06	1.89	1.35	1.53	1.57

Table A 3.16 Post-training plasma $[Na^+]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	140.0	139.0	141.0	141.0	139.0	143.0	142.0	142.0	141.0	140.0	140.0	140.0	140.0	140.0
2	139.0	139.0	140.0	141.0	138.0	142.0	143.0	144.0	145.0	143.0	141.0	141.0	141.0	142.0
3	140.0	139.0	141.0	143.0	139.0	140.0	142.0	142.0	143.0	142.0	140.0	139.0	139.0	139.0
4	138.0	138.0	140.0	141.0	137.0	143.0	141.0	146.0	143.0	142.0	140.0	139.0	138.0	138.0
5	137.0	138.0	140.0	140.0	138.0	144.0	141.0	144.0	142.0	139.0	139.0	137.0	137.0	138.0
6	141.0	143.0	144.0	142.0	139.0	141.0	143.0	143.0	144.0	142.0	141.0	141.0	139.0	139.0
7	137.0	137.0	140.0	140.0	137.0	138.0	142.0	143.0	145.0	144.0	140.0	138.0	136.0	136.0
8	141.0	139.0	143.0	143.0	139.0	140.0	144.0	143.0	144.0	141.0	140.0	140.0	140.0	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	139.13	139.00	141.13	141.38	138.25	141.38	142.25	143.38	143.38	141.63	140.13	139.38	138.75	138.86
SD	1.64	1.77	1.55	1.19	0.89	2.00	1.04	1.30	1.41	1.60	0.64	1.41	1.67	1.86

Control Group

1	142.0	142.0	145.0	148.0	146.0	147.0	148.0	148.0	148.0	147.0	146.0	143.0	141.0	141.0
2	140.0	140.0	144.0	147.0	147.0		147.0	147.0	146.0	144.0	143.0	140.0	140.0	140.0
3	138.0	139.0	142.0	143.0	138.0	143.0	144.0	145.0	145.0	144.0	142.0	140.0	139.0	140.0
4	139.0	140.0	143.0	145.0	140.0	142.0	148.0	147.0	147.0	145.0	143.0	141.0	140.0	139.0
5	139.0	139.0	142.0	144.0	140.0	144.0	144.0	146.0	146.0	144.0	142.0	140.0	140.0	140.0
6	138.0	136.0	138.0	139.0	137.0	137.0	142.0	141.0	143.0	142.0	141.0	138.0	136.0	137.0
7	140.0	141.0	140.0	139.0	139.0	140.0	144.0	146.0	146.0	144.0	141.0	139.0	138.0	138.0
8	139.0	138.0	141.0	142.0	139.0	140.0	142.0	142.0	144.0	142.0	139.0	139.0	138.0	138.0
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	139.38	139.38	141.88	143.38	140.75	141.86	144.88	145.25	145.63	144.00	142.13	140.00	139.00	139.13
SD	1.30	1.85	2.23	3.34	3.69	3.24	2.47	2.49	1.60	1.60	2.03	1.51	1.60	1.36

Table A 3.17 Pre-training plasma $[Na^+]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise						Recovery					
		Time (min)											
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	139.0	140.0	141.0	141.0	141.0	141.0	142.0	141.0	144.0	143.0	144.0	124.0	140.0	
2	142.0	143.0	143.0	144.0	143.0	143.0	145.0	145.0	146.0	146.0	145.0	144.0	143.0	142.0
3	141.0	140.0	140.0	141.0	141.0	141.0	144.0	144.0	146.0	146.0	144.0	143.0	141.0	141.0
4	138.0	138.0	139.0	140.0	140.0	140.0	143.0	142.0	144.0	143.0	142.0	140.0	139.0	140.0
5	139.0	140.0	140.0	141.0	139.0	140.0	142.0		142.0	141.0	140.0	139.0	136.0	138.0
6	140.0	140.0	141.0	142.0	142.0	141.0	142.0	141.0	142.0	141.0	140.0	139.0	141.0	140.0
7	138.0	138.0	138.0	138.0	140.0	139.0	136.0		140.0	141.0	138.0	137.0	136.0	137.0
8	140.0	141.0	142.0	143.0	143.0	145.0	145.0	146.0	146.0	145.0	144.0	143.0	141.0	140.0
n	8	8	8	8	8	8	8	6	8	8	8	8	8	7
Mean	139.63	140.00	140.50	141.25	141.13	141.25	142.38	143.17	143.75	143.25	142.13	138.63	139.63	139.71
SD	1.41	1.60	1.60	1.83	1.46	1.91	2.88	2.14	2.25	2.19	2.53	6.39	2.50	1.70

Control Group

1	142.0	141.0	141.0	141.0	141.0	142.0	142.0	143.0	142.0	142.0	141.0	140.0	139.0	139.0
2	139.0	139.0	138.0	141.0		140.0	140.0	142.0	141.0	141.0				
3	141.0	141.0	140.0	141.0	140.0	141.0		144.0	144.0	144.0	142.0	140.0	139.0	140.0
4	140.0	141.0	141.0	142.0	141.0	141.0	144.0	144.0	145.0	145.0	143.0	141.0	141.0	141.0
5	141.0	142.0	142.0	144.0	143.0	142.0		143.0	144.0	145.0	144.0	142.0	141.0	141.0
6	139.0	139.0	139.0	139.0	139.0	140.0	143.0	141.0	144.0	144.0	143.0	141.0	139.0	139.0
7	142.0	142.0	142.0	142.0	143.0	143.0	144.0	144.0	144.0	145.0	145.0	142.0	141.0	141.0
8	137.0	137.0	137.0	138.0	140.0	139.0	142.0	140.0	143.0	142.0	140.0	139.0	138.0	138.0
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	140.13	140.25	140.00	141.00	141.00	141.00	142.50	142.63	143.38	143.50	142.57	140.71	139.71	139.86
SD	1.73	1.75	1.85	1.85	1.53	1.31	1.52	1.51	1.30	1.60	1.72	1.11	1.25	1.21

Table A 3.18 Post-training plasma $[Na^+]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	141.0	140.0	140.0	141.0	140.0	140.0	142.0	143.0	142.0	142.0	142.0	141.0	141.0	141.0
2	139.0	140.0	139.0	140.0	140.0	142.0	144.0	143.0	145.0	145.0	143.0	142.0	142.0	142.0
3	140.0	140.0	140.0	141.0	140.0	142.0	141.0	142.0	143.0	142.0	141.0	140.0	140.0	140.0
4	138.0	138.0	138.0	139.0	138.0	140.0	141.0	139.0	143.0	141.0	140.0	139.0	139.0	139.0
5	137.0	138.0	139.0	139.0	141.0	139.0	138.0	139.0	141.0	140.0	139.0	137.0	138.0	139.0
6	141.0	139.0	140.0	129.0	140.0	139.0	141.0	140.0	142.0	141.0	139.0	140.0	139.0	140.0
7	138.0	139.0	140.0	140.0	140.0	139.0	141.0	142.0	141.0	141.0	140.0	138.0	137.0	137.0
8	140.0	141.0	141.0	142.0	142.0	142.0	144.0	142.0	144.0	142.0	140.0	141.0	140.0	140.0
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	139.25	139.38	139.63	138.88	140.13	140.38	141.50	141.25	142.63	141.75	140.50	139.75	139.50	139.75
SD	1.49	1.06	0.92	4.12	1.13	1.41	1.93	1.67	1.41	1.49	1.41	1.67	1.60	1.49

Control Group

1	143.0	143.0	143.0	143.0	145.0	146.0	148.0	146.0	148.0	147.0	146.0	144.0	142.0	142.0
2	140.0	140.0	141.0	143.0	142.0	141.0	144.0	142.0		144.0				
3	139.0	140.0	141.0	141.0	139.0	141.0	144.0	142.0	144.0	145.0	144.0	141.0	140.0	140.0
4	139.0	140.0	140.0	141.0	141.0	142.0	145.0	144.0	147.0	146.0	144.0	140.0	140.0	140.0
5	140.0	140.0	141.0	141.0	143.0	142.0	143.0	143.0	146.0	146.0	144.0	141.0	140.0	141.0
6	137.0	138.0	137.0	137.0	138.0	137.0	141.0	140.0	141.0	140.0	140.0	139.0	138.0	137.0
7	141.0	142.0	140.0	141.0	140.0	141.0	141.0	141.0	142.0	142.0	142.0	139.0	139.0	139.0
8	139.0	139.0	142.0	142.0	139.0	140.0	141.0	142.0	144.0	142.0	141.0	140.0	138.0	138.0
n	8	8	8	8	8	8	8	8	7	8	7	7	7	7
Mean	139.75	140.25	140.63	141.13	140.88	141.25	143.38	142.50	144.57	144.00	143.00	140.57	139.57	139.57
SD	1.75	1.58	1.77	1.89	2.36	2.49	2.45	1.85	2.57	2.45	2.08	1.72	1.40	1.72

Table A 3.19 Pre-training plasma $[Ca^{2+}]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.14	1.14	1.2	1.21	1.17	1.19	1.22	1.21	1.26	1.16	1.23	1.21	1.19	0.84
2	1.21	1.23	1.27	1.27	1.22	1.23	1.25	1.27	1.31	1.28	1.26	1.25	1.23	1.23
3	1.23	1.15	1.23	1.25	1.14	1.16	1.26	1.3	1.35	1.31	1.31	1.29	1.24	1.21
4	1.16	1.19	1.22	1.24	1.2	1.24	1.29	1.27	1.29	1.28	1.26	1.25	1.22	1.25
5	1.15	1.2	1.25	1.23	1.18	1.21	1.22		1.24	1.23	1.15	1.2	1.2	1.17
6	1.17	1.13	1.21	1.26	1.19	1.18		1.21	1.23	1.19	1.16	1.15	1.13	1.12
7	1.16	1.12	1.18	1.22	1.17	1.21	1.19		1.25	1.25	1.24	1.22	1.22	1.19
8	1.19	1.17	1.25	1.28	1.24	1.26	1.28	1.3	1.27	1.26	1.25	1.21	1.24	1.22
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	1.18	1.17	1.23	1.25	1.19	1.21	1.24	1.26	1.28	1.25	1.23	1.22	1.21	1.15
SD	0.03	0.04	0.03	0.02	0.03	0.03	0.04	0.04	0.04	0.05	0.05	0.04	0.04	0.13

Control Group

1	1.23	1.20	1.30	1.30	1.27	1.29	1.25	1.27	1.30	1.28	1.27	1.26	1.25	1.24
2	1.17	1.16	1.23	1.23		1.22		1.25						
3	1.23	1.25	1.30	1.32	1.25	1.23	1.28	1.30	1.36	1.33	1.29	1.28	1.25	1.25
4	1.25	1.30	1.32	1.25	1.25	1.28								
5	1.17	1.20	1.26	1.27	1.22	1.22		1.23	1.26	1.23	1.22	1.20	1.20	1.18
6	1.16	1.17	1.21	1.24	1.18	1.24	1.28	1.28	1.29	1.27	1.25	1.24	1.22	1.23
7	1.24	1.24	1.28	1.30	1.25	1.25	1.30	1.29	1.30	1.30	1.28	1.24	1.24	1.23
8	1.17	1.20	1.23	1.20	1.20	1.21	1.23	1.23	1.25	1.22	1.22	1.19	1.18	1.20
n	8	8	8	8	7	8	5	7	6	6	6	6	6	6
Mean	1.20	1.22	1.27	1.26	1.23	1.24	1.27	1.26	1.29	1.27	1.26	1.24	1.22	1.22
SD	0.04	0.05	0.04	0.04	0.03	0.03	0.03	0.03	0.04	0.04	0.03	0.03	0.03	0.03

Table A 3.20 Post-training plasma $[Ca^{2+}]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.18	1.15	1.22	1.19	1.18	1.25	1.22	1.25	1.21	1.20	1.21	1.19	1.19	1.19
2	1.17	1.17	1.21	1.22	1.15	1.23	1.22	1.25	1.28	1.26	1.22	1.19	1.19	1.17
3	1.19	1.18	1.23	1.24	1.19	1.20	1.26	1.27	1.29	1.28	1.25	1.20	1.18	1.19
4	1.22	1.23	1.24	1.25	1.21	1.28	1.24	1.32	1.27	1.26	1.22	1.24	1.22	1.24
5	1.21	1.20	1.24	1.22	1.20	1.24	1.25	1.27	1.25	1.23	1.27	1.25	1.19	1.21
6	1.20	1.22	1.22	1.24	1.18	1.21	1.26	1.26	1.28	1.27	1.21	1.30	1.20	1.17
7	1.23	1.24	1.27	1.27	1.23	1.19	1.29	1.29	1.34	1.32	1.29	1.24	1.22	1.22
8	1.20	1.21	1.23	1.22	1.17	1.16	1.29	1.22	1.24	1.23	1.21	1.21	1.20	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	1.20	1.20	1.23	1.23	1.19	1.22	1.25	1.27	1.27	1.26	1.24	1.23	1.20	1.20
SD	0.02	0.03	0.02	0.02	0.02	0.04	0.03	0.03	0.04	0.04	0.03	0.04	0.01	0.03

Control Group

1	1.25	1.25	1.28	1.28	1.30	1.32	1.30	1.31	1.33	1.31	1.29	1.26	1.24	1.24
2	1.21	1.21	1.24	1.31	1.26		1.21	1.34	1.30	1.29	1.26	1.24	1.19	1.22
3	1.21	1.20	1.25	1.26	1.19	1.27	1.21	1.28	1.27	1.27	1.21	1.22	1.19	1.16
4	1.16	1.16	1.22	1.27	1.21	1.20	1.31	1.33	1.35	1.29	1.25	1.26	1.22	1.20
5	1.19	1.17	1.24	1.27	1.20	1.24	1.26	1.28	1.31	1.29	1.22	1.22	1.19	1.21
6	1.19	1.16	1.19	1.22	1.20	1.18	1.25	1.25	1.29	1.26	1.27	1.25	1.23	1.24
7	1.20	1.21	1.19	1.17	1.17	1.20	1.24	1.29	1.31	1.28	1.22	1.22	1.20	1.22
8	1.23	1.23	1.30	1.31	1.27	1.27	1.28	1.30	1.30	1.29	1.29	1.28	1.27	1.27
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	1.20	1.19	1.23	1.26	1.21	1.23	1.25	1.30	1.30	1.28	1.25	1.24	1.21	1.22
SD	0.02	0.03	0.04	0.05	0.04	0.04	0.04	0.03	0.02	0.01	0.03	0.02	0.03	0.03

Table A 3.21 Pre-training plasma $[Ca^{2+}]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.17	1.14	1.16	1.20	1.21	1.25	1.23	1.30	1.28	1.29	1.23	0.92	1.22	
2	1.20	1.23	1.23	1.27	1.24	1.22	1.26	1.27	1.26	1.26	1.27	1.25	1.23	1.23
3	1.18	1.11	1.16	1.20	1.16	1.20	1.25	1.31	1.31	1.30	1.25	1.23	1.21	1.18
4	1.19	1.15	1.14	1.16	1.13	1.22	1.18	1.24	1.25	1.20	1.22	1.24	1.24	1.25
5	1.17	1.21	1.22	1.22	1.18	1.22	1.24		1.25	1.23	1.23	1.18	1.15	1.19
6	1.13	1.12	1.17	1.16	1.16	1.17	1.18	1.17	1.20	1.19	1.14	1.13	1.07	1.11
7	1.15	1.15	1.20	1.16	1.20	1.23	1.07		1.22	1.23	1.18	1.22	1.20	1.19
8	1.17	1.21	1.22	1.27	1.21	1.28	1.27	1.29	1.27	1.22	1.27	1.26	1.25	1.20
n	8	8	8	8	8	8	8	6	8	8	8	8	8	7
Mean	1.17	1.17	1.19	1.21	1.19	1.22	1.21	1.26	1.26	1.24	1.22	1.18	1.20	1.19
SD	0.02	0.05	0.03	0.05	0.04	0.03	0.07	0.05	0.03	0.04	0.04	0.11	0.06	0.04

Control Group

1	1.20	1.27	1.32	1.30	1.27	1.33	1.29	1.29	1.28	1.27	1.27	1.26	1.22	1.23
2	1.17	1.18	1.15	1.16		1.19	1.21	1.22	1.22	1.24				
3	1.26	1.25	1.18	1.19	1.21	1.17		1.33	1.34	1.32	1.23	1.24	1.21	1.17
4	1.22	1.21	1.18	1.18	1.21	1.19	1.26	1.26	1.25	1.27	1.26	1.23	1.19	1.19
5	1.20	1.17	1.16	1.21	1.17	1.17		1.22	1.18	1.17	1.12	1.19	1.20	1.19
6	1.14	1.20	1.21	1.23	1.21	1.24	1.27	1.24	1.26	1.28	1.25	1.25	1.23	1.22
7	1.20	1.25	1.25	1.25	1.25	1.24	1.27	1.25	1.19	1.26	1.28	1.25	1.23	1.25
8	1.19	1.21	1.21	1.2	1.2	1.18	1.23	1.21	1.16	1.18	1.24	1.23	1.22	1.22
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	1.20	1.22	1.21	1.22	1.22	1.21	1.26	1.25	1.24	1.25	1.24	1.24	1.21	1.21
SD	0.03	0.04	0.06	0.04	0.03	0.05	0.03	0.04	0.06	0.05	0.05	0.02	0.02	0.03

Table A 3.22 Post-training plasma $[Ca^{2+}]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.17	1.15	1.20	1.18	1.19	1.22	1.19	1.26	1.21	1.21	1.21	1.19	1.19	1.18
2	1.16	1.18	1.15	1.19	1.19	1.23	1.25	1.22	1.27	1.26	1.22	1.21	1.18	1.19
3	1.19	1.22	1.24	1.23	1.24	1.28	1.26	1.27	1.28	1.28	1.26	1.24	1.22	1.18
4	1.21	1.23	1.22	1.26	1.20	1.26	1.26	1.25	1.29	1.27	1.25	1.26	1.21	1.22
5	1.19	1.18	1.13	1.16	1.01	1.08	1.27	1.23	1.26	1.25	1.28	1.24	1.22	1.21
6	1.17	1.10	1.16	0.93	1.21	1.19	1.24	1.22	1.23	1.23	1.21	1.22	1.19	1.15
7	1.26	1.26	1.24	1.24	1.23	1.22	1.24	1.33	1.26	1.25	1.25	1.26	1.23	1.21
8	1.21	1.21	1.24	1.24	1.18	1.22	1.27	1.24	1.26	1.22	1.22	1.23	1.20	1.21
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	1.20	1.19	1.20	1.18	1.18	1.21	1.25	1.25	1.26	1.25	1.24	1.23	1.21	1.19
SD	0.03	0.05	0.04	0.11	0.07	0.06	0.03	0.04	0.03	0.02	0.03	0.02	0.02	0.02

Control Group

1	1.25	1.23	1.25	1.23	1.26	1.31	1.33	1.31	1.33	1.32	1.31	1.31	1.28	1.27
2	1.23	1.24	1.26	1.28	1.25	1.25	1.29	1.27		1.29				
3	1.20	1.11	1.11	1.18	1.16	1.22	1.16	1.25	1.27	1.28	1.12	1.16	1.18	1.16
4	1.19	1.20	1.22	1.20	1.20	1.25	1.28	1.28	1.34	1.29	1.29	1.22	1.21	1.19
5	1.21	1.23	1.22	1.21	1.27	1.25	1.28	1.28	1.32	1.32	1.25	1.22	1.21	1.19
6	1.18	1.19	1.17	1.15	1.16	1.18	1.22	1.23	1.25	1.21	1.20	1.27	1.20	1.22
7	1.21	1.23	1.24	1.22	1.16	1.25	1.25	1.27	1.27	1.27	1.24	1.24	1.24	1.23
8	1.23	1.26	1.27	1.27	1.27	1.24	1.27	1.28	1.29	1.27	1.27	1.27	1.25	1.25
n	8	8	8	8	8	8	8	8	7	8	7	7	7	7
Mean	1.21	1.21	1.21	1.22	1.21	1.23	1.25	1.27	1.29	1.28	1.23	1.23	1.22	1.21
SD	0.02	0.05	0.06	0.05	0.05	0.03	0.05	0.02	0.03	0.03	0.06	0.04	0.03	0.03

Table A 3.23 Pre-training plasma $[Cl^-]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	108.0	109.0	110.0	110.0	109.0	112.0	112.0	111.0	116.0	115.0	109.0	109.0	108.0	107.0
2	106.0	107.0	110.0	111.0	108.0	110.0	111.0	111.0	112.0	110.0	108.0	107.0	108.0	107.0
3	103.0	104.0	107.0	109.0	105.0	107.0	109.0	109.0	110.0	108.0	107.0	104.0	105.0	105.0
4	107.0	108.0	111.0	113.0	109.0	107.0	111.0	111.0	112.0	110.0	108.0	107.0	107.0	106.0
5	107.0	108.0	109.0	110.0	108.0	112.0	112.0		111.0	110.0	112.0	108.0	112.0	109.0
6	107.0	109.0	111.0	111.0	108.0	111.0		112.0	110.0	109.0	109.0	109.0	109.0	108.0
7	106.0	108.0	110.0	110.0	109.0	109.0	109.0		109.0	108.0	107.0	107.0	107.0	109.0
8	107.0	108.0	111.0	114.0	110.0	116.0	111.0	115.0	112.0	111.0	110.0	109.0	107.0	108.0
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	106.38	107.63	109.88	111.00	108.25	110.50	110.71	111.50	111.50	110.13	108.75	107.50	107.88	107.38
SD	1.51	1.60	1.36	1.69	1.49	2.98	1.25	1.97	2.14	2.23	1.67	1.69	2.03	1.41

Control Group

1	111.0	107.0	109.0	112.0	111.0	113.0	112.0	108.0	108.0	107.0	106.0	106.0	106.0	106.0
2	106.0	107.0	111.0	113.0		113.0		113.0						
3	107.0	107.0	110.0	111.0	107.0	108.0	111.0	109.0	110.0	108.0	107.0	106.0	107.0	106.0
4	107.0	107.0	110.0	112.0	108.0	112.0	112.0	114.0	113.0	111.0	109.0	108.0	108.0	108.0
5	107.0	106.0	108.0	110.0	106.0	110.0		110.0	111.0	109.0	108.0	107.0	106.0	107.0
6	108.0	108.0	111.0	111.0	110.0	109.0	112.0	111.0	113.0	112.0	109.0	108.0	108.0	107.0
7	105.0	106.0	109.0	111.0	108.0	108.0	111.0	111.0	112.0	110.0	107.0	107.0	106.0	107.0
8	108.0	106.0	109.0	111.0	107.0	109.0	110.0	110.0	112.0	110.0	107.0	107.0	108.0	107.0
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	107.38	106.75	109.63	111.38	108.14	110.25	111.33	110.75	111.29	109.57	107.57	107.00	107.00	106.86
SD	1.77	0.71	1.06	0.92	1.77	2.12	0.82	1.98	1.80	1.72	1.13	0.82	1.00	0.69

Table A 3.24 Post-training plasma $[Cl^-]_a$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	105.0	107.0	107.0	109.0	107.0	111.0	109.0	110.0	108.0	106.0	106.0	106.0	106.0	106.0
2	108.0	109.0	112.0	114.0	111.0	111.0	111.0	112.0	112.0	110.0	109.0	109.0	108.0	107.0
3	106.0	106.0	110.0	111.0	107.0	109.0	107.0	108.0	108.0	107.0	105.0	106.0	106.0	106.0
4	105.0	105.0	108.0	110.0	106.0	112.0	108.0	113.0	109.0	109.0	108.0	106.0	106.0	105.0
5	103.0	104.0	105.0	106.0	104.0	112.0	106.0	111.0	106.0	106.0	104.0	103.0	122.0	104.0
6	107.0	105.0	111.0	110.0	108.0	111.0	113.0	113.0	111.0	108.0	109.0	106.0	107.0	107.0
7	101.0	101.0	103.0	105.0	103.0	105.0	106.0	105.0	108.0	107.0	105.0	104.0	103.0	103.0
8	108.0	108.0	111.0	112.0	109.0	110.0	111.0	112.0	112.0	110.0	110.0	108.0	108.0	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	105.38	105.63	108.38	109.63	106.88	110.13	108.88	110.50	109.25	107.88	107.00	106.00	108.25	105.43
SD	2.45	2.50	3.20	2.97	2.59	2.30	2.59	2.78	2.19	1.64	2.27	1.93	5.78	1.51

Control Group

1	105.0	106.0	111.0	114.0	119.0	109.0	113.0	113.0	113.0	111.0	110.0	109.0	107.0	107.0
2	106.0	106.0	110.0	112.0	131.0		115.0	111.0	109.0	109.0	109.0	108.0	107.0	107.0
3	106.0	107.0	110.0	112.0	109.0	110.0	112.0	110.0	112.0	109.0	110.0	109.0	109.0	111.0
4	109.0	110.0	113.0	116.0	111.0	115.0	115.0	114.0	114.0	112.0	112.0	107.0	108.0	108.0
5	106.0	108.0	110.0	112.0	109.0	109.0	108.0	112.0	110.0	108.0	108.0	106.0	106.0	106.0
6	104.0	105.0	108.0	109.0	108.0	109.0	109.0	108.0	110.0	108.0	106.0	106.0	105.0	104.0
7	107.0	108.0	108.0	110.0	109.0	112.0	114.0	116.0	113.0	112.0	111.0	110.0	109.0	108.0
8	104.0	105.0	107.0	108.0	105.0	108.0	109.0	108.0	109.0	108.0	105.0	105.0	105.0	105.0
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	105.88	106.88	109.63	111.63	112.63	110.29	111.88	111.50	111.25	109.63	108.88	107.50	107.00	107.00
SD	1.64	1.73	1.92	2.62	8.45	2.43	2.85	2.83	1.98	1.77	2.42	1.77	1.60	2.14

Table A 3.25 Pre-training plasma $[Cl^-]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	107.0	113.0	111.0	112.0	110.0	109.0	111.0	107.0	111.0	111.0	113.0	110.0	108.0	
2	106.0	106.0	106.0	106.0	107.0	109.0	108.0	108.0	109.0	110.0	108.0	108.0	107.0	107.0
3	105.0	108.0	107.0	107.0	109.0	107.0	107.0	105.0	107.0	109.0	108.0	107.0	107.0	107.0
4	105.0	109.0	111.0	112.0	113.0	107.0	112.0	110.0	111.0	112.0	110.0	107.0	107.0	106.0
5	107.0	106.0	106.0	108.0	109.0	108.0	110.0		110.0	109.0	108.0	109.0	111.0	109.0
6	108.0	109.0	107.0	110.0	110.0	110.0	111.0	111.0	111.0	111.0	111.0	111.0	112.0	109.0
7	108.0	107.0	106.0	109.0	112.0	106.0	108.0		107.0	105.0	110.0	107.0	108.0	109.0
8	108.0	107.0	108.0	109.0	111.0	110.0	110.0	110.0	111.0	113.0	110.0	107.0	107.0	108.0
n	8	8	8	8	8	8	8	6	8	8	8	8	8	7
Mean	106.75	108.13	107.75	109.13	110.13	108.25	109.63	108.50	109.63	110.00	109.75	108.25	108.38	107.86
SD	1.28	2.30	2.12	2.17	1.89	1.49	1.77	2.26	1.77	2.45	1.75	1.58	2.00	1.21

Control Group

1	109.0	106.0	105.0	106.0	107.0	107.0	107.0	107.0	108.0	108.0	107.0	106.0	107.0	109.0
2	106.0	106.0	108.0	110.0		109.0	108.0	109.0	110.0	108.0				
3	105.0	105.0	109.0	110.0	108.0	111.0		106.0	107.0	108.0	110.0	108.0	109.0	109.0
4	105.0	106.0	108.0	110.0	108.0	110.0	109.0	109.0	113.0	111.0	110.0	108.0	108.0	108.0
5	105.0	107.0	107.0	107.0	107.0	108.0		107.0	110.0	111.0	112.0	107.0	106.0	106.0
6	109.0	107.0	107.0	108.0	108.0	106.0	110.0	108.0	111.0	110.0	109.0	108.0	108.0	108.0
7	106.0	104.0	106.0	106.0	107.0	107.0	107.0	109.0	113.0	110.0	108.0	108.0	107.0	106.0
8	106.0	104.0	104.0	107.0	108.0	108.0	108.0	107.0	112.0	111.0	107.0	106.0	106.0	106.0
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	106.38	105.63	106.75	108.00	107.57	108.25	108.17	107.75	110.50	109.63	109.00	107.29	107.29	107.43
SD	1.69	1.19	1.67	1.77	0.53	1.67	1.17	1.16	2.20	1.41	1.83	0.95	1.11	1.40

Table A 3.26 Post-training plasma $[Cl^-]_v$ (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	105.0	106.0	104.0	105.0	105.0	104.0	108.0	106.0	107.0	106.0	107.0	106.0	106.0	106.0
2	108.0	109.0	111.0	110.0	110.0	108.0	110.0	111.0	111.0	110.0	109.0	108.0	108.0	107.0
3	106.0	104.0	106.0	106.0	106.0	104.0	105.0	105.0	105.0	105.0	105.0	105.0	104.0	105.0
4	106.0	105.0	106.0	106.0	108.0	108.0	108.0	106.0	109.0	108.0	107.0	105.0	107.0	106.0
5	103.0	104.0	108.0	107.0	114.0	110.0	105.0	105.0	106.0	106.0	106.0	103.0	104.0	107.0
6	107.0	109.0	105.0	107.0	109.0	108.0	109.0	109.0	110.0	110.0	108.0	108.0	108.0	108.0
7	101.0	100.0	103.0	103.0	103.0	103.0	105.0	101.0	105.0	106.0	106.0	104.0	103.0	104.0
8	106.0	107.0	108.0	109.0	111.0	110.0	110.0	110.0	112.0	111.0	109.0	108.0	109.0	109.0
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	105.25	105.50	106.38	106.63	108.25	106.88	107.50	106.63	108.13	107.75	107.13	105.88	106.13	106.50
SD	2.25	2.98	2.56	2.20	3.54	2.80	2.20	3.25	2.75	2.31	1.46	1.96	2.23	1.60

Control Group

1	105.0	106.0	107.0	110.0	109.0	107.0	110.0	109.0	111.0	111.0	109.0	108.0	107.0	106.0
2	104.0	105.0	105.0	108.0	108.0	107.0	109.0	108.0		109.0				
3	106.0	110.0	111.0	110.0	110.0	106.0	112.0	108.0	111.0	109.0	115.0	112.0	109.0	109.0
4	107.0	107.0	109.0	111.0	111.0	108.0	110.0	110.0	111.0	112.0	109.0	110.0	109.0	109.0
5	105.0	104.0	105.0	106.0	105.0	105.0	105.0	106.0	107.0	106.0	107.0	106.0	105.0	107.0
6	104.0	103.0	107.0	109.0	109.0	107.0	109.0	106.0	107.0	109.0	109.0	105.0	106.0	105.0
7	106.0	105.0	106.0	107.0	109.0	107.0	108.0	108.0	107.0	108.0	109.0	109.0	108.0	108.0
8	105.0	105.0	108.0	107.0	106.0	107.0	110.0	107.0	111.0	108.0	107.0	106.0	106.0	106.0
n	8	8	8	8	8	8	8	8	7	8	7	7	7	7
Mean	105.25	105.63	107.25	108.50	108.38	106.75	109.13	107.75	109.29	109.00	109.29	108.00	107.14	107.14
SD	1.04	2.13	2.05	1.77	2.00	0.89	2.03	1.39	2.14	1.85	2.69	2.52	1.57	1.57

Table A 3.27 Pre-training plasma pH_a at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.41	7.44	7.38	7.35	7.34	7.40	7.26	7.27	7.22	7.18	7.18	7.19	7.25	7.33
2	7.42	7.42	7.37	7.34	7.34	7.37	7.26	7.29	7.19	7.19	7.17	7.20	7.29	7.34
3	7.40	7.45	7.36	7.32	7.33	7.37	7.20	7.19	7.14	7.16	7.13	7.16	7.23	7.33
4	7.40	7.42	7.37	7.34	7.32	7.30	7.21	7.23	7.17	7.17	7.16	7.16	7.26	7.32
5	7.40	7.38	7.35	7.34	7.35	7.34	7.29		7.21	7.20	7.22	7.26	7.32	7.36
6	7.43	7.43	7.36	7.29	7.29	7.34		7.27	7.22	7.23	7.23	7.28	7.36	7.38
7	7.41	7.44	7.39	7.36	7.33	7.31	7.37		7.24	7.22	7.23	7.25	7.32	7.33
8	7.41	7.45	7.33	7.27	7.26	7.27	7.21	7.19	7.17	7.17	7.15	7.15	7.24	7.29
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	7.41	7.43	7.36	7.33	7.32	7.34	7.26	7.24	7.19	7.19	7.18	7.21	7.28	7.34
SD	0.01	0.02	0.02	0.03	0.03	0.04	0.06	0.04	0.03	0.03	0.04	0.05	0.05	0.03

Control Group

1	7.41	7.41	7.41	7.31	7.26	7.33	7.26	7.31	7.24	7.26	7.25	7.29	7.34	7.38
2	7.44	7.45	7.37	7.27		7.28		7.22						
3	7.37	7.43	7.35	7.32	7.31	7.32	7.24	7.25	7.20	7.18	7.17	7.19	7.27	7.32
4	7.42	7.43	7.35	7.29	7.31	7.38	7.20	7.22	7.11	7.13	7.10	7.15	7.29	7.34
5	7.39	7.40	7.34	7.31	7.31	7.37		7.30	7.23	7.22	7.21	7.23	7.30	7.35
6	7.41	7.43	7.34	7.33	7.34	7.35	7.22	7.24	7.20	7.18	7.15	7.16	7.21	7.23
7	7.33	7.26	7.17	7.14	7.16	7.17	7.24	7.21	7.31	7.27	7.30	7.35	7.39	7.39
8	7.36	7.34	7.23	7.22	7.21	7.23	7.28	7.26	7.37	7.31	7.35	7.36	7.39	7.37
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	7.39	7.05	6.99	6.96	6.93	6.97	6.78	6.75	6.86	6.85	6.85	6.87	6.93	6.97
SD	0.03	1.71	1.70	1.69	1.73	1.69	1.79	1.75	1.71	1.71	1.71	1.71	1.73	1.74

Table A 3.28 Post-training plasma pH_a at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**3**	**4**	**5**	**6**	**7**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.43	7.49	7.40	7.39	7.38	7.41	7.28	7.30	7.28	7.30	7.35	7.38	7.38	7.34
2	7.42	7.45	7.38	7.35	7.37	7.39	7.25	7.29	7.20	7.19	7.21	7.27	7.35	7.41
3	7.39	7.42	7.35	7.31	7.30	7.34	7.22	7.23	7.15	7.14	7.13	7.21	7.32	7.37
4	7.41	7.43	7.37	7.34	7.34	7.29	7.26	7.24	7.20	7.19	7.21	7.25	7.32	7.38
5	7.39	7.39	7.37	7.36	7.37	7.36	7.22	7.27	7.18	7.18	7.16	7.24	7.31	7.34
6	7.40	7.41	7.36	7.30	7.32	7.32	7.17	7.22	7.23	7.23	7.25	7.27	7.29	7.33
7	7.44	7.43	7.40	7.37	7.37	7.45	7.26	7.31	7.19	7.17	7.12	7.14	7.24	7.32
8	7.39	7.39	7.35	7.32	7.33	7.37	7.16	7.24	7.15	7.17	7.17	7.22	7.32	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	7.41	7.43	7.37	7.34	7.35	7.37	7.23	7.26	7.20	7.19	7.20	7.25	7.32	7.35
SD	0.02	0.03	0.02	0.03	0.03	0.05	0.05	0.03	0.04	0.05	0.07	0.07	0.04	0.03

Control Group

1	7.41	7.42	7.37	7.34	7.32	7.33	7.29	7.29	7.27	7.25	7.27	7.25	7.29	7.34
2	7.45	7.44	7.38	7.28	7.33		7.20	7.13	7.13	7.13	7.13	7.20	7.32	7.36
3	7.37	7.40	7.33	7.32	7.30	7.30	7.21	7.22	7.19	7.17	7.16	7.16	7.22	7.30
4	7.41	7.42	7.33	7.26	7.25	7.30	7.17	7.10	7.10	7.08	7.08	7.13	7.23	7.32
5	7.38	7.39	7.32	7.27	7.27	7.33	7.23	7.28	7.21	7.19	7.19	7.23	7.31	7.35
6	7.37	7.41	7.36	7.34	7.32	7.37	7.27	7.26	7.23	7.22	7.18	7.18	7.12	7.14
7	7.39	7.39	7.38	7.40	7.39	7.41	7.25	7.22	7.18	7.17	7.16	7.20	7.30	7.33
8	7.39	7.43	7.38	7.35	7.34	7.38	7.25	7.25	7.20	7.19	7.19	7.23	7.32	7.36
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	7.40	7.41	7.36	7.32	7.31	7.34	7.23	7.22	7.19	7.17	7.17	7.20	7.26	7.31
SD	0.03	0.02	0.02	0.05	0.04	0.04	0.04	0.07	0.05	0.05	0.05	0.04	0.07	0.07

Table A 3.29 Pre-training plasma pH_v at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.36	7.37	7.37	7.36	7.33	7.32	7.30	7.30	7.25	7.23	7.19	7.20	7.24	
2	7.40	7.38	7.35	7.31	7.30	7.31	7.26	7.26	7.24	7.20	7.17	7.21	7.29	7.33
3	7.36	7.36	7.34	7.28	7.28	7.29	7.15	7.18	7.16	7.16	7.15	7.12	7.23	7.32
4	7.36	7.39	7.38	7.34	7.30	7.30	7.25	7.23	7.21	7.18	7.16	7.19	7.26	7.31
5	7.35	7.34	7.32	7.31	7.31	7.30		7.25	7.21	7.20	7.20	7.26	7.31	7.33
6	7.44	7.40	7.39	7.33	7.30	7.30	7.26	7.26	7.23	7.23	7.23	7.26	7.33	7.35
7	7.38	7.39	7.36	7.33	7.33	7.30	7.30		7.25	7.23	7.25	7.24	7.31	7.31
8	7.40	7.39	7.34	7.28	7.27	7.20	7.20	7.17	7.16	7.16	7.14	7.14	7.23	7.29
n	8	8	8	8	8	8	7	7	8	8	8	8	8	7
Mean	7.38	7.38	7.36	7.32	7.30	7.29	7.24	7.23	7.21	7.20	7.19	7.20	7.27	7.32
SD	0.03	0.02	0.02	0.03	0.02	0.04	0.05	0.05	0.04	0.03	0.04	0.05	0.04	0.02

Control Group

1	7.39	7.35	7.30	7.27	7.27	7.28	7.19	7.20	7.21	7.23	7.23	7.26	7.32	7.34
2	7.42	7.39	7.36	7.28		7.22	7.21	7.20	7.20	7.18				
3	7.34	7.35	7.34	7.33	7.30	7.29		7.21	7.21	7.20	7.19	7.20	7.26	7.30
4	7.40	7.37	7.35	7.31	7.29	7.30	7.19	7.20	7.14	7.13	7.09	7.16	7.28	7.33
5	7.34	7.32	7.31	7.26	7.28	7.28		7.25	7.24	7.22	7.21	7.21	7.29	7.33
6	7.37	7.39	7.35	7.32	7.32	7.32	7.25	7.25	7.22	7.19	7.16	7.17	7.21	7.22
7	7.35	7.33	7.32	7.30	7.26	7.27	7.22	7.22	7.20	7.18	7.15	7.16	7.26	7.31
8	7.37	7.34	7.34	7.31	7.29	7.30	7.26	7.26	7.23	7.22	7.19	7.23	7.30	7.33
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	7.37	7.36	7.33	7.30	7.29	7.28	7.22	7.22	7.20	7.19	7.17	7.20	7.27	7.31
SD	0.03	0.03	0.02	0.03	0.02	0.03	0.03	0.03	0.03	0.03	0.05	0.04	0.04	0.04

Table A 3.30 Post-training plasma pH_v at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	7.40	7.39	7.39	7.37	7.36	7.36	7.30	7.28	7.27	7.28	7.29	7.33	7.35	7.37
2	7.38	7.39	7.39	7.36	7.34	7.34	7.26	7.27	7.21	7.19	7.20	7.27	7.35	7.38
3	7.36	7.35	7.30	7.27	7.25	7.25	7.23	7.21	7.17	7.16	7.16	7.19	7.29	7.34
4	7.38	7.38	7.35	7.31	7.32	7.31	7.26	7.26	7.20	7.20	7.21	7.24	7.33	7.37
5	7.39	7.38	7.36	7.34	7.33	7.33	7.27	7.26	7.19	7.18	7.17	7.18	7.30	7.33
6	7.37	7.39	7.37	7.30	7.25	7.30	7.25	7.26	7.24	7.22	7.23	7.32	7.33	7.35
7	7.38	7.37	7.33	7.30	7.33	7.33	7.28	7.26	7.23	7.21	7.18	7.16	7.25	7.30
8	7.33	7.34	7.30	7.25	7.23	7.27	7.14	7.19	7.14	7.15	7.17	7.22	7.31	7.31
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	7.37	7.37	7.35	7.31	7.30	7.31	7.25	7.25	7.21	7.20	7.20	7.24	7.31	7.34
SD	0.02	0.02	0.04	0.04	0.05	0.04	0.05	0.03	0.04	0.04	0.04	0.06	0.04	0.03

Control Group

1	7.40	7.39	7.38	7.36	7.33	7.31	7.29	7.29	7.27	7.26	7.24	7.24	7.28	7.33
2	7.39	7.38	7.36	7.28	7.26	7.27	7.19	7.20						
3	7.33	7.36	7.34	7.32	7.29	7.28	7.23	7.23	7.21	7.16	7.16	7.16	7.22	7.27
4	7.38	7.37	7.31	7.27	7.26	7.24	7.16	7.17	7.05	7.07	7.08	7.13	7.23	7.31
5	7.34	7.34	7.33	7.30	7.27	7.29	7.23	7.25	7.18	7.17	7.18	7.20	7.31	7.33
6	7.37	7.35	7.33	7.33	7.31	7.30	7.27	7.26	7.25	7.26	7.22	7.20	7.16	7.13
7	7.32	7.32	7.31	7.30	7.31	7.30	7.24	7.23	7.22	7.21	7.19	7.19	7.25	7.28
8	7.38	7.41	7.27	7.31	7.32	7.30	7.24	7.23	7.21	7.20	7.19	7.21	7.32	7.37
n	8	8	8	8	8	8	8	8	7	7	7	7	7	7
Mean	7.36	7.36	7.33	7.31	7.29	7.29	7.23	7.23	7.20	7.19	7.18	7.19	7.25	7.29
SD	0.03	0.03	0.03	0.03	0.03	0.02	0.04	0.04	0.07	0.06	0.05	0.04	0.06	0.08

Table A 3.31 Pre-training plasma Lac^-_a (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.90	0.90	2.90	4.30	5.20	5.00	11.00	11.60	13.40	14.00	16.00	14.40	11.70	8.50
2	0.60	0.60	4.00	7.20	6.40	6.00	13.80	14.40	19.00	19.00	18.00	16.00	10.80	7.00
3	1.00	0.80	4.20	6.60	6.20	5.20	11.50	11.90	12.70	13.20	11.70	12.10	9.30	6.60
4	0.60	0.60	3.90	7.90	9.20	9.30	14.80	15.00	17.00	17.00	16.00	16.00	10.50	7.70
5	1.00	0.90	2.90	3.80	3.30	3.80	6.40		7.50	7.50	7.20	6.40	4.90	3.90
6	1.20	1.00	3.70	5.50	5.60	5.60		6.80	7.00	7.30	6.00	6.80	4.80	4.40
7	1.30	1.30	3.30	6.00	6.60	8.20	8.80		12.70	13.50	12.90	11.40	7.90	5.10
8	0.60	0.90	5.10	10.10	10.20	12.10	16.00	17.00	17.00	17.00	16.00	15.00	11.90	8.60
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	0.90	0.88	3.75	6.43	6.59	6.90	11.76	12.78	13.29	13.56	12.98	12.26	8.98	6.48
SD	0.28	0.23	0.73	2.03	2.20	2.75	3.40	3.56	4.37	4.30	4.41	3.87	2.85	1.82

Control Group

1	0.40	0.60	0.80	6.80	12.20	9.40	11.90	8.90	12.10	12.10	11.70	10.00	6.90	5.00
2	0.90	1.00	6.40	11.90		12.30		15.00						
3	0.90	0.60	3.10	5.70	6.90	6.50	11.60	11.30	12.60	13.10	13.10	11.80	8.60	6.00
4	0.40	0.80	4.50	8.30	8.00	6.70	14.30	16.00	19.00	17.00	17.00	14.90	11.20	7.90
5	0.70	0.70	3.40	5.20	5.70	5.40		10.40	13.10	13.30	14.80	13.00	8.60	5.80
6	0.40	0.40	2.30	4.10	4.10	4.30	11.30	12.00	13.10	13.90	15.00	13.40	11.00	8.40
7	0.90	0.90	3.70	7.80	10.40	9.40	15.00	15.00	18.00	18.00	18.00	15.00	11.10	6.30
8	1.60	1.60	3.30	5.00	5.60	5.50	8.30	8.40	9.10	9.70	9.40	8.20	5.50	3.70
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	0.78	0.83	3.44	6.85	7.56	7.44	12.07	12.13	13.86	13.87	14.14	12.33	8.99	6.16
SD	0.41	0.37	1.62	2.49	2.87	2.69	2.39	2.92	3.47	2.84	2.99	2.52	2.24	1.61

Table A 3.32 Post-training plasma Lac^-_a (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.60	0.70	2.30	3.60	3.80	5.70	11.90	12.50	11.70	11.10	9.70	6.60	4.40	3.30
2	0.70	0.90	3.40	5.40	4.90	5.30	12.60	13.10	17.00	17.00	14.90	11.10	6.60	4.10
3	0.90	0.60	3.90	7.50	7.30	6.70	12.70	13.70	17.00	17.00	16.00	11.70	6.40	4.10
4	0.90	1.00	4.00	7.20	8.40	9.80	13.30	14.50	17.00	17.00	14.80	12.90	7.20	4.30
5	0.50	0.40	1.90	2.70	3.10	6.00	11.20	14.40	16.00	16.00	14.60	11.60	8.30	5.80
6	0.50	0.50	3.40	6.80	4.80	4.60	8.60	11.30	14.20	14.30	12.70	10.60	6.70	5.10
7	0.80	0.80	2.80	4.50	4.70	4.60	14.50	14.70	20.00	20.00	19.00	17.00	12.30	8.50
8	1.30	1.30	4.10	5.90	5.50	5.10	9.40	9.30	10.00	9.90	9.30	8.50	6.00	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	0.78	0.78	3.23	5.45	5.31	5.98	11.78	12.94	15.36	15.29	13.88	11.25	7.24	5.03
SD	0.27	0.29	0.82	1.74	1.75	1.70	1.98	1.87	3.24	3.36	3.23	3.06	2.32	1.73

Control Group

1	1.20	1.20	4.20	8.70	10.60	12.10	14.90	16.00	17.00	17.00	17.00	16.00	13.00	10.00
2	1.20	1.10	6.80	13.80	4.20		19.00	23.00	22.00	22.00	21.00	19.00	13.20	8.90
3	0.70	0.60	3.60	5.80	6.40	6.80	12.20	12.80	14.40	16.00	15.00	13.80	9.80	7.30
4	0.90	1.40	5.40	9.70	9.70	10.10	16.00	18.00	18.00	17.00	16.00	15.00	12.30	8.40
5	0.80	0.60	3.60	6.90	7.70	7.70	12.20	13.10	14.40	15.00	13.70	12.10	7.40	4.80
6	0.70	0.80	2.50	3.90	4.20	4.00	6.90	7.10	7.20	7.40	7.30	7.10	6.40	5.40
7	0.80	0.90	1.20	1.20	1.30	2.10	9.10	10.00	10.70	10.80	10.90	9.60	7.20	4.80
8	1.70	0.90	3.90	6.20	6.60	5.80	13.50	13.70	16.00	16.00	16.00	13.30	8.10	4.80
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	1.00	0.94	3.90	7.03	6.34	6.94	12.98	14.21	14.96	15.15	14.61	13.24	9.68	6.80
SD	0.35	0.28	1.70	3.81	3.07	3.43	3.83	4.88	4.52	4.38	4.12	3.71	2.80	2.12

Table A 3.33 Pre-training plasma Lac^-_v (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	1.50	1.00	0.70	1.70	2.10	2.80	3.90	4.00	6.20	7.70	9.90	13.40	10.70	
2	0.90	0.90	1.60	3.20	5.30	4.30	8.70	8.20	8.80	13.20	17.00	13.40	9.80	6.70
3	1.20	0.90	1.90	3.60	4.60	4.70	7.70	8.20	9.50	11.00	10.40	11.10	8.40	6.30
4	0.80	0.70	1.20	3.30	6.20	5.10	7.80	10.20	11.00	12.50	13.40	13.80	10.40	7.90
5	1.10	1.20	1.80	2.50	2.70	2.80	5.20		6.90	7.00	7.00	6.50	5.30	4.10
6	1.30	1.20	1.50	3.30	4.20	4.30	5.20	5.80	6.60	6.80	6.70	6.10	5.30	4.40
7	1.40	1.50	1.90	2.90	2.90	5.60	4.30		9.00	9.60	9.80	10.80	7.40	6.10
8	0.70	0.90	2.50	5.30	6.70	8.70	11.40	12.30	12.80	12.30	13.30	15.00	12.50	9.50
n	8	8	8	8	8	8	8	6	8	8	8	8	8	7
Mean	1.11	1.04	1.64	3.23	4.34	4.79	6.78	8.12	8.85	10.01	10.94	11.26	8.73	6.43
SD	0.29	0.25	0.53	1.03	1.68	1.87	2.57	2.97	2.29	2.60	3.47	3.36	2.60	1.89

Control Group

1	0.60	0.90	1.80	3.40	5.60	5.50	7.40	7.70	9.10	8.70	8.40	8.10	5.70	4.80
2	0.90	1.40	2.80	5.50		10.90	12.20	10.20	12.30	13.80				
3	0.90	0.90	1.10	2.30	3.80	4.00		6.90	8.10	8.80	9.80	9.30	7.70	5.60
4	0.70	1.20	1.50	2.70	4.20	4.60	8.90	9.00	11.50	14.80	16.00	14.50	9.60	7.60
5	1.00	1.00	1.30	3.00	3.30	3.60		5.10	5.80	8.30	10.10	11.50	8.20	5.80
6	0.60	0.60	1.50	2.50	3.50	3.20	7.40	6.90	9.10	12.10	12.80	11.50	10.00	8.00
7	0.90	0.90	1.60	2.50	4.20	4.40	6.30	6.50	7.90	9.40	13.60	14.50	10.40	6.40
8	1.50	1.50	1.80	2.60	3.50	3.30	5.10	4.60	7.10	7.30	8.90	8.20	5.80	4.00
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	0.89	1.05	1.68	3.06	4.01	4.94	7.88	7.11	8.86	10.40	11.37	11.09	8.20	6.03
SD	0.29	0.30	0.51	1.04	0.78	2.53	2.47	1.86	2.17	2.78	2.81	2.71	1.93	1.43

Table A 3.34 Post-training plasma Lac^-_v (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	0.80	0.90	1.20	1.50	2.30	2.30	4.60	7.10	7.80	7.10	8.10	6.40	4.60	3.80
2	0.90	1.10	1.30	2.70	3.50	3.80	9.00	9.20	13.00	14.50	14.10	10.60	6.10	4.40
3	1.00	0.80	2.60	3.60	5.10	5.10	6.20	7.00	9.10	8.70	9.70	9.50	6.60	4.60
4	0.90	0.90	1.80	4.20	6.50	6.30	10.50	8.80	14.90	12.80	14.90	11.80	7.00	4.50
5	0.60	0.50	0.80	1.40	1.70	1.60	4.60	5.30	13.10	12.40	12.70	10.50	5.70	6.70
6	0.70	0.90	1.00	2.20	3.60	3.60	6.90	6.70	9.40	10.90	11.30	9.40	7.20	5.30
7	0.80	0.80	1.50	3.00	3.10	2.90	5.20	6.30	7.40	8.40	12.40	13.50	10.60	7.20
8	1.40	1.30	2.60	4.00	4.50	4.80	7.30	7.90	8.30	8.80	8.80	7.90	5.50	4.00
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	0.89	0.90	1.60	2.83	3.79	3.80	6.79	7.29	10.38	10.45	11.50	9.95	6.66	5.06
SD	0.24	0.23	0.69	1.08	1.55	1.55	2.12	1.29	2.86	2.60	2.47	2.21	1.80	1.25

Control Group

1	1.20	1.40	1.80	3.90	5.60	6.90	11.60	10.00	13.90	16.00	16.00	16.00	12.30	10.10
2	1.50	1.50	2.60	7.80	10.50	10.90	14.10	14.10		15.00				
3	0.90	0.60	1.00	2.90	5.30	4.20	8.00	7.70	10.70	14.20	11.50	12.00	10.00	6.50
4	1.20	1.70	3.00	4.20	6.90	6.30	10.40	9.60	13.00	14.40	16.00	14.10	11.50	8.10
5	0.90	0.80	0.90	1.80	5.10	4.10	5.60	6.50	8.90	10.40	12.50	12.50	7.60	4.60
6	0.80	0.90	1.50	2.30	3.40	3.20	4.90	4.50	5.10	5.00	5.00	6.00	5.70	4.60
7	0.90	1.10	1.20	1.40	1.30	1.50	3.00	3.70	4.20	4.70	5.50	8.20	5.80	4.50
8	1.70	1.00	3.90	4.50	6.00	4.80	10.20	9.20	14.00	14.50	15.00	12.40	8.20	5.00
n	8	8	8	8	8	8	8	8	7	8	7	7	7	7
Mean	1.14	1.13	1.99	3.60	5.51	5.24	8.48	8.16	9.97	11.78	11.64	11.60	8.73	6.20
SD	0.32	0.38	1.08	2.04	2.66	2.84	3.77	3.34	4.07	4.57	4.69	3.42	2.63	2.17

Table A 3.35 Pre-training plasma Glu_a (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise							Recovery					
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	5.8	6.4	6.6	6.7	6.4	6.4	6.6	6.6	6.8	6.7	6.9	6.9	7.3	7.3
2	5.1	5.1	5.1	5.0	4.7	4.7	4.9	5.4	5.5	5.9	6.0	5.7	5.5	5.2
3	5.6	5.8	5.9	5.6	5.7	5.6	5.7	6.5	6.4	6.9	7.0	6.7	5.9	5.0
4	4.5	4.5	4.8	4.8	4.7	4.8	5.1	5.2	5.3	5.6	5.5	5.3	5.0	4.6
5	6.1	5.4	5.5	5.3	5.0	4.7	5.2		5.3	5.3	5.0	5.3	5.0	5.1
6	6.3	6.1	6.0	5.8	5.5	5.5		5.5	5.5	5.6	4.5	5.1	4.6	4.7
7	5.4	4.9	5.3	5.3	5.0	5.0	5.3		5.7	5.9	5.5	5.4	5.0	4.6
8	5.3	5.1	5.2	5.2	5.4	5.6	6.1	6.4	6.5	6.6	6.6	6.2	5.8	5.5
n	8	8	8	8	8	8	7	6	8	8	8	8	8	8
Mean	5.51	5.41	5.55	5.46	5.30	5.29	5.56	5.93	5.88	6.06	5.88	5.83	5.51	5.25
SD	0.57	0.64	0.58	0.59	0.58	0.60	0.61	0.63	0.60	0.59	0.91	0.69	0.85	0.89

Control Group

1	5.7	6.2	6.2	6.7	6.6	6.6	6.5	6.4	6.7	6.7	6.6	6.6	6.6	6.4
2	5.8	5.8	6.0	5.9		6.3		6.8						
3	5.1	5.2	5.1	5.1	4.7	4.7	4.7	5.1	5.2	5.2	5.1	5.0	4.7	4.8
4	5.5	6.0	6.0	6.0	6.3	6.4	6.8	7.1	7.2	7.9	7.6	7.2	6.5	5.6
5	5.3	5.5	5.8	5.8	5.2	5.0		5.1	5.3	5.4	5.3	4.9	4.5	4.5
6	6.0	6.4	6.2	6.2	5.6	5.6	5.6	5.6	5.4	5.5	5.4	5.0	5.6	5.7
7	5.5	5.6	5.5	5.4	5.1	5.1	5.2	5.4	5.5	5.7	5.9	5.6	5.8	5.7
8	7.6	7.5	5.9	5.5	5.1	5.1	5.0	5.0	5.0	5.2	5.5	5.1	5.1	4.8
n	8	8	8	8	7	8	6	8	7	7	7	7	7	7
Mean	5.81	6.03	5.84	5.83	5.51	5.60	5.63	5.81	5.76	5.94	5.91	5.63	5.54	5.36
SD	0.78	0.71	0.37	0.50	0.70	0.74	0.85	0.83	0.84	1.00	0.89	0.91	0.83	0.68

Table A 3.36 Post-training plasma Glu_a (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	5.5	5.7	5.7	5.6	5.6	5.9	5.9	6.1	6.5	6.5	6.5	6.4	6.2	6.1
2	7.0	6.5	5.9	5.3	4.8	4.8	4.6	4.7	4.7	5.0	4.8	4.5	4.7	4.7
3	5.8	5.8	5.7	5.5	4.6	5.4	5.5	5.8	6.0	6.0	6.0	5.9	5.7	5.6
4	4.8	4.8	4.9	4.8	4.6	4.6	4.7	5.0	5.0	5.0	4.5	4.8	4.7	4.5
5	4.9	5.0	5.2	5.0	5.0	4.7	4.6	5.2	5.3	5.3	5.0	4.9	5.2	4.7
6	5.1	5.1	5.3	5.1	4.7	4.9	4.8	5.0	5.3	5.4	5.0	4.9	4.9	5.0
7	4.8	5.1	5.5	5.5	5.2	5.4	5.5	5.7	5.8	6.3	6.4	5.8	5.3	4.8
8	5.4	5.1	5.2	5.2	5.0	5.0	5.5	5.6	5.7	5.9	5.7	5.3	4.9	
n	8	8	8	8	8	8	8	8	8	8	8	8	8	7
Mean	5.41	5.39	5.43	5.25	4.94	5.09	5.14	5.39	5.54	5.68	5.49	5.31	5.20	5.06
SD	0.74	0.57	0.33	0.28	0.34	0.44	0.52	0.48	0.58	0.58	0.76	0.66	0.53	0.58

Control Group

1	6.0	6.2	6.2	6.2	6.1	6.3	6.2	6.4	6.5	6.4	6.7	6.6	6.6	6.4
2	5.7	6.0	5.8	6.0	2.3		6.3	7.2	7.3	7.4	7.5	7.3	6.7	6.4
3	5.1	5.2	5.1	5.1	4.7	4.7	4.7	5.2	5.2	5.2	5.1	5.0	4.7	4.8
4	5.2	5.6	5.8	6.0	6.8	7.0	7.6	7.7	7.6	8.0	7.8	7.4	6.5	5.3
5	5.4	5.5	5.6	5.5	5.1	5.2	5.2	5.3	5.2	5.5	5.2	5.1	4.8	5.0
6	6.1	6.1	6.1	6.1	5.8	5.7	5.9	6.0	5.8	5.8	5.8	5.9	5.7	5.6
7	6.2	6.0	5.7	5.5	5.6	5.9	6.2	6.4	6.6	6.7	6.3	6.1	5.5	5.0
8	8.1	6.9	6.9	6.7	6.3	5.2	5.3	5.3	5.6	5.9	6.4	6.5	6.1	5.5
n	8	8	8	8	8	7	8	8	8	8	8	8	8	8
Mean	5.98	5.94	5.90	5.89	5.34	5.71	5.93	6.19	6.23	6.36	6.35	6.24	5.83	5.50
SD	0.95	0.52	0.52	0.50	1.39	0.77	0.89	0.92	0.92	0.96	0.98	0.90	0.79	0.62

Table A 3.37 Pre-training plasma Glu_v (mM) at rest, pre-exercise, during and following high-intensity cycling

Pre-Training

Training Group

		Exercise								Recovery				
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	4.4	4.0	3.5	5.0	5.0	5.3	4.9	5.4	5.3	5.3	5.7	6.1	6.7	
2	4.8	4.8	4.7	4.7	4.6	4.5	4.7	4.8	4.8	5.3	5.8	5.5	5.4	5.2
3	4.9	4.8	5.0	5.0	4.8	5.1	5.4	5.7	5.8	6.2	6.3	6.3	5.7	4.8
4	4.4	4.3	4.2	4.2	4.1	4.6	4.3	4.8	4.8	4.9	5.1	5.2	5.1	4.6
5	5.7	5.2	5.0	4.9	4.7	4.9	4.9		5.2	5.3	5.3	5.1	5.1	5.0
6	5.9	5.8	5.9	5.5	5.2	5.3	5.0	5.2	5.4	5.4	5.0	4.7	4.3	4.6
7	4.9	4.8	4.6	4.5	4.5	4.9	4.4		5.2	5.3	5.0	5.2	4.9	4.6
8	4.9	4.8	4.9	4.9	5.0	5.3	5.8	6.0	6.1	5.9	6.2	6.3	6.0	5.6
n	8	8	8	8	8	8	8	6	8	8	8	8	8	7
Mean	4.99	4.81	4.73	4.84	4.74	4.99	4.93	5.32	5.33	5.45	5.55	5.55	5.40	4.91
SD	0.55	0.54	0.69	0.39	0.35	0.32	0.49	0.48	0.45	0.41	0.53	0.61	0.73	0.38

Control Group

1	5.2	6.1	6.0	6.0	5.9	6.3	5.8	6.0	6.2	6.2	6.3	6.4	6.2	6.0
2	5.6	5.7	5.5	5.4		6.3	6.3	6.4	6.6	6.8				
3	4.3	4.7	4.4	4.3	4.4	4.1		4.8	4.9	4.8	4.6	4.6	4.4	4.3
4	5.1	5.4	5.1	4.9	5.4	5.5	6.0	6.0	6.2	7.3	7.5	7.1	6.3	5.7
5	4.4	4.4	4.5	4.6	4.2	4.4		4.4	4.2	4.5	4.5	4.7	4.4	4.3
6	5.7	6.1	5.9	5.9	5.7	5.6	5.5	5.4	5.4	5.4	5.4	5.2	5.6	5.5
7	4.8	4.6	4.8	4.6	4.5	4.5	4.4	4.5	4.1	4.8	5.5	5.4	5.4	5.5
8	6.9	7.4	5.9	5.5	5.2	4.9	5.0	4.7	4.7	4.7	5.3	5.2	5.1	4.8
n	8	8	8	8	7	8	6	8	8	8	7	7	7	7
Mean	5.25	5.55	5.26	5.15	5.04	5.20	5.50	5.28	5.29	5.56	5.59	5.51	5.34	5.16
SD	0.84	1.00	0.65	0.64	0.68	0.85	0.70	0.78	0.96	1.07	1.04	0.91	0.77	0.69

Table A 3.38 Post-training plasma Glu_v (mM) at rest, pre-exercise, during and following high-intensity cycling

Post-Training

Training Group

		Exercise							Recovery					
		Time (min)												
Subject	**Rest**	**0**	**2**	**4**	**6**	**6.5**	**8.5**	**9**	**+1**	**+2**	**+5**	**+10**	**+20**	**+30**
1	5.2	5.0	5.1	4.9	5.2	5.3	5.0	5.5	5.9	5.9	5.9	6.0	5.9	5.8
2	5.6	4.3	4.3	4.5	4.2	4.7	4.4	4.6	4.4	4.9	4.8	4.5	4.0	4.3
3	5.4	5.0	5.0	5.1	5.1	5.3	5.2	5.3	5.3	5.8	5.6	5.5	5.2	5.2
4	4.5	4.5	4.5	4.6	4.4	4.5	4.5	4.7	4.6	5.0	4.8	4.8	4.6	4.4
5	4.9	4.8	4.5	4.5	3.8	3.9	4.5	4.6	5.1	5.1	4.9	4.9	4.4	3.4
6	4.7	4.7	5.0	4.7	4.3	4.6	4.8	4.8	4.8	5.0	5.0	4.4	4.9	5.0
7	4.0	4.4	4.6	4.8	4.8	4.8	4.6	5.0	4.8	5.0	5.5	5.5	5.1	4.7
8	4.8	4.8	4.9	4.8	4.5	4.7	4.9	5.2	5.4	5.6	5.6	5.2	4.7	5.0
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	4.89	4.69	4.74	4.74	4.54	4.73	4.74	4.96	5.04	5.29	5.26	5.10	4.85	4.73
SD	0.51	0.26	0.30	0.21	0.47	0.45	0.28	0.34	0.49	0.41	0.43	0.55	0.57	0.71

Control Group

1	5.9	5.7	5.8	5.8	5.8	5.9	6.1	6.0	6.3	6.6	7.0	6.9	6.6	6.5
2	5.7	5.6	5.6	5.7	6.1	6.3	6.4	6.1		6.6				
3	4.3	4.7	4.4	4.3	4.4	4.1	4.6	4.8	4.9	4.8	4.6	4.6	4.4	4.3
4	4.7	5.1	5.3	5.1	6.1	5.9	6.5	6.5	6.9	7.4	7.9	7.3	6.3	5.1
5	5.1	5.3	5.1	4.9	5.1	5.1	4.9	4.9	5.0	5.2	5.3	5.1	4.9	4.7
6	5.8	5.7	5.4	5.3	5.3	5.4	5.4	5.4	5.4	5.1	5.0	5.5	5.6	5.5
7	5.2	4.9	5.1	5.2	4.6	5.4	5.2	5.3	5.3	5.4	5.2	5.6	5.2	4.7
8	7.9	6.7	5.9	6.0	5.1	4.7	5.0	4.8	5.2	5.6	6.2	6.3	6.0	5.4
n	8	8	8	8	8	8	8	8	7	8	7	7	7	7
Mean	5.58	5.46	5.33	5.29	5.31	5.35	5.51	5.48	5.57	5.84	5.89	5.90	5.57	5.17
SD	1.09	0.62	0.48	0.55	0.64	0.71	0.73	0.65	0.74	0.92	1.20	0.97	0.79	0.72

Table A 3.39 Pre-training MVC (Nm), following high-intensity cycling, during recovery and expressed as a percentage of pre-exercise

Pre-Training								% of pre-exercise					
Training		Pre-exercise	4 min	Wingate 1	Wingate 2	+10 min	+30 min	100%	4 min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	leg length	MVC (Nm)						MVC (%)					
1	0.32	89.81	63.80	58.20	72.93	59.03	77.93	100.00	71.04	64.80	81.20	64.80	86.77
2	0.32	51.86	51.47	53.80	55.61	59.26	60.27	100.00	99.24	103.74	107.23	103.74	107.23
3	0.32	56.58	62.69	65.42	70.26	75.93	62.72	100.00	110.80	115.63	115.63	124.18	110.86
4	0.33	64.70	65.90	60.36	48.19	42.01	39.65	100.00	101.87	93.30	74.48	64.94	61.29
5	0.32	108.84	108.78	104.39	100.19	115.43	95.95	100.00	99.94	95.91	92.05	106.05	88.15
6	0.32	64.21	36.64	47.23	40.76	26.25	32.41	100.00	57.07	73.56	73.56	40.88	50.48
7	0.32	115.00	98.73	103.96	93.42	91.80	91.80	100.00	85.85	90.40	90.40	81.24	79.82
8	0.37	42.53	41.10	28.11	26.20	34.26	33.49	100.00	96.66	66.10	61.61	80.55	78.75
n		**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean		**74.19**	**66.14**	**65.18**	**63.44**	**63.00**	**61.78**		**89.15**	**87.86**	**85.51**	**84.91**	**83.27**
SD		**27.02**	**25.66**	**26.56**	**25.58**	**30.22**	**25.31**		**17.98**	**18.26**	**18.05**	**26.99**	**20.57**

Control		Pre-exercise	4 min	Wingate 1	Wingate 2	+10 min	+30 min	100%	4 min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	leg length	MVC (Nm)						MVC (%)					
1	0.32	107.25	106.98	99.03	81.68	91.48	94.73	100.00	99.74	92.33	76.16	76.16	88.33
2	0.32	77.01	68.59	63.26	66.57	62.66	60.91	100.00	89.07	82.15	86.45	81.37	86.45
3	0.32	105.11	58.59	48.18	35.80	69.84	76.92	100.00	55.74	45.84	34.06	34.06	73.18
4	0.33	54.87	46.19	29.07	47.45	42.77	41.92	100.00	84.18	52.97	86.46	77.95	76.39
5	0.32	75.59	78.78	58.24	58.13	38.36	56.36	100.00	104.22	77.05	76.90	76.90	74.56
6	0.32	102.46	94.17	59.47	76.78	73.27	65.58	100.00	91.90	58.04	74.94	74.94	64.01
7	0.32	73.43	70.66	49.05	50.45	50.71	70.53	100.00	96.23	66.79	68.71	68.71	96.05
8	0.37	121.04	123.94	104.48	92.09	99.26	101.44	100.00	102.39	86.32	76.08	82.00	83.81
n		**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean		**89.60**	**80.99**	**63.85**	**63.62**	**66.04**	**71.05**		**90.39**	**71.26**	**71.01**	**73.71**	**79.30**
SD		**22.45**	**25.83**	**25.67**	**19.12**	**21.95**	**19.70**		**15.58**	**16.86**	**16.62**	**15.68**	**10.19**

Table A 3.40 Post-training MVC (Nm), following high-intensity cycling, during recovery and expressed as a percentage of pre-exercise

Post-Training								% of pre-exercise					
Training		Pre-exercise	4 min	Wingate 1	Wingate 2	+10 min	+30 min	100%	4 min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	leg length	MVC (Nm)						MVC (%)					
1	0.32	68.57	88.00	64.27	60.27	63.65	64.54	100	128.34	93.74	87.90	92.82	94.13
2	0.32	74.32	56.84	66.61	62.40	56.17	47.90	100	76.48	89.62	83.96	75.58	64.45
3	0.32	65.07	60.45	60.61	56.46	42.55	66.24	100	92.91	93.15	86.77	65.40	101.80
4	0.33	91.49	79.67	79.25	86.02	91.23	91.71	100	87.08	86.63	94.02	99.72	100.24
5	0.32	116.94	110.08	104.88	95.50	103.23	89.58	100	94.13	89.69	81.67	88.28	76.60
6	0.32	61.41	29.49	43.27	47.81	39.89	32.88	100	48.02	70.47	77.86	64.95	53.54
7	0.32	107.30	94.42	104.52	96.86	84.22	82.01	100	88.00	97.41	90.27	78.49	76.44
8	0.37	42.84	40.50	42.65	45.36	44.76	39.18	100	94.55	99.56	105.89	104.48	91.47
n		**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean		**78.49**	**69.93**	**70.76**	**68.84**	**65.71**	**64.25**		**89.10**	**90.15**	**87.70**	**83.72**	**81.86**
SD		**24.89**	**27.76**	**24.15**	**20.88**	**24.32**	**22.66**		**22.23**	**8.97**	**8.62**	**14.99**	**17.48**

Control		Pre-exercise	4 min	Wingate 1	Wingate 2	+10 min	+30 min	100%	4 min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	leg length	MVC (Nm)						MVC (%)					
1	0.32	108.32	97.36	90.71	82.98	87.08	99.34	100	89.89	83.74	76.61	80.39	91.71
2	0.32	64.86	65.72	65.92	48.32	42.11	39.55	100	101.32	101.63	74.49	64.92	60.97
3	0.32	81.56	49.63	44.92	38.05	42.71	78.18	100	60.85	55.07	46.65	52.37	95.85
4	0.33	58.73	63.51	57.13	46.06	41.95	58.50	100	108.12	97.27	78.42	71.43	99.60
5	0.32	63.38	63.04	40.84	29.78	33.38	51.63	100	99.48	64.43	46.98	52.66	81.46
6	0.32	102.46	94.17	59.47	56.78	73.27	63.54	100	91.90	58.04	55.42	71.51	62.01
7	0.32	73.88	55.56	60.20	57.38	65.21	73.59	100	75.20	81.48	77.67	88.26	99.61
8	0.37	123.09	110.40	97.68	78.69	112.07	116.65	100	89.69	79.36	63.93	91.04	94.76
n		**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean		**84.54**	**74.92**	**64.61**	**54.75**	**62.22**	**72.62**		**88.63**	**76.43**	**64.77**	**73.60**	**85.91**
SD		**23.89**	**22.37**	**20.11**	**18.52**	**27.42**	**25.36**		**15.20**	**17.25**	**13.73**	**14.67**	**16.03**

Table A 3.41 Pre-training 1 Hz stimulations separated by 3 s at 50, 60, 70, 80, 90 and 100% of magnetic stimulator output

Pre-Training

Training

	50%			60%			70%			80%						90%						100%					
Subject	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV
1	1.90	1.61	1.25	2.09	2.84	2.93	5.27	5.60	5.07	7.01	8.95	8.97	8.31	0.08	1.01	10.66	9.87	10.49	12.97	0.94	7.28	11.07	12.83	12.33	14.30	0.44	3.05
2	2.67	2.64	2.83	3.55	3.42	3.47	4.24	4.28	4.24	8.97	8.73	8.80	8.83	0.08	0.93	9.62	9.40	10.89	9.97	0.80	8.07	11.88	11.66	11.32	11.62	0.28	2.40
3	3.26	3.38	3.40	3.96	4.04	4.41	4.75	4.87	4.62	6.77	6.06	6.08	6.30	0.08	1.23	6.86	6.97	6.98	6.94	0.07	0.97	7.32	7.96	7.51	7.60	0.33	4.32
4	0.94	1.12	1.94	1.28	1.06	1.26	2.15	2.01	2.18	5.40	5.54	5.40	5.45	0.26	4.71	6.70	6.04	6.74	6.49	0.39	6.04	6.67	6.71	6.74	6.70	0.04	0.56
5	0.79	0.84	0.72	1.68	1.60	1.64	2.22	2.89	2.53	10.02	11.48	11.54	11.01	0.73	6.63	12.28	12.70	12.64	12.54	0.23	1.84	13.75	13.89	12.77	13.47	0.61	4.56
6	1.11	1.53	1.94	2.35	2.43	2.27	4.35	4.96	4.56	6.11	8.53	8.94	7.86	0.30	3.78	8.07	9.11	9.71	8.96	0.83	9.21	9.35	9.43	10.27	9.85	0.59	5.97
7	2.30	2.26	2.58	3.91	3.44	3.39	7.48	7.64	7.62	18.28	18.41	19.83	18.84	0.70	3.72	19.22	19.77	20.31	19.77	0.54	2.74	20.62	20.69	20.69	20.67	0.04	0.19
8	0.76	0.72	0.75	1.40	1.09	1.05	2.22	2.02	1.96	3.14	3.96	3.94	3.68	0.49	13.40	4.28	4.13	4.01	4.14	0.13	3.25	4.01	4.62	4.65	4.43	0.36	8.22
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
mean	1.72	1.76	1.92	2.53	2.49	2.55	4.08	4.28	4.10	8.21	8.96	9.19	8.79	0.34	4.43	10.89	10.73	11.47	10.22	0.49	4.93	11.87	11.64	12.00	11.08	0.34	3.66
SD	0.96	0.93	0.98	1.12	1.14	1.19	1.86	1.93	1.87	4.58	4.49	4.94	4.64	0.27	4.15	5.30	4.82	4.92	4.89	0.34	3.11	5.59	5.78	5.41	5.15	0.22	2.70
										0.07	0.07	0.06	0.06	0.26	0.43	0.07	0.07	0.07	0.09	0.29	0.61	0.09	0.12	0.10	0.13	0.33	0.94

Control

	50%			60%			70%			80%						90%						100%					
Subject	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV
1	3.94	4.42	4.25	6.35	6.55	6.79	10.13	10.07	10.30	13.31	15.64	15.76	14.90	1.38	9.24	16.57	16.58	17.97	17.04	0.81	4.73	17.79	17.98	17.78	17.85	0.11	0.64
2	1.01	1.01	1.01	1.63	1.50	1.53	2.46	2.30	2.46	4.77	5.66	5.61	5.34	0.50	9.37	5.44	5.09	6.92	5.82	0.97	16.67	6.99	7.06	7.31	7.12	0.17	2.35
3	1.85	1.93	1.55	4.37	3.91	4.03	6.74	6.72	6.39	10.23	11.67	12.60	11.50	1.19	10.37	14.59	14.08	14.44	14.37	0.26	1.82	16.32	14.57	15.85	15.58	0.91	5.81
4	3.26	3.40	3.38	6.67	7.82	7.51	8.07	9.11	9.71	11.59	11.03	10.12	10.92	0.74	6.80	12.44	12.37	13.11	12.64	0.41	3.24	13.87	13.79	13.21	13.62	0.36	2.63
5	5.62	6.27	5.94	8.95	9.16	9.98	16.40	17.36	18.50	22.24	22.40	22.73	22.46	0.25	1.12	23.50	23.14	26.26	24.30	1.71	7.03	27.10	27.15	26.95	27.06	0.10	0.39
6	2.19	2.17	2.12	3.66	2.90	2.61	2.95	2.92	2.88	11.84	12.70	13.55	12.70	0.86	6.75	13.16	12.63	13.35	13.05	0.37	2.86	13.51	13.38	12.83	13.24	0.36	2.72
7	1.11	1.06	1.09	3.94	4.27	4.45	5.16	6.24	5.97	13.67	13.18	14.93	13.92	0.90	6.50	15.20	15.26	15.20	15.22	0.04	0.23	15.15	16.08	15.98	15.73	0.51	3.26
8	1.58	1.57	1.57	2.94	2.73	2.72	4.42	4.51	4.25	7.69	7.29	8.44	7.81	0.58	7.49	9.99	8.02	9.73	9.25	1.07	11.59	11.23	10.40	10.38	10.67	0.48	4.53
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
mean	2.57	2.73	2.61	4.81	4.86	4.95	7.04	7.40	7.56	11.92	12.45	12.97	12.44	0.80	7.20	9.93	9.20	10.52	13.96	0.70	6.02	10.78	10.20	10.93	15.11	0.38	2.79
SD	1.60	1.85	1.76	2.36	2.70	2.89	4.57	4.86	5.27	5.12	5.14	5.21	5.12	0.37	2.85	5.80	5.99	6.00	5.47	0.54	5.55	6.38	6.52	6.07	5.86	0.27	1.81

Table A 3.42 Post-training 1 Hz stimulations separated by 3 s at 50, 60, 70, 80, 90 and 100% of magnetic stimulator output

Post-Training

Training

	50%			60%			70%			80%						90%						100%					
Subject	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV
1	0.76	0.76	0.76	2.09	1.84	1.93	4.01	4.30	4.10	9.67	9.87	9.08	9.54	0.41	4.30	11.27	11.32	12.25	10.34	0.42	4.04	13.08	12.76	12.96	12.93	0.16	1.24
2	2.50	2.59	2.50	3.86	3.57	3.62	4.43	4.31	4.26	9.00	8.87	8.91	8.93	0.07	0.73	10.22	11.88	11.66	11.25	0.90	8.01	12.83	12.63	12.35	12.61	0.24	1.90
3	1.77	1.13	2.77	1.78	2.11	2.04	4.46	3.23	3.19	6.05	6.03	5.98	6.02	0.04	0.59	6.84	7.03	7.99	7.29	0.62	8.46	8.97	8.42	8.83	8.74	0.29	3.29
4	0.94	1.12	1.94	1.28	1.06	1.26	2.15	2.01	2.18	5.40	5.54	5.40	5.45	0.08	1.48	5.70	6.04	6.74	6.16	0.53	8.63	6.67	6.71	6.74	6.70	0.04	0.56
5	1.05	0.96	0.94	1.27	1.28	1.31	2.02	1.72	1.98	3.92	3.76	4.87	4.18	0.60	14.25	4.23	4.12	4.29	4.21	0.08	1.99	4.58	4.51	5.57	4.89	0.59	12.09
6	3.94	4.42	4.25	6.35	6.55	6.79	10.13	10.07	10.30	14.31	15.64	15.76	15.24	0.80	5.26	16.57	16.58	16.97	16.71	0.23	1.37	16.79	17.98	17.78	17.52	0.64	3.64
7	2.15	2.37	2.55	5.03	5.06	4.94	7.50	7.15	6.91	11.77	15.17	16.00	14.31	2.24	15.66	17.47	17.20	18.14	17.60	0.48	2.74	18.22	19.64	19.42	19.09	0.77	4.01
8	0.77	1.00	1.07	1.97	1.81	1.78	2.81	2.68	2.77	3.74	3.71	4.93	4.13	0.70	16.92	4.23	4.29	4.36	4.29	0.07	1.57	4.82	4.98	5.82	5.20	0.54	10.34
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
mean	1.73	1.79	2.10	2.95	2.91	2.96	4.69	4.43	4.46	7.98	8.57	8.87	8.47	0.62	7.40	9.13	8.52	9.79	9.73	0.42	4.60	10.03	9.44	10.25	10.96	0.41	4.63
SD	1.11	1.26	1.18	1.91	1.98	2.00	2.81	2.85	2.83	3.84	4.75	4.63	4.37	0.72	7.03	5.98	6.00	6.17	5.24	0.28	3.23	6.51	6.69	6.32	5.46	0.26	4.26
										0.09	0.16	0.13	0.12	0.26	0.81	0.13	0.21	0.19	0.16	0.23	0.85	0.16	0.24	0.25	0.21	0.29	0.70

Control

	50%			60%			70%			80%						90%						100%					
Subject	1	2	3	1	2	3	1	2	3	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV	1	2	3	mean	SD	CV
1	4.44	4.28	4.31	12.39	11.50	12.28	15.60	15.57	15.40	16.64	16.56	16.85	16.68	0.15	0.88	17.30	17.29	17.12	17.23	0.10	0.58	18.23	19.96	19.17	19.12	0.86	4.52
2	1.01	1.01	1.01	1.30	1.19	1.77	2.01	2.03	2.02	4.55	5.54	5.53	5.21	0.57	10.94	5.86	5.99	6.60	6.15	0.40	6.44	6.59	6.70	6.73	6.67	0.08	1.14
3	2.07	2.08	2.29	4.08	4.29	4.08	6.51	6.72	7.12	10.01	11.93	12.48	11.47	1.30	11.29	12.42	13.42	12.61	12.82	0.53	4.14	13.55	13.77	13.46	13.59	0.16	1.16
4	3.26	3.40	3.38	6.67	7.82	7.51	8.07	9.11	9.71	11.59	11.03	10.12	10.92	0.74	6.80	12.44	12.37	13.11	12.64	0.41	3.24	13.87	13.79	13.21	13.62	0.36	2.63
5	4.67	4.05	3.67	6.27	5.94	6.77	9.29	9.61	9.64	17.73	17.94	17.94	17.87	0.12	0.68	18.14	20.81	20.79	19.91	1.54	7.71	21.29	21.75	21.21	21.42	0.29	1.34
6	2.19	2.17	2.12	3.66	2.90	2.61	5.95	5.92	6.88	10.84	11.70	11.55	11.36	0.46	4.04	13.16	12.63	12.35	12.72	0.41	3.22	13.51	13.38	13.83	13.58	0.23	1.70
7	2.04	1.72	1.49	2.56	2.25	2.07	4.92	4.89	4.79	11.64	12.77	12.73	12.38	0.64	5.20	13.59	13.47	14.78	13.95	0.73	5.20	15.39	15.34	15.53	15.42	0.10	0.63
8	1.96	1.96	1.91	2.64	2.60	2.72	3.84	2.86	3.74	5.35	5.79	5.63	5.59	0.22	4.00	7.19	6.65	7.87	7.24	0.61	8.45	8.91	8.46	8.48	8.62	2.72	31.55
n	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
mean	2.70	2.58	2.52	4.95	4.81	4.98	7.02	7.09	7.41	11.04	11.66	11.60	11.43	0.53	5.48	8.71	8.33	9.38	12.83	0.59	4.87	9.65	9.19	9.96	14.00	0.60	5.59
SD	1.29	1.18	1.15	3.52	3.45	3.65	4.16	4.34	4.21	4.66	4.42	4.54	4.52	0.39	4.03	5.51	5.80	5.58	4.58	0.42	2.61	5.99	6.36	5.87	4.88	0.89	10.56

Table A 3.43 Pre-training Q_{twpot} force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

							% of pre-exercise					
Training	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Twitch (Nm)						**Twitch (%)**					
1	11.08	5.17	5.19	3.62	3.78	5.26	100	46.63	46.82	32.64	34.10	47.48
2	13.22	7.37	9.21	5.18	10.21	11.15	100	55.79	69.71	39.18	77.26	84.33
3	20.73	15.28	12.45	11.01	16.51	16.54	100	73.72	60.06	53.12	79.63	79.78
4	10.25	6.49	6.67	6.73	8.10	9.52	100	63.38	65.06	65.69	79.10	92.93
5	32.61	25.20	23.89	22.77	28.85	29.53	100	77.27	73.26	69.80	88.45	90.55
6	26.01	20.86	16.51	13.79	16.71	19.45	100	80.21	63.47	53.03	64.24	74.80
7	25.56	16.85	14.70	14.70	17.57	17.57	100	65.94	57.54	57.54	68.73	68.73
8	8.94	3.89	3.50	3.08	7.56	8.02	100	43.54	39.22	34.47	84.63	89.79
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**18.55**	**13.71**	**12.42**	**11.04**	**15.07**	**14.63**		**63.31**	**59.39**	**50.69**	**72.02**	**78.55**
SD	**8.89**	**8.00**	**6.78**	**6.79**	**7.94**	**7.81**		**13.74**	**11.44**	**13.99**	**17.21**	**15.06**

Control	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Twitch (Nm)						**Twitch (%)**					
1	16.31	15.81	5.08	5.70	15.84	15.75	100	96.94	31.13	34.98	97.14	96.57
2	10.53	7.87	4.66	3.77	7.16	9.82	100	74.72	44.29	35.78	68.04	93.27
3	22.55	9.89	7.82	10.83	11.87	14.40	100	43.87	34.68	48.04	52.63	63.87
4	14.01	7.30	4.54	4.37	10.28	12.62	100	52.15	32.39	31.24	73.37	90.08
5	30.09	16.01	10.33	7.53	24.97	24.76	100	53.21	34.34	25.03	82.98	82.29
6	22.56	17.54	15.13	11.77	13.38	21.94	100	77.74	67.10	52.16	59.34	97.28
7	18.29	14.44	6.08	7.89	16.01	18.58	100	78.96	33.22	43.16	87.56	101.56
8	28.64	14.12	8.80	7.26	11.15	14.96	100	49.30	30.71	25.35	38.92	52.24
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**20.37**	**12.87**	**7.80**	**7.39**	**13.83**	**16.60**		**65.86**	**38.48**	**36.97**	**70.00**	**84.64**
SD	**6.87**	**3.95**	**3.63**	**2.84**	**5.36**	**4.91**		**18.76**	**12.33**	**10.05**	**19.31**	**17.64**

Table A 3.44 Post-training Q_{twpot} force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

							% of pre-exercise					
Training	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Twitch (Nm)						**Twitch (%)**					
1	18.26	11.08	9.97	8.95	8.51	9.22	100	60.67	54.62	49.05	46.64	50.51
2	11.55	12.72	10.26	12.96	10.65	14.52	100	110.13	88.79	112.12	92.15	125.69
3	16.43	10.12	12.05	12.37	10.56	10.66	100	61.56	73.33	75.29	64.27	64.89
4	10.25	9.60	9.27	4.75	5.35	4.31	100	93.71	90.52	46.36	52.17	42.12
5	9.21	6.86	6.75	10.42	9.71	9.81	100	74.43	73.21	113.05	105.36	106.46
6	22.85	19.10	14.34	15.03	18.42	17.32	100	83.60	62.77	65.77	80.62	75.80
7	30.83	23.57	12.05	12.75	14.32	21.05	100	76.45	39.09	41.34	46.44	68.29
8	8.56	5.40	5.08	3.61	7.27	6.21	100	63.07	59.31	42.19	84.95	72.60
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**15.99**	**12.31**	**9.97**	**10.10**	**10.60**	**11.64**		**76.95**	**62.35**	**63.18**	**66.27**	**72.78**
SD	**8.37**	**6.61**	**3.23**	**4.38**	**4.36**	**6.00**		**17.40**	**17.37**	**29.85**	**22.39**	**27.75**

Control	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Twitch (Nm)						**Twitch (%)**					
1	22.88	15.17	9.42	9.17	10.10	12.56	100	66.28	41.17	40.08	44.14	54.90
2	10.25	7.87	8.15	6.61	7.17	9.41	100	76.79	79.57	64.48	69.98	91.83
3	21.31	13.62	8.06	7.99	12.56	14.29	100	63.90	37.81	37.51	58.97	67.08
4	14.70	8.52	6.24	6.22	7.69	8.86	100	57.94	42.41	42.29	52.33	60.28
5	25.65	14.08	9.82	7.33	12.32	17.97	100	54.89	38.27	28.58	48.04	70.06
6	21.94	17.54	15.13	11.77	13.41	22.56	100	79.92	68.98	53.62	61.12	102.80
7	21.03	18.48	14.98	12.52	17.36	17.36	100	87.90	71.24	59.52	82.54	82.54
8	12.53	7.89	5.23	5.35	11.15	14.96	100	63.02	41.77	42.67	88.98	119.43
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**18.79**	**12.90**	**9.63**	**8.37**	**11.47**	**14.75**		**68.83**	**52.65**	**46.09**	**63.26**	**81.11**
SD	**5.70**	**4.53**	**3.97**	**2.79**	**3.49**	**4.85**		**11.51**	**17.40**	**12.06**	**16.12**	**22.35**

Table A 3.45 Pre-training doublet force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

							% of pre-exercise					
Training	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Doublet (Nm)						**Doublet (%)**					
1	22.28	11.50	14.24	14.55	10.57	21.41	100	51.61	63.93	65.31	47.43	96.12
2	24.51	26.36	18.40	15.80	19.55	20.27	100	107.55	75.08	64.46	79.77	82.70
3	37.63	30.43	18.51	19.35	21.13	20.20	100	80.88	49.19	51.41	56.15	53.67
4	18.94	10.50	11.55	11.42	15.39	14.08	100	55.41	60.99	60.28	81.25	74.31
5	35.90	25.22	26.98	18.15	23.23	29.26	100	70.25	75.16	50.54	64.71	81.49
6	38.10	19.50	17.01	14.20	26.25	33.82	100	51.18	44.65	37.27	68.91	88.76
7	46.12	35.03	29.73	29.65	35.03	34.09	100	75.96	64.46	64.29	75.96	73.91
8	16.32	6.97	4.44	5.04	6.39	11.39	100	42.72	27.19	30.91	39.13	69.81
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**29.98**	**20.69**	**17.61**	**16.02**	**19.69**	**23.06**		**66.94**	**57.58**	**53.06**	**64.16**	**77.60**
SD	**10.81**	**10.22**	**8.09**	**7.06**	**9.04**	**8.55**		**21.18**	**16.37**	**13.13**	**15.44**	**12.91**

Control	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Doublet (Nm)						**Doublet (%)**					
1	24.49	24.61	16.31	19.66	20.11	26.02	100	100.48	66.60	80.30	82.12	106.25
2	18.13	23.73	10.23	10.86	18.22	22.36	100	130.84	56.41	59.87	100.47	123.29
3	39.62	25.84	16.81	18.64	19.82	26.31	100	65.21	42.44	47.06	50.04	66.42
4	23.20	21.09	10.31	12.01	17.51	23.69	100	90.91	44.45	51.78	75.45	102.09
5	55.95	49.85	21.37	14.42	36.12	50.15	100	89.10	38.19	25.76	64.56	89.63
6	53.08	51.29	32.63	22.99	34.37	49.65	100	96.63	61.47	43.31	64.74	93.54
7	25.01	19.88	13.11	14.10	25.69	28.34	100	79.47	52.39	56.38	102.68	113.29
8	60.59	53.78	25.89	9.59	17.74	22.16	100	88.77	42.73	15.82	29.28	36.58
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**37.51**	**33.76**	**18.33**	**15.28**	**23.70**	**31.08**		**92.68**	**50.58**	**47.54**	**71.17**	**91.39**
SD	**17.01**	**14.96**	**7.88**	**4.70**	**7.59**	**11.80**		**18.87**	**10.22**	**20.07**	**24.72**	**27.95**

Table A 3.46 Post-training doublet force (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

							% of pre-exercise					
Training	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Doublet (Nm)						**Doublet (%)**					
1	16.58	20.71	12.18	13.70	21.71	24.80	100	124.92	73.47	82.60	130.91	149.55
2	21.81	17.21	15.23	12.61	33.45	33.25	100	78.95	69.83	57.85	153.38	152.47
3	24.85	19.82	21.30	21.97	19.66	17.82	100	79.78	85.70	88.40	79.11	71.73
4	10.48	6.71	6.74	8.14	10.34	9.08	100	64.06	64.26	77.68	98.62	86.64
5	17.23	14.76	15.97	11.03	18.55	17.26	100	85.67	92.68	64.02	107.69	100.19
6	34.61	21.57	17.98	17.95	30.11	28.45	100	62.32	51.96	51.87	86.99	82.20
7	49.80	38.31	33.98	21.43	29.47	35.15	100	76.92	68.22	43.04	59.17	70.57
8	14.14	10.89	10.77	8.94	12.39	14.25	100	77.04	76.17	63.19	87.63	100.80
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**23.69**	**18.47**	**17.42**	**14.58**	**21.96**	**22.51**		**81.21**	**72.79**	**66.08**	**100.44**	**101.77**
SD	**13.58**	**10.13**	**8.71**	**5.81**	**8.44**	**9.36**		**19.36**	**12.59**	**15.67**	**29.98**	**32.39**

Control	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Doublet (Nm)						**Doublet (%)**					
1	38.91	22.11	22.94	12.55	26.20	31.03	100	56.81	58.97	32.25	67.32	79.74
2	21.23	13.24	13.06	11.34	15.19	18.79	100	62.36	61.53	53.41	71.56	88.50
3	32.97	31.79	16.22	13.56	25.14	33.27	100	96.44	49.19	41.12	76.27	100.93
4	19.86	11.55	7.34	6.07	13.61	16.27	100	58.17	36.96	30.55	68.54	81.91
5	43.49	32.76	21.24	17.37	23.65	27.61	100	75.32	48.83	39.93	54.37	63.47
6	53.08	51.29	32.63	22.99		34.37	100	96.63	61.47	43.31	0.00	64.74
7	31.19	24.93	22.20	19.85	29.14	38.36	100	79.93	71.18	63.64	93.44	122.99
8	24.12	12.45	11.33	9.59	17.74	22.16	100	51.59	46.96	39.73	73.53	91.88
n	**8**	**8**	**8**	**8**	**7**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Mean	**33.11**	**25.01**	**18.37**	**14.16**	**21.52**	**27.73**		**72.16**	**54.38**	**42.99**	**63.13**	**86.77**
SD	**12.27**	**13.54**	**8.03**	**5.58**	**5.98**	**7.94**		**17.76**	**10.83**	**10.88**	**27.72**	**19.43**

Table A 3.47 Pre-training 20 Hz Tetani (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

							% of pre-exercise					
Training	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Tetani (Nm)						**Tetani (%)**					
1	45.49	26.22	37.49	50.15	34.37	31.06	100	57.63	82.42	110.25	75.55	68.28
2	63.22	38.37	32.38	37.06	35.92	38.47	100	60.70	51.23	58.63	56.82	60.85
3	37.67	57.10	55.45	47.05			100	151.57	147.20	124.89		
4	26.20	17.42	17.22	22.30	25.16	27.04	100	66.48	65.72	85.15	96.07	103.22
5	41.84	31.84	30.14	23.65	38.16	37.19	100	76.10	72.04	56.53	91.22	88.90
6	36.27	36.35	44.60	33.24	58.87	70.01	100	100.21	122.95	91.63	162.29	193.02
7	85.54	61.51	77.69	66.62	66.58	66.58	100	71.92	90.83	77.89	77.84	77.84
8	16.51	15.53			11.35	13.12	100	94.08			68.73	79.45
n	**8**	**8**	**7**	**7**	**7**	**7**	**8**	**8**	**7**	**7**	**7**	**7**
Mean	**44.09**	**35.54**	**42.14**	**40.01**	**38.63**	**40.50**		**84.84**	**90.34**	**86.42**	**89.79**	**95.94**
SD	**21.63**	**16.81**	**19.70**	**15.79**	**18.90**	**20.76**		**30.89**	**33.74**	**25.21**	**34.58**	**44.95**
Control	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Tetani (Nm)						**Tetani (%)**					
1	48.89				42.39	42.97	100				86.71	87.90
2	47.57	36.86	36.42	26.87	36.42	38.84	100	77.50	76.57	56.48	76.57	81.65
3	46.43	43.54	32.84	32.84	40.65	40.17	100	93.78	70.74	70.74	87.55	86.52
4	36.28	42.77		25.58	30.72	32.56	100	117.89	0.00	70.51	84.66	89.74
5	79.14	75.31	58.97	49.04		71.31	100	95.16	74.51	61.97	0.00	90.10
6	70.73		52.67	62.90	62.62		100	0.00	74.46	88.92	88.53	0.00
7	61.57	35.45	37.30	36.79		38.34	100	57.58	60.59	59.75	0.00	62.27
8	56.52		28.72	17.44	21.53	29.80	100	0.00	50.81	30.86	38.09	52.71
n	**8**	**5**	**6**	**7**	**6**	**7**	**8**	**7**	**7**	**7**	**8**	**8**
Mean	**55.89**	**46.79**	**41.16**	**35.92**	**39.05**	**42.00**		**63.13**	**58.24**	**62.75**	**57.76**	**68.86**
SD	**14.07**	**16.33**	**11.92**	**15.49**	**13.80**	**13.69**		**46.85**	**27.30**	**17.68**	**39.29**	**31.10**

Table A 3.48 Post-training 20 Hz Tetani (Nm) evoked via magnetic stimulation and expressed as a percentage of pre-exercise

							% of pre-exercise					
Training	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Tetani (Nm)						**Tetani (%)**					
1	26.69	19.48			16.38	27.92	100	73.01			61.38	104.63
2	35.92	26.98	26.69	22.15	58.38	38.47	100	75.12	74.31	61.68	162.54	107.10
3	28.90	29.33	26.13	25.89	26.57	28.91	100	101.50	90.42	89.60	91.94	100.02
4	13.88	9.90	9.90	12.50	16.15	15.54	100	71.35	71.35	90.10	116.36	111.99
5	70.25	45.79	42.09	31.30	43.80	63.06	100	65.19	59.92	44.56	62.36	89.78
6	62.78	38.81	35.82	35.26	50.44	63.01	100	61.83	57.07	56.17	80.35	100.37
7	78.37	55.84	64.89	61.55	63.38	63.16	100	71.25	82.80	78.54	80.87	80.60
8	21.38	18.65	16.28		18.96	19.46	100	87.22	76.15		88.68	91.01
n	**8**	**8**	**7**	**6**	**8**	**8**	**8**	**8**	**7**	**6**	**8**	**8**
Mean	**42.27**	**30.60**	**31.69**	**31.44**	**36.76**	**39.94**		**75.81**	**73.15**	**70.11**	**93.06**	**98.19**
SD	**24.52**	**15.33**	**18.24**	**16.71**	**19.54**	**20.32**		**12.80**	**11.82**	**18.81**	**33.05**	**10.36**
Control	**Pre-exercise**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**	**100%**	**4 min**	**Wingate 1**	**Wingate 2**	**+10 min**	**+30 min**
Subject	Tetani (Nm)						**Tetani (%)**					
1	69.67		35.04	24.37	49.10	60.20	100		50.29	34.98	70.47	86.41
2	26.21	26.27	17.44	22.48	25.07	27.04	100	100.25	66.54	85.79	95.66	103.19
3	72.21	54.88	49.63	46.45	60.34	74.62	100	76.00	68.73	64.33	83.57	103.34
4	26.84	16.22			16.44	16.27	100	60.44	0.00	0.00	61.25	60.62
5	49.61	41.59	35.02	25.02	36.82	44.18	100	83.83	70.60	50.44	74.22	89.05
6	70.73	67.84	62.90	52.67		62.62	100	95.91	88.92	74.46	0.00	88.53
7	68.38	59.20	50.94	52.33	56.10	58.38	100	86.57	74.49	76.52	82.04	85.38
8	37.00	29.58	27.44	21.53	29.80	35.81	100	79.95	74.17	58.20	80.53	96.79
n	**8**	**7**	**7**	**7**	**7**	**8**	**8**	**7**	**8**	**8**	**8**	**8**
Mean	**52.58**	**42.23**	**39.77**	**34.98**	**39.09**	**47.39**		**83.28**	**61.72**	**55.59**	**68.47**	**89.17**
SD	**20.24**	**19.13**	**15.56**	**14.69**	**16.54**	**19.95**		**13.19**	**27.12**	**27.60**	**29.46**	**13.59**

Table A 3.49 Pre-training Q_{twpot} vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Pre-Training
VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.4	1.3	1.0	1.2	1.8	1.5	100	53.3	42.5	49.6	75.8	64.2
2	7.6	3.9	2.9	2.9	8.0	8.7	100	51.2	38.0	38.0	105.3	114.5
3	1.2	1.0	0.5	0.5	1.1	1.3	100	85.8	41.7	41.7	91.7	108.3
4	2.3	1.7	1.1	1.0	1.3	2.0	100	73.9	47.0	44.8	26.5	26.5
5	3.2	1.9	1.1	1.1	2.6	2.8	100	59.4	34.4	34.4	59.4	34.4
6	3.3	1.5	1.7	1.7	1.8	2.6	100	44.2	51.5	51.5	54.5	78.8
7	6.7	4.9	5.5	3.9	7.3	7.5	100	73.1	82.1	58.2	109.0	111.9
8	3.9	3.8	4.1	3.9	3.4	3.1	100	97.4	105.1	100.0	87.2	79.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**3.83**	**2.50**	**2.24**	**2.03**	**3.42**	**3.69**		**67.31**	**55.28**	**52.27**	**76.17**	**77.26**
SD	**2.22**	**1.47**	**1.77**	**1.35**	**2.72**	**2.81**		**18.4**	**25.0**	**20.7**	**28.0**	**34.1**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	6.9	4.7	1.9	1.7	3.8	4.7	100	68.1	27.4	24.6	54.3	67.6
2	3.1	2.3	2.4	2.5	2.7	2.9	100	74.2	77.4	80.6	87.1	93.5
3	4.1	1.9	1.6	4.5	4.3	2.5	100	46.3	39.0	109.8	104.9	61.0
4	1.8	2.2	2.4	3.0	3.1	3.2	100	122.2	133.3	166.7	172.2	177.8
5	6.1	2.5	2.8	2.2	4.8	4.2	100	41.0	45.9	36.1	78.7	68.9
6	2.2	2.0	1.3	0.7	2.2	2.5	100	89.5	57.9	31.6	100.0	111.4
7	3.2	2.1	2.1	2.1	3.6	3.2	100	65.6	65.6	65.6	112.5	100.0
8	3.2	2.8	3.2	4.5	4.2	2.8	100	87.5	100.0	140.6	131.3	87.5
n	**8**	**8**	**8**	**8**	**7**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**3.83**	**2.56**	**2.21**	**2.65**	**3.59**	**3.25**		**74.31**	**68.32**	**81.95**	**105.12**	**95.95**
SD	**1.80**	**0.91**	**0.62**	**1.32**	**0.86**	**0.79**		**25.9**	**34.8**	**52.9**	**35.6**	**37.4**

Table A 3.50 Post-training Q_{twpot} vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Post-Training
VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	5.5	2.4	1.5	2.2		5.1	100	43.6	27.3	40.0		92.7
2	5.5	4.4	5.8	6.4	7.9	4.1	100	80.0	105.5	116.4	143.6	74.5
3	3.1	2.8	0.6		4.4	5.3	100	90.3	19.4		141.9	171.0
4	1.4	1.6	1.3	1.4	1.4	1.2	100	114.3	92.9	100.0	100.0	85.7
5	0.7	0.5	0.4	0.5	1.3	0.7	100	71.4	57.1	71.4	185.7	100.0
6	3.3	3.5	3.4	2.8	2.3	2.5	100	106.1	103.0	84.8	69.7	75.8
7	5.2	6.7	2.0	1.9	5.8	4.8	100	128.8	38.5	36.5	111.5	92.3
8	4.1	4.0	3.7	4.8	9.4	4.2	100	97.6	90.2	117.1	229.3	102.4
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**3.60**	**3.24**	**2.34**	**2.86**	**4.64**	**3.49**		**91.52**	**66.73**	**80.89**	**140.26**	**99.31**
SD	**1.84**	**1.89**	**1.84**	**2.06**	**3.21**	**1.79**		**26.7**	**35.3**	**33.4**	**53.9**	**30.7**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	4.4	2.2	2.1	2.7	3.4	3.2	100	50.0	47.7	61.4	77.3	72.7
2	4.8	4.8	4.9	3.9	3.4	3.9	100	100.0	102.1	81.3	70.8	81.3
3	12.5	10.8	5.5	8.1	11.5	12.2	100	86.4	44.0	64.8	92.0	97.6
4	2.1	3.1	3.8	4	3.6	4.1	100	147.6	181.0	190.5	171.4	195.2
5	9.1	8.8	9.1	8.7	8.3	8.6	100	96.7	100.0	95.6	91.2	94.5
6	5.5	9.4	2.5	6.3	8.2		100	170.9	45.5	114.5	149.1	0.0
7	3.1	4	2.2	2.2	2.5	2.2	100	129.0	71.0	71.0	80.6	71.0
8	4.1	4.7	4.3		9.4		100	114.6	104.9		229.3	
n	**7**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**7**
mean	**5.89**	**5.98**	**4.30**	**5.13**	**6.29**	**5.70**		**111.91**	**87.01**	**97.00**	**120.22**	**87.47**
SD	**3.67**	**3.22**	**2.32**	**2.59**	**3.44**	**3.87**		**37.6**	**46.2**	**45.2**	**57.1**	**57.7**

Table A 3.51 Pre-training Q_{twpot} vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	46	69	53	55	48	48	100	150.0	115.2	119.6	104.3	104.3
2	36	41	37	39	37	37	100	113.9	102.8	113.9	102.8	108.3
3	32	47	46	48	42	37	100	146.9	143.8	150.0	131.3	115.6
4	24	38	35	38	22	27	100	158.3	91.7	112.5	145.8	158.3
5	32	45	41	40	27	30	100	140.6	128.1	84.4	140.6	128.1
6	27	45	48	49	36	31	100	166.7	177.8	181.5	133.3	114.8
7	42	58	49	46	34	35	100	138.1	116.7	109.5	81.0	83.3
8	36	72	64	71	34	48	100	200.0	177.8	197.2	94.4	133.3
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**34.38**	**51.88**	**46.63**	**48.25**	**35.00**	**36.63**		**151.81**	**131.72**	**133.57**	**116.70**	**118.28**
SD	**7.29**	**12.90**	**9.33**	**10.87**	**8.09**	**7.84**		**25.0**	**32.4**	**39.0**	**24.0**	**22.2**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	37	65	46	47	30	30	100	175.7	124.3	127.0	81.1	81.1
2	42	42	43	52	40	42	100	100.0	102.4	123.8	95.2	100.0
3	38	45	35	51	33	33	100	118.4	92.1	134.2	86.8	86.8
4	38	36	38	58	53	43	100	94.7	100.0	152.6	139.5	113.2
5	34	40	40	35	29	35	100	117.6	117.6	102.9	85.3	102.9
6	26	38	37	37	22	21	100	146.2	142.3	141.0	83.3	79.5
7	38	42	42	56	44	34	100	110.5	110.5	147.4	115.8	89.5
8	27	31	34	53	47	32	100	114.8	125.9	196.3	174.1	118.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**35.00**	**42.38**	**39.38**	**48.58**	**37.21**	**33.71**	**100.00**	**122.25**	**114.40**	**140.66**	**107.64**	**96.44**
SD	**5.68**	**10.10**	**4.14**	**8.53**	**10.54**	**7.01**	**0.00**	**26.5**	**16.4**	**27.3**	**33.5**	**14.6**

Table A 3.52 Post-training Q_{twpot} vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	43	52	49	50		44	100	120.9	114.0	116.3		102.3
2	37	48	49	42	34	42	100	129.7	132.4	113.5	91.9	113.5
3	48	46	41		51	39	100	95.8	85.4		106.3	81.3
4	32	40	38	38	28	23	100	125.0	118.8	118.8	87.5	71.9
5	45	36	39	62	39	39	100	80.0	86.7	137.8	86.7	86.7
6	36	42	45	34	41	43	100	116.7	125.0	94.4	113.9	119.4
7	33	52	43	41	32	30	100	157.6	130.3	124.2	97.0	90.9
8	45	52	54	60	41	37	100	115.6	120.0	133.3	91.1	82.2
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**39.88**	**46.00**	**44.75**	**46.71**	**38.00**	**37.13**		**117.66**	**114.07**	**119.76**	**96.33**	**93.53**
SD	**6.10**	**6.14**	**5.57**	**10.90**	**7.53**	**7.20**		**23.0**	**18.3**	**14.3**	**10.2**	**16.7**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	38	39	42	23	25	20	100	102.6	110.5	60.5	65.8	52.6
2	46	53	57	61	42	30	100	115.2	123.9	132.6	91.3	65.2
3	33	49	51	51	40	33	100	148.5	154.5	154.5	121.2	100.0
4	46	51	51	53	40	39	100	110.9	110.9	115.2	87.0	84.8
5	53	61	54	71	46	42	100	115.1	101.9	134.0	86.8	79.2
6	59	56	98	64	59		100	94.9	166.1	108.5	100.0	
7	36	33	29	29	35	24	100	91.7	80.6	80.6	97.2	66.7
8	45	60	43		41		100	133.3	95.6		91.1	
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**6**
mean	**44.50**	**50.25**	**53.13**	**50.29**	**41.00**	**31.33**		**114.03**	**117.99**	**112.27**	**92.55**	**74.76**
SD	**8.73**	**9.84**	**20.17**	**17.97**	**9.59**	**8.48**		**19.2**	**29.2**	**32.6**	**15.5**	**16.8**

Table A 3.53 Pre-training Q_{twpot} vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	41	11	11	11	34	33	100	26.8	26.8	26.8	82.9	80.5
2	48	10	10	10	46	57	100	20.8	20.8	20.8	95.8	118.8
3	18	7	8	4	18	18	100	38.9	44.4	22.2	100.0	100.0
4	32	7	3	3	7	8	100	21.9	9.4	9.4	21.9	25.0
5	21	15	15	15	29	29	100	71.4	71.4	71.4	138.1	71.4
6	13	9	11	9	18	17	100	69.2	84.6	69.2	138.5	130.8
7	48	28	31	38	64	64	100	58.3	64.6	79.2	133.3	133.3
8	38	45	50	52	31	33	100	118.4	131.6	136.8	81.6	86.8
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**32**	**17**	**17**	**18**	**31**	**32**		**53.23**	**56.71**	**54.49**	**99.01**	**93.33**
SD	**14**	**13**	**16**	**18**	**18**	**19**		**33.4**	**40.1**	**42.9**	**39.3**	**36.0**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	13	14	7	31	6	5	100	107.7	53.8	238.5	46.2	38.5
2	27	18	20	13	18	18	100	66.7	74.1	48.1	66.7	66.7
3	21	10	14	23	27	20	100	47.6	66.7	109.5	128.6	95.2
4	14	17	18	34	35	27	100	121.4	128.6	242.9	250.0	192.9
5	32	64	30	23	50	23	100	200.0	93.8	71.9	156.3	71.9
6	46	81	48	57	85	50	100	176.1	104.3	123.9	184.8	108.7
7	17	20	20	22	33	33	100	117.6	117.6	129.4	194.1	194.1
8	26	46	27	48	34	20	100	176.9	103.8	184.6	130.8	76.9
n	**8**	**8**	**8**	**8**	**7**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**25**	**34**	**23**	**31**	**36**	**25**		**126.76**	**92.84**	**143.60**	**144.66**	**105.60**
SD	**11**	**27**	**12**	**15**	**24**	**13**		**54.3**	**25.9**	**72.2**	**67.1**	**58.0**

Table A 3.54 Post-training Q_{twpot} vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	45	24	17	24		45	100	53.3	37.8	53.3		100.0
2	48	37	46	58	63	27	100	77.1	95.8	120.8	131.3	56.3
3	28	23	1		30	26	100	82.1	3.6		107.1	92.9
4	6	11	4	5	4	7	100	183.3	66.7	83.3	66.7	116.7
5	5	4	3	5	6	6	100	80.0	60.0	100.0	120.0	120.0
6	22	25	24	61	18	20	100	113.6	109.1	277.3	81.8	90.9
7	29	12	26	36	62	55	100	41.4	89.7	124.1	213.8	189.7
8	39	28	45	57	82	36	100	71.8	115.4	146.2	210.3	92.3
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**28**	**21**	**21**	**35**	**38**	**28**		**87.84**	**72.25**	**129.29**	**132.99**	**107.33**
SD	**16**	**11**	**18**	**25**	**31**	**17**		**44.1**	**38.1**	**71.9**	**58.2**	**38.5**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	45	15	19	18	22	15	100	33.3	42.2	40.0	48.9	33.3
2	35	41	44	28	26	26	100	117.1	125.7	80.0	74.3	74.3
3	70	77	59	50	82	70	100	110.0	84.3	71.4	117.1	100.0
4	20	28	38	42	24	36	100	140.0	190.0	210.0	120.0	180.0
5	82	81	82	87	52	55	100	98.8	100.0	106.1	63.4	67.1
6	39	1	21	65	71		100	2.6	53.8	166.7	182.1	
7	13	19	21	21	24	18	100	146.2	161.5	161.5	184.6	138.5
8	39	57	42		82		100	146.2	107.7		210.3	
n	**7**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**6**
mean	**43**	**40**	**41**	**44**	**48**	**37**		**99.27**	**108.16**	**119.39**	**125.08**	**98.86**
SD	**25**	**29**	**22**	**25**	**27**	**22**		**53.7**	**50.4**	**61.3**	**61.3**	**53.0**

Table A 3.55 Pre-training Q_{twpot} vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	0.5	0.5	0.4	0.4	0.6	0.7	100	87.0	66.7	68.5	105.6	120.4
2	1.8	0.6	0.6	1.5	1.9	1.8	100	34.9	34.9	85.7	105.7	102.3
3	2.9	2.1	2.1	2.1	3.2	3.4	100	72.4	72.4	72.4	110.3	117.2
4	4.9	2.2	1.7	1.7	2.8	3.9	100	44.3	35.5	34.7	57.1	79.6
5	5.2	3.2	2.8	2.5	4.6	4.4	100	61.5	53.8	48.1	88.5	84.6
6	5.0	4.9	2.5	2.1	4.5	4.6	100	97.4	49.7	41.7	89.5	91.5
7	8.9	8.1	5.0	3.5	8.6	8.5	100	91.0	56.2	39.3	96.6	95.5
8	5.6	5.5	4.2	3.8	5.3	5.3	100	98.2	75.0	67.9	94.6	94.6
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**4.35**	**3.38**	**2.41**	**2.20**	**3.93**	**4.07**		**73.35**	**55.52**	**57.29**	**93.49**	**98.21**
SD	**2.59**	**2.63**	**1.61**	**1.10**	**2.45**	**2.36**		**24.4**	**15.4**	**18.6**	**16.7**	**14.5**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	4.2	3.4	2.5	1.9	3.07	2.8	100	81.0	59.5	45.2	73.1	66.7
2	1.6	2.1	1.7	1.9	1.8	1.9	100	131.3	106.3	118.8	112.5	118.8
3	2.5	1.5	4	3.2	3.2	3.6	100	60.0	160.0	128.0	128.0	144.0
4	2.6	2.5	2.5	1.9	2.7	3.3	100	96.2	96.2	73.1	103.8	126.9
5	3.2	2.8	3	3.1	3	3.3	100	87.5	93.8	96.9	93.8	103.1
6	2.6	2.5	2.5	1.9	2.7	3.3	100	96.2	96.2	73.1	103.8	126.9
7	5.2	2.1	1.9	1.9	4.3	4.7	100	40.4	36.5	36.5	82.7	90.4
8	1.6	1.5	1.4	1.5	1.5	1.3	100	93.8	87.5	93.8	93.8	81.3
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**2.94**	**2.30**	**2.44**	**2.16**	**2.78**	**3.03**		**85.77**	**91.98**	**83.16**	**98.93**	**107.25**
SD	**1.24**	**0.64**	**0.82**	**0.63**	**0.86**	**1.05**		**27.0**	**35.9**	**32.5**	**17.2**	**26.4**

Table A 3.56 Post-training Q_{twpot} vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.8	2.3	2.1	2.7	3.5	3.9	100	82.1	75.0	96.4	125.0	139.3
2	2.1	2.8	2.9	2.6	2.8	3.8	100	133.3	138.1	123.8	133.3	181.0
3	3.9	2.9	1.5			4.6	100	74.4	38.5			117.9
4	1.1	1.5	0.9	0.9	1.1	1.2	100	141.5	88.7	84.9	103.8	113.2
5	1.0	1.1	1.2	1.0	1.9	1.7	100	110.0	120.0	100.0	190.0	170.0
6	4.1	3.8	4.1	3.6	4.2	3.8	100	92.7	100.0	87.8	102.4	92.7
7	6.8	6.0	9.3	6.6	3.5	3.3	100	88.2	136.8	97.1	51.5	48.5
8	3.8	3.5	3.8	4.3	4.0	3.9	100	92.1	100.0	113.2	105.3	102.6
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**3.20**	**2.99**	**3.23**	**3.10**	**3.00**	**3.28**		**101.80**	**99.63**	**100.45**	**115.90**	**120.65**
SD	**1.91**	**1.53**	**2.72**	**1.98**	**1.14**	**1.19**		**24.3**	**33.3**	**13.8**	**41.8**	**42.7**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.6	2.7	2.5	2.3	2.4	1.8	100	103.8	96.2	88.5	92.3	69.2
2	1.3	1.1	1.1	1	1.2	1.6	100	84.6	84.6	76.9	92.3	123.1
3	1.6	1.7	1.2	1.6	1.3	1.3	100	106.3	75.0	100.0	81.3	81.3
4	3.5	3.2	2.1	3.1	3.5	2.5	100	91.4	60.0	88.6	100.0	71.4
5	8.8	8.2	8.8	8	6.6	6.5	100	93.2	100.0	90.9	75.0	73.9
6	5.1	4.9	3.1	2.8	3.2		100	96.1	60.8	54.9	62.7	
7	3.9	3.5	3.3	3	2.8	3.2	100	89.7	84.6	76.9	71.8	82.1
8	3.8	4.2	3.9		3.9		100	110.5	102.6		102.6	
n	**7**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**6**
mean	**4.00**	**3.69**	**3.25**	**3.11**	**3.11**	**2.82**		**96.96**	**82.98**	**82.38**	**84.75**	**83.48**
SD	**2.50**	**2.20**	**2.45**	**2.29**	**1.71**	**1.93**		**9.0**	**16.6**	**14.6**	**14.3**	**20.1**

Table A 3.57 Pre-training Q_{twpot} vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	46	48	54	69	50	48	100	104.3	117.4	150.0	108.7	104.3
2	24	28	38	38	27	30	100	73.7	158.3	63.2	71.1	78.9
3	37	42	57	49	45	42	100	113.5	154.1	132.4	121.6	113.5
4	40	48	45	44	32	36	100	120.0	112.5	110.0	80.0	90.0
5	44	49	50	49	45	44	100	111.4	102.0	100.0	91.8	89.8
6	42	47	40	40	33	35	100	111.9	95.2	95.2	78.6	83.3
7	51	60	50	54	37	36	100	117.6	98.0	105.9	72.5	70.6
8	33	46	47	51	34	36	100	139.4	142.4	154.5	103.0	109.1
n	**30**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**32.34**	**46.00**	**47.63**	**49.25**	**37.88**	**38.38**		**111.48**	**122.50**	**113.91**	**90.92**	**92.45**
SD	**8.37**	**8.90**	**6.52**	**9.68**	**7.94**	**5.80**		**18.4**	**25.5**	**30.5**	**18.6**	**15.2**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	40	34	34	96	25	24	100	85.0	85.0	240.0	62.5	60.0
2	40	39	42	31	35	27	100	97.5	105.0	77.5	87.5	67.5
3	31	40	52	40	33	33	100	129.0	167.7	129.0	106.5	106.5
4	25	26	26	31	29	41	100	104.0	104.0	124.0	116.0	164.0
5	32	40	40	36	30	26	100	125.0	125.0	112.5	93.8	81.3
6	24	27	28	33	29	41	100	112.5	116.7	137.5	120.8	170.8
7	45	49	55	55	50	46	100	108.9	122.2	122.2	111.1	102.2
8	31	54	57	66	52	43	100	174.2	183.9	212.9	167.7	138.7
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**33.50**	**38.63**	**41.75**	**48.50**	**35.38**	**35.13**		**117.01**	**126.19**	**144.46**	**108.24**	**111.37**
SD	**7.50**	**9.74**	**12.03**	**22.95**	**10.10**	**8.68**		**27.1**	**33.4**	**54.1**	**30.5**	**42.5**

Table A 3.58 Post-training Q_{twpot} vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	58	46	42	57	38	44	100	79.3	72.4	98.3	65.5	75.9
2	42	44	37	31	42	34	100	104.8	88.1	73.8	100.0	81.0
3	34	42	41			31	100	123.5	120.6			91.2
4	20	22	38	38	23	23	100	110.0	190.0	190.0	115.0	115.0
5	36	40	38	63	37	37	100	111.1	105.6	175.0	102.8	102.8
6	32	35	36	25	30	25	100	109.4	112.5	78.1	93.8	78.1
7	52	46	46	43	48	42	100	88.5	88.5	82.7	92.3	80.8
8	44	52	54	48	37	33	100	118.2	122.7	109.1	84.1	75.0
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**39.75**	**40.88**	**41.50**	**43.57**	**36.43**	**33.63**		**105.59**	**112.54**	**115.28**	**93.35**	**87.46**
SD	**11.97**	**9.09**	**6.00**	**13.61**	**8.06**	**7.41**		**14.8**	**35.9**	**47.7**	**15.6**	**14.5**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	39	40	40	39	33	38	100	102.6	102.6	100.0	84.6	97.4
2	38	40	48	45	29	24	100	105.3	126.3	118.4	76.3	63.2
3	55	51	48	63	45	51	100	92.7	87.3	114.5	81.8	92.7
4	32	39	35	34	23	24	100	121.9	109.4	106.3	71.9	75.0
5	51	58	51	65	46	33	100	113.7	100.0	127.5	90.2	64.7
6	36	42	98	65	50		100	116.7	272.2	180.6	138.9	0.0
7	36	38	54	52	32	32	100	105.6	150.0	144.4	88.9	88.9
8	27	59	33		31		100	218.5	122.2		114.8	
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**7**
mean	**39.25**	**45.88**	**50.88**	**51.86**	**36.13**	**33.67**		**122.11**	**133.75**	**127.38**	**93.43**	**68.85**
SD	**9.35**	**8.77**	**20.48**	**12.92**	**9.60**	**10.09**		**40.0**	**59.2**	**27.6**	**22.4**	**33.2**

Table A 3.59 Pre-training Q_{twpot} vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	11	12	11	12	13	11	100	109.1	100.0	109.1	118.2	100.0
2	19	16	16	16	18	17	100	84.2	84.2	84.2	94.7	89.5
3	23	17	17	17	20	27	100	85.0	135.0	115.0	87.0	117.4
4	28	15	13	13	23	25	100	89.3	46.4	82.1	53.6	89.3
5	33	28	25	23	30	29	100	84.8	75.8	69.7	90.9	87.9
6	41	47	41	38	35	41	100	114.6	100.0	92.7	85.4	100.0
7	64	48	28	44	49	49	100	75.0	43.8	68.8	76.6	76.6
8	44	41	32	48	29	29	100	93.2	72.7	109.1	65.9	65.9
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**33**	**28**	**23**	**26**	**27**	**29**		**91.91**	**82.23**	**91.33**	**84.02**	**90.81**
SD	**17**	**15**	**10**	**15**	**11**	**12**		**13.4**	**30.0**	**18.1**	**19.5**	**15.6**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	18	20	20	20	18	18	100	111.1	111.1	111.1	100.0	100.0
2	7	7	7	6	10	10	100	100.0	100.0	85.7	142.9	142.9
3	30	28	10	38	20	20	100	93.3	33.3	126.7	66.7	66.7
4	18	22	13	17	14	11	100	122.2	72.2	94.4	77.8	61.1
5	89	85	86	89	62	51	100	95.5	96.6	100.0	69.7	57.3
6	33	39	54	29	23	21	100	118.2	163.6	87.9	69.7	63.6
7	34	26	31	28	20	24	100	76.5	91.2	82.4	58.8	70.6
8	22	40	29	26	25	24	100	181.8	131.8	118.2	113.6	109.1
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**31**	**33**	**31**	**32**	**24**	**22**		**112.33**	**99.99**	**100.79**	**87.39**	**83.91**
SD	**25**	**23**	**27**	**25**	**16**	**13**		**31.7**	**38.7**	**16.3**	**29.0**	**30.4**

Table A 3.60 Post-training Q_{twpot} vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	30	29	29	37	27	34	100	96.7	96.7	123.3	90.0	113.3
2	29	25	23	22	26	22	100	86.2	79.3	75.9	89.7	75.9
3	21	23	7			27	100	109.5	33.3			128.6
4	6	9	5	6	6	7	100	150.0	83.3	100.0	100.0	116.7
5	9	9	10	10	13	12	100	100.0	111.1	111.1	144.4	133.3
6	27	26	27	23	27	23	100	96.3	100.0	85.2	100.0	85.2
7	44	39	66	47	35	30	100	88.6	150.0	106.8	79.5	68.2
8	30	32	33	35	28	26	100	106.7	110.0	116.7	93.3	86.7
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**25**	**24**	**25**	**26**	**23**	**23**		**104.25**	**95.47**	**102.71**	**99.57**	**100.98**
SD	**12**	**10**	**20**	**15**	**10**	**9**		**20.1**	**33.2**	**17.0**	**21.0**	**25.0**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	20	20	20	20	18	18	100	100.0	100.0	100.0	90.0	90.0
2	7	7	7	6	10	10	100	100.0	100.0	85.7	142.9	142.9
3	35	28	10	38	20	20	100	80.0	28.6	108.6	57.1	57.1
4	18	22	13	17	14	11	100	122.2	72.2	94.4	77.8	61.1
5	86	85	86	89	62	51	100	98.8	100.0	103.5	72.1	59.3
6	33	39	54	29	19		100	118.2	163.6	87.9	57.6	0.0
7	36	26	31	28	20	24	100	72.2	86.1	77.8	55.6	66.7
8	22	40	29		25		100	181.8	131.8		113.6	
n	**7**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**7**
mean	**34**	**33**	**31**	**32**	**24**	**22**		**109.16**	**97.79**	**93.98**	**83.33**	**68.15**
SD	**25**	**23**	**27**	**27**	**16**	**15**		**33.8**	**39.8**	**10.9**	**31.1**	**42.7**

Table A 3.61 Pre-training doublet vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Pre-Training
VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.9	0.8	0.9	0.6	1.6	1.6	100	28.28	31.72	21.03	55.17	55.17
2	8.1	8.3	1.7	3.5	4.5	8.3	100	102.47	20.99	43.21	55.56	102.47
3	2.5	1.9	1.3	1.3	3.1	2.6	100	75.60	52.00	52.00	122.80	104.00
4	4.0	1.3	0.8	0.5	1.4	1.3	100	33.33	18.94	13.13	35.35	32.07
5	2.3	1.3	1.1	1.1	1.5	1.6	100	56.52	46.96	46.96	63.04	69.57
6	2.6	2.9	2.8	2.2	2.3	2.1	100	112.94	109.80	86.27	90.20	82.35
7	8.2	7.2	4.6	3.4	5.3	5.5	100	87.80	56.10	41.46	64.63	67.07
8	3.0	3.8	3.3	3.6	3.1	2.7	100	126.67	110.00	120.00	103.33	90.00
n	**8**	**0**			**0**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**4.19**	**3.44**	**2.06**	**2.03**	**2.84**	**3.21**		**77.95**	**55.81**	**53.01**	**73.76**	**75.34**
SD	**2.50**	**2.84**	**1.37**	**1.32**	**1.45**	**2.45**		**36.29**	**36.05**	**34.79**	**29.03**	**24.50**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	3.7	1.4	2	2.5	2.6	3.6	100	37.84	54.05	67.57	70.27	97.30
2	3.3	2.7	1.9	2.6	2.7	2.9	100	81.82	57.58	78.79	81.82	87.88
3	2.7	2.2	2.2	2.5	4.1	2.7	100	81.48	81.48	92.59	151.85	100.00
4	2.6	2.4	2.3	3.0	1.8	2.2	100	92.31	88.46	115.38	69.23	84.62
5	6.4	4.4	2.2	1.2	3.2	4.8	100	68.75	34.38	18.75	75.00	75.00
6	4.7	4.0	1.9	1.8	5.1	5.2	100	85.01	40.01	37.51	107.51	110.01
7	5.8	2.2	2.2	1.8	2.3	3.1	100	38.07	38.45	31.17	38.93	53.82
8	2.3	1.9	1.8	1.7	2.4	2.4	100	75.25	80.80	73.24	101.50	100.47
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**			**8**	**8**
mean	**3.95**	**2.76**	**2.10**	**2.14**	**3.01**	**3.36**		**70.07**	**59.40**	**64.38**	**87.01**	**88.64**
SD	**1.54**	**1.07**	**0.17**	**0.60**	**1.08**	**1.11**		**20.97**	**21.59**	**32.95**	**33.62**	**17.79**

Table A 3.62 Post-training doublet vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Post-Training
VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.5	2.4	3.6	2.8	0.7	3.7	100	96.00	144.00	112.00	26.40	148.00
2	4.2	2.3	5.6	11.5	11.9	8.9	100	54.76	133.33	273.81	283.33	211.90
3	4.5	1.6	1.6			1.6	100	35.56	35.56			35.56
4	1.0	1.5	1.5	2.1	1.1	1.1	100	145.63	145.63	203.88	106.80	106.80
5	1.9	1.3	1.7	1.8	1.8	1.7	100	70.27	91.89	97.30	97.30	91.89
6	2.9	2.7	1.8	2.7	3.8	2.9	100	93.10	62.07	93.10	131.03	100.00
7	4.3	10.5	9.1	10.0	11.6	12.2	100	244.19	211.63	232.56	269.77	283.72
8	4.3	4.5	4.1	4.4	4.4	4.6	100	104.65	95.35	102.33	102.33	106.98
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**3.20**	**3.35**	**3.63**	**5.04**	**5.04**	**4.59**		**105.52**	**114.93**	**159.28**	**145.28**	**135.61**
SD	**1.32**	**3.06**	**2.67**	**4.01**	**4.78**	**4.27**		**65.24**	**55.40**	**75.47**	**95.32**	**78.15**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	3.8	4.7	4.2	4.1	4.1	2.7	100	123.68	110.53	107.89	107.89	71.05
2	3.7	3.1	4.2	4.2	4.9	3.4	100	83.78	113.51	113.51	132.43	91.89
3	6.3	6.6	5.1	5.9	7.7	6.3	100	104.76	80.95	93.65	122.22	100.00
4	2.1	2.5	2.3	2.9	3.6	2.4	100	119.05	109.52	138.10	171.43	114.29
5	8.1	7.4	7.2	8.7	6.6	8.5	100	91.36	88.89	107.41	81.48	104.94
6	3.2	1.9	2.2	2.1	1.8		100	59.38	68.75	65.63	56.25	
7	8.4	3.4	3.5	2	2.9	3.7	100	40.48	41.67	23.81	34.52	44.05
8	4.3	4.5	4.2		4.3		100	104.65	97.67		100.00	
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**6**
mean	**4.99**	**4.26**	**4.11**	**4.27**	**4.49**	**4.50**		**90.89**	**88.94**	**92.86**	**100.78**	**87.70**
SD	**2.33**	**1.94**	**1.60**	**2.38**	**1.91**	**2.40**		**28.87**	**24.72**	**37.46**	**43.51**	**25.91**

Table A 3.63 Pre-training doublet vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	77	80	86	87	77	77	100	103.90	111.69	112.99	100.00	100.00
2	72	75	76	77	73	70	100	104.17	105.56	106.94	101.39	97.22
3	64	73	89	89	62	66	100	114.06	139.06	139.06	96.88	103.13
4	75	79	72	67	60	75	100	105.33	96.00	89.33	80.00	100.00
5	72	76	78	86	75	71	100	105.56	108.33	119.44	104.17	98.61
6	82	83	85	93	80	73	100	101.22	103.66	113.41	97.56	89.02
7	80	84	93	81	74	80	100	105.00	116.25	101.25	92.50	100.00
8	87	95	96	96	92	87	100	109.20	110.34	110.34	105.75	100.00
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**			**8**	**8**
mean	**76.13**	**80.63**	**84.38**	**84.50**	**74.13**	**74.88**	**100.00**	**106.05**			**97.28**	**98.50**
SD	**7.08**	**6.95**	**8.43**	**9.32**	**10.08**	**6.53**		**3.92**	**12.71**	**14.38**	**8.15**	**4.17**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	72	88	79	79	76	76	100	122.22	109.72	109.72	105.56	105.56
2	86	88	84	84	77	82	100	102.33	97.67	97.67	89.53	95.35
3	69	78	69	71	71	71	100	113.04	100.00	102.90	102.90	102.90
4	89	91	87	94	80	70	100	102.25	97.75	105.62	89.89	78.65
5	82	89	87	77	89	88	100	108.54	106.10	93.90	108.54	107.32
6	62	78	73	72	65	65	100	127.03	118.92	116.22	104.86	105.94
7	84	88	98	95	90	86	100	104.76	116.67	113.10	107.14	102.38
8	82	91	87	89	86	84	100	110.98	106.10	108.54	104.88	102.44
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**			**8**	**8**
mean	**78.21**	**86.42**	**83.04**	**82.58**	**79.21**	**77.79**		**111.39**	**106.62**	**105.96**	**101.66**	**100.07**
SD	**9.54**	**5.24**	**9.10**	**9.45**	**8.89**	**8.39**		**9.12**	**8.15**	**7.56**	**7.56**	**9.39**

Table A 3.64 Post-training doublet vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	72	98	98	94	77	76	100	136.11	136.11	130.56	106.94	105.56
2	87	79	78	86	85	75	100	90.80	89.66	98.85	97.70	86.21
3	72	73	82			69	100	101.39	113.89			95.83
4	69	86	79	77	72	71	100	124.64	114.49	111.59	104.35	102.90
5	71	75	77	91	82	87	100	105.63	108.45	128.17	115.49	122.54
6	81	90	76	75	96	77	100	111.11	93.83	92.59	118.52	95.06
7	81	74	70	78	82	81	100	91.36	86.42	96.30	101.23	100.00
8	90	78	87	85	86	87	100	86.67	96.67	94.44	95.56	96.67
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**77.88**	**81.63**	**80.88**	**83.71**	**82.86**	**77.88**		**105.96**	**104.94**	**107.50**	**105.69**	**100.59**
SD	**7.97**	**8.90**	**8.46**	**7.30**	**7.54**	**6.71**		**17.41**	**16.58**	**16.17**	**8.66**	**10.61**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	86	85	75	74	85	72	100	98.84	87.21	86.05	98.84	83.72
2	75	84	83	87	83	73	100	112.00	110.67	116.00	110.67	97.33
3	82	92	81	92	82	80	100	112.20	98.78	112.20	100.00	97.56
4	89	90	93	90	92	87	100	101.12	104.49	101.12	103.37	97.75
5	75	84	81	96	75	79	100	112.00	108.00	112.00	100.00	105.33
6	92	79	95	95	79		100	85.87	103.26	103.26	85.87	0.00
7	71	90	78	85	72	73	100	126.76	109.86	119.72	101.41	102.82
8	96	78	98		86		100	81.25	102.08	0.00	89.58	0.00
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**83.25**	**85.25**	**85.50**	**88.43**	**81.75**	**77.33**		**103.75**	**103.04**	**93.79**	**98.72**	**73.06**
SD	**9.00**	**5.15**	**8.59**	**7.50**	**6.36**	**5.82**		**15.09**	**7.57**	**39.34**	**7.78**	**45.54**

Table A 3.65 Pre-training doublet vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	7	5	4	5	6	5	100	71.43	57.14	71.43	85.71	71.43
2	92	95	25	28	47	93	100	103.26	27.17	30.43	51.09	101.09
3	30	14	8	12	22	22	100	46.67	26.67	40.00	73.33	73.33
4	12	10	9	8	17	14	100	83.33	75.00	66.67	141.67	116.67
5	23	17	15	15	19	19	100	73.91	65.22	65.22	82.61	82.61
6	40	40	22	22	29	29	100	100.00	55.00	55.00	72.50	72.50
7	98	71	45	45	10	15	100	72.45	45.92	45.92	10.20	15.31
8	98	71	68	57	80	82	100	72.45	69.39	58.16	81.63	83.67
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**50.00**	**40.38**	**24.50**	**24.00**	**28.75**	**34.88**		**77.94**	**52.69**	**54.10**	**74.84**	**77.08**
SD	**39.45**	**34.38**	**21.85**	**18.49**	**24.22**	**33.33**		**17.94**	**18.26**	**14.27**	**36.72**	**29.52**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	56	28	22	19	30	29	100	50.00	39.29	33.93	53.57	51.79
2	34	38	43	30	32	38	100	111.76	126.47	88.24	94.12	111.76
3	34	36	37	64	51	50	100	105.88	108.82	188.24	150.00	147.06
4	38	54	24	57	16	30	100	142.11	63.16	150.00	42.11	78.95
5	76	56	53	44	36	34	100	73.68	69.74	57.89	47.37	44.74
6	34	36	37	36	51	50	100	105.88	108.82	105.88	150.00	147.06
7	41	40	32	32	45	43	100	97.56	78.05	78.05	109.76	104.88
8	75	55	52	42	36	33	100	73.33	69.33	56.00	48.00	44.00
n	**8**	**8**			**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**48.50**	**42.88**	**37.50**	**40.50**	**37.13**	**38.38**		**95.03**	**82.96**	**94.78**	**86.86**	**91.28**
SD	**18.17**	**10.63**	**11.55**	**14.66**	**11.79**	**8.43**		**28.52**	**29.07**	**51.82**	**45.87**	**43.00**

Table A 3.66 Post-training doublet vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	23	64	60	47	13	51	100	278.26	260.87	204.35	56.52	221.74
2	76	26	87	120	104	80	100	34.21	114.47	157.89	136.84	105.26
3	38	38	19			18	100	100.00	50.00			47.37
4	21	26	21	17	17	22	100	123.81	100.00	80.95	80.95	104.76
5	13	13	12	13	12	13	100	100.00	92.31	100.00	92.31	100.00
6	41	41	23	38	32	30	100	100.00	56.10	92.68	78.05	73.17
7	79	94	80	143	138	111	100	118.99	101.27	181.01	174.68	140.51
8	87	71	65	71	78	77	100	81.61	74.71	81.61	89.66	88.51
n	**8**	**8**	**8**	**7**	**7**	**8**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**47.25**	**46.63**	**45.88**	**64.14**	**56.29**	**50.25**		**117.11**	**106.22**	**128.36**	**101.29**	**110.16**
SD	**29.25**	**27.33**	**30.31**	**50.33**	**50.65**	**35.71**		**70.74**	**66.45**	**51.53**	**40.47**	**52.52**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	66	53	41	68	68	31	100	80.30	62.12	103.03	103.03	46.97
2	59	54	68	68	67	37	100	91.53	115.25	115.25	113.56	62.71
3	133	172	114	163	168	129	100	129.32	85.71	122.56	126.32	96.99
4	44	63	59	71	71	59	100	143.18	134.09	161.36	161.36	134.09
5	129	145	129	165	113	131	100	112.40	100.00	0.04	87.60	101.55
6	44	119	47	94	91		100	270.45	106.82	213.64	206.82	0.00
7	66	41	44	38	41	42	100	62.12	66.67	57.58	62.12	63.64
8	87	77	77		78		100	88.51	88.51		89.66	
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**7**	**8**	**7**
mean	**78.50**	**90.50**	**72.38**	**95.29**	**87.13**	**71.50**		**122.23**	**94.90**	**110.49**	**118.81**	**72.28**
SD	**35.19**	**48.63**	**32.93**	**49.68**	**38.67**	**46.27**		**65.47**	**24.25**	**68.86**	**46.18**	**43.43**

Table A 3.67 Pre-training doublet vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.4	1.6	0.8	0.6	1.2	2.1	100	66.10	33.90	24.15	49.15	88.98
2	3.3	2.4	2.2	1.4	1.8	2.1	100	72.73	66.67	42.42	54.55	63.64
3	5.2	3.9	3.4	2.6	4.7	4.2	100	75.00	65.38	50.00	90.38	80.77
4	5.1	3.4	2.1	2.3	2.6	2.4	100	196.15	79.62	130.77	88.85	47.25
5	1.6	1.1	1.3	1.0	1.1	1.3	100	69.75	80.25	61.73	80.25	80.25
6	4.7	5.1	5.1	4.5	4.2	4.7	100	108.51	108.51	95.74	89.36	100.00
7	10.5	10.1	7.9	7.2	7.6	8.4	100	127.85	132.91	106.33	96.20	80.00
8	5.2	5.3	4.7	5.1	3.0	4.2	100	101.92	90.38	98.08	57.69	80.77
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**4.75**	**4.11**	**3.43**	**3.09**	**3.27**	**3.68**		**102.25**	**82.20**	**76.15**	**75.80**	**77.71**
SD	**2.70**	**2.86**	**2.37**	**2.31**	**2.19**	**2.27**		**43.90**	**29.76**	**36.82**	**18.87**	**15.95**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	5.7	3.5	3.0	5.5	4.8	3.8	100	61.40	52.63	96.49	84.21	66.67
2	3.2	1.9	2.8	2.7	3.7	3.1	100	168.42	147.37	194.74	142.11	96.88
3	3.8	2.2	1.4	1.7	2.5	3.2	100	57.89	36.84	44.74	65.79	84.21
4	3.5	1.8	2.7	1.7	2.5	4.2	100	51.43	77.14	48.57	71.43	120.00
5	3.8	3.9	3.2	3.4	3.9	3.8	100	102.63	84.21	100.00	89.47	100.00
6	2.4	1.2	0.7	0.7	1.1	2.0	100	85.01	45.00	30.02	50.00	85.01
7	5.7	4.9	4.5	2.7	4.7	4.7	100	108.89	126.67	104.44	104.44	82.46
8	4.1	3.6	3.5	3.2	5.5	4.3	100	86.79	86.20	132.77	104.04	104.04
n	**8**	**8**			**8**	**7**	**8**	**8**			**8**	**8**
mean	**4.02**	**2.87**	**2.73**	**2.71**	**3.58**	**3.54**		**90.31**	**82.01**	**93.97**	**88.94**	**92.41**
SD	**1.16**	**1.28**	**1.19**	**1.44**	**1.47**	**0.87**		**37.87**	**38.89**	**53.97**	**28.48**	**16.29**

Table A 3.68 Post-training doublet vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	4.4		3.4	1.9	0.66	3.8	100		77.27	43.18	15.00	86.36
2	2.1	4.2	4.7	4.9	5	4.6	100	50.00	111.90	119.05	116.67	219.05
3	4.8	4.3	1.6			3.8	100	89.58	33.33			79.17
4	1.9	1.5	1.1	1.2	1.2	1.5	100	78.95	57.89	63.16	63.16	78.95
5	1.1	0.8	0.7	1.1	1.3	1.4	100	72.73	63.64	127.27	100.00	127.27
6	5.1	4.5	4.5	4.9	4.6	5.5	100	107.84	90.20	96.08	88.24	107.84
7	7.4	8.9	8.3	5.2	7.1	8.5	100	107.23	89.16	102.41	85.54	114.86
8	3.6	4.5	4.1	4.2	3.8	4.1	100	125.00	113.89	105.56	113.89	113.89
n	**8**	**7**	**8**	**7**	**7**	**8**	**8**	**7**	**8**	**7**	**7**	**8**
mean	**3.80**	**4.10**	**3.55**	**3.34**	**3.38**	**4.16**		**90.19**	**79.66**	**93.81**	**83.21**	**115.92**
SD	**2.06**	**2.62**	**2.48**	**1.86**	**2.40**	**2.44**		**25.37**	**27.50**	**30.21**	**35.18**	**45.40**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	3.4	3.2	3.2	2.2	4	4.1	100	94.12	94.12	64.71	117.65	120.59
2	2.8	1	1.1	1.8	0.7	2.2	100	35.71	39.29	64.29	25.00	78.57
3	4.3	3.4	1.8	3.2	3.9	3.4	100	79.07	41.86	74.42	90.70	79.07
4	3.7	3.7	2.9	3.9	4	2.9	100	100.00	78.38	105.41	108.11	78.38
5	4.1	5.4	6.2	6.6	5.3	6.5	100	131.71	151.22	160.98	129.27	158.54
6	2.1	2.8	1.6	1.2	2.5		100	133.33	76.19	57.14	119.05	0.00
7	4.3	3.4	3.1	3.2	3.5	3.6	100	79.07	72.09	74.42	81.40	83.72
8	3.6	4.5	4.4		3.7		100	125.00	122.22	0.00	102.78	0.00
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**3.54**	**3.43**	**3.04**	**3.16**	**3.45**	**3.78**		**97.25**	**84.42**	**75.17**	**96.74**	**74.86**
SD	**0.77**	**1.28**	**1.66**	**1.78**	**1.35**	**1.48**		**33.22**	**37.97**	**45.48**	**32.90**	**54.01**

Table A 3.69 Pre-training doublet vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	67	68	76	78	69	62	100	101.49	113.43	116.42	102.99	92.54
2	74	79	76	89	75	72	100	106.76	102.70	120.27	101.35	97.30
3	62	76	89	95	58	63	100	122.58	143.55	153.23	93.55	101.61
4	82	74	76	75	80	75	100	90.24	92.68	91.46	97.56	91.46
5	72	76	96	87	75	72	100	105.56	133.33	120.83	104.17	100.00
6	74	86	86	98	80	74	100	116.22	116.22	132.43	108.11	100.00
7	82	98	96	96	82	85	100	119.51	117.07	117.07	100.00	103.66
8	75	90	98	96	80	81	100	120.00	130.67	128.00	106.67	108.00
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**			**8**	**8**
mean	**73.50**	**80.88**	**86.63**	**89.25**	**74.88**	**73.00**	**100.00**	**110.29**	**118.71**	**122.46**	**101.80**	**99.32**
SD	**6.80**	**9.76**	**9.64**	**8.75**	**8.01**	**7.89**		**11.21**	**16.67**	**17.36**	**4.78**	**5.51**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	77	73	91	98	73	78	100	94.81	118.18	127.27	94.81	101.30
2	74	76	78	82	70	73	100	102.70	105.41	110.81	94.59	98.65
3	73	89	78	84	77	72	100	121.92	106.85	115.07	105.48	98.63
4	74	80	71	79	75	82	100	108.11	95.95	106.76	101.35	110.81
5	74	84	85	82	80	84	100	113.51	114.86	110.81	108.11	113.51
6	63	80	72	72	62	66	100	125.79	113.16	113.16	97.37	103.69
7	90	92	97	97	94	90	100	102.22	107.78	107.78	104.44	100.00
8	74	84	86	88	84	81	100	113.51	116.22	118.92	113.51	109.46
n	**8**	**8**			**8**	**8**	**8**	**8**			**8**	**8**
mean	**74.92**	**82.21**	**82.21**	**85.21**	**76.83**	**78.21**		**110.32**	**109.80**	**113.82**	**102.46**	**104.51**
SD	**7.30**	**6.36**	**9.18**	**8.90**	**9.64**	**7.73**		**10.44**	**7.29**	**6.69**	**6.71**	**5.92**

Table A 3.70 Post-training doublet vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	98		98	94	77	76	100		100.00	95.92	78.57	77.55
2	88	74	79	84	75	74	100	84.09	89.77	95.45	85.23	84.09
3	75	75	82			76	100	100.00	109.33			101.33
4	74	72	69	70	72	71	100	97.30	93.24	94.59	97.30	95.95
5	74	81	93	75	79	88	100	109.46	125.68	101.35	106.76	118.92
6	82	82	70	80	74	77	100	100.00	85.37	97.56	90.24	93.90
7	93	90	95	81	87	86	100	96.77	102.15	87.10	93.55	92.47
8	87	82	87	85	83	84	100	94.25	100.00	97.70	95.40	96.55
n	**8**	**7**	**8**	**7**	**7**	**8**	**8**	**7**	**8**	**7**	**7**	**8**
mean	**83.88**	**79.43**	**84.13**	**81.29**	**78.14**	**79.00**		**97.41**	**100.69**	**95.67**	**92.44**	**95.10**
SD	**9.16**	**6.21**	**11.06**	**7.65**	**5.30**	**6.16**		**7.60**	**12.60**	**4.37**	**9.02**	**12.23**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	85	80	80	83	85	80	100	94.12	94.12	97.65	100.00	94.12
2	81	84	88	90	88	74	100	103.70	108.64	111.11	108.64	91.36
3	93	98	92	94	93	92	100	105.38	98.92	101.08	100.00	98.92
4	74	75	93	80	71	92	100	101.35	125.68	108.11	95.95	124.32
5	85	88	97	98	98	87	100	103.53	114.12	98.82	115.29	102.35
6	98	98	98	78	72		100	100.00	100.00	79.59	73.47	0.00
7	76	79	84	90	77	76	100	103.95	110.53	118.42	101.32	100.00
8	97	92	98		79		100	94.85	101.03	0.00	81.44	0.00
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**86.13**	**86.75**	**91.25**	**87.57**	**82.88**	**83.50**		**100.86**	**106.63**	**89.35**	**97.01**	**76.38**
SD	**9.14**	**8.73**	**6.73**	**7.44**	**9.79**	**7.94**		**4.27**	**10.21**	**37.88**	**13.65**	**48.18**

Table A 3.71 Pre-training doublet vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	5	4	3	1	3	5	100	80.00	60.00	20.00	60.00	100.00
2	49	35	32	24	32	32	100	71.43	65.31	48.98	65.31	65.31
3	47	25	23	21	31	29	100	53.19	48.94	44.68	65.96	61.70
4	56	75	38	68	46	42	100	133.93	67.86	121.43	82.14	75.00
5	22	17	19	15	17	17	100	77.27	86.36	68.18	77.27	77.27
6	67	73	73	89	82	67	100	108.96	108.96	132.84	122.39	100.00
7	105	115	111	121	101	93	100	109.52	105.71	115.24	96.19	88.57
8	63	79	83	91	47	54	100	125.40	131.75	144.44	74.60	85.71
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**51.75**	**52.88**	**47.75**	**53.75**	**44.88**	**42.38**		**94.96**			**80.48**	**81.70**
SD	**30.03**	**38.19**	**37.16**	**44.07**	**32.56**	**28.36**		**28.51**	**28.77**	**47.00**	**20.39**	**14.47**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	61	43	46	37	53	59	100	70.49	75.41	60.66	86.89	96.72
2	24	32	27	40	25	31	100	133.33	112.50	166.67	104.17	129.17
3	50	66	47	33	18	40	100	132.00	94.00	66.00	36.00	80.00
4	33	37	33	29	29	52	100	112.12	100.00	87.88	87.88	157.58
5	49	42	57	53	42	59	100	85.71	116.33	108.16	85.71	120.41
6	50	66	33	33	39	46	100	132.00	66.00	66.00	78.00	92.00
7	84	80	81	76	80	80	100	95.24	96.43	90.48	95.24	95.24
8	48	41	55	53	42	58	100	85.42	114.58	110.42	87.50	120.83
n	**8**	**8**			**8**	**8**	**8**	**8**			**8**	**8**
mean	**49.88**	**50.88**	**47.38**	**44.25**	**41.00**	**53.13**		**105.79**	**96.91**	**94.53**	**82.67**	**111.49**
SD	**17.92**	**17.29**	**17.37**	**15.66**	**19.27**	**14.78**		**24.92**	**18.39**	**34.80**	**20.35**	**25.23**

Table A 3.72 Post-training doublet vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	65		61	47	12	50	100		93.85	72.31	18.46	76.92
2	48	53	49	69	41	43	100	110.42	102.08	143.75	85.42	89.58
3	52	53	19			45	100	101.92	36.54			86.54
4	34	21	15	18	17	22	100	61.76	44.12	52.94	50.00	64.71
5	22	17	9	22	21	29	100	77.27	40.91	100.00	95.45	131.82
6	57	56	47	54	52	51	100	98.25	82.46	94.74	91.23	89.47
7	92	90	115	79	79	92	100	97.83	125.00	85.87	85.87	100.00
8	66	72	65	71	61	66	100	109.09	98.48	107.58	92.42	100.00
n	**8**	**7**	**8**	**7**	**7**	**8**	**8**	**7**	**8**	**7**	**7**	**8**
mean	**54.50**	**51.71**	**47.50**	**51.43**	**40.43**	**49.75**		**93.79**	**77.93**	**93.88**	**74.12**	**92.38**
SD	**21.31**	**25.97**	**34.64**	**24.02**	**25.10**	**21.78**		**17.85**	**33.21**	**28.63**	**28.95**	**19.74**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	44	48	49	29	46	37	100	109.09	111.36	65.91	104.55	84.09
2	28	24	22	24	22	22	100	85.71	78.57	85.71	78.57	78.57
3	53	70	34	49	65	52	100	132.08	64.15	92.45	122.64	98.11
4	39	46	41	46	35	41	100	117.95	105.13	117.95	89.74	105.13
5	107	112	87	142	119	98	100	104.67	81.31	0.04	111.21	91.59
6	50	70	64	40	48		100	140.00	128.00	80.00	96.00	0.00
7	48	50	56	59	49	49	100	104.17	116.67	122.92	102.08	102.08
8	72	70	77		60		100	97.22	106.94	0.00	83.33	0.00
n	**8**	**8**	**8**	**7**	**8**	**6**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**55.13**	**61.25**	**53.75**	**55.57**	**55.50**	**49.83**		**111.36**	**99.02**	**70.62**	**98.52**	**69.95**
SD	**24.43**	**25.99**	**21.84**	**39.92**	**28.97**	**25.86**		**17.94**	**21.88**	**47.45**	**14.66**	**44.06**

Table A 3.73 Pre-training 20Hz Tetani vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Pre-Training
VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	2.5	0.9	0.4	0.4	1.4	1.4	100	36.8	17.2	17.2	54.8	56.4
2	10.5	6.5	5.3	3.2	4.4	6.5	100	61.9	50.5	30.5	41.9	61.9
3	5.4	4.7	3.1	3.4	4.4	5.8	100	87.0	56.5	62.0	80.4	106.5
4	1.9	0.8	0.6	0.5	0.9	0.5	100	42.3	30.2	27.5	47.1	27.5
5	4.8	1.1	1.2	1.1	4.4	4.8	100	22.9	25.0	22.9	91.7	100.0
6	10.2	2.7	2.0	1.7	7.8	9.4	100	26.5	19.9	16.7	76.5	92.2
7	7.1	5.3	3.2	1.5	4.0	5.7	100	74.6	45.1	21.1	56.3	80.3
8	2.2	1.1	1.6	1.3	1.5	1.4	100	50.0	72.7	59.1	68.2	63.6
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**5.58**	**2.89**	**2.18**	**1.64**	**3.59**	**4.87**		**50.25**	**39.63**	**32.13**	**64.61**	**73.55**
SD	**3.44**	**2.30**	**1.63**	**1.11**	**2.28**	**3.04**		**22.79**	**19.73**	**18.18**	**17.42**	**26.25**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	0.9	0.7	0.6	0.6	0.3	0.8	100	82.4	71.8	70.6	32.9	94.1
2	3.6	2.5	1.1	1.1	2.3	2.4	100	69.4	30.6	30.6	63.9	66.7
3	11.4	8.1	4.7	3.9	5.6	5.7	100	71.1	41.2	34.2	49.1	50.0
4	3.4	1.7	1.1	1.2	1.1	2.2	100	50.0	32.4	35.3	32.4	64.7
5	6.5	2.8	1.8	0.9	4.0	4.1	100	43.1	27.7	13.7	61.5	63.1
6	4.7	4.4	3.1	2.7	4.2	3.9	100	92.5	65.0	57.2	88.3	82.6
7	2.6	2.7	1.8	1.9	2.7	2.5	100	103.8	69.2	72.7	103.8	96.2
8	3.7	2.1	1.1	1.1	2.7	3.0	100	58.1	30.0	29.0	74.2	80.7
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**4.59**	**3.12**	**1.91**	**1.67**	**2.86**	**3.09**		**71.29**	**45.98**	**42.90**	**63.27**	**74.74**
SD	**3.19**	**2.26**	**1.35**	**1.12**	**1.72**	**1.60**		**20.91**	**19.29**	**21.34**	**25.27**	**16.23**

Table A 3.74 Post-training 20Hz Tetani vastus medialis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Post-Training
VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	1.8	2.1	2.9			1.9	100	116.7	161.1			105.6
2	6.5	2.3	7.7	2.8	8.4	2.6	100	35.4	118.5	43.1	129.2	40.0
3	1.5	1.6	1.2			2.1	100	106.7	80.0			140.0
4	0.9	0.7	0.7	0.6	1.2	0.9	100	77.6	77.6	70.6	141.2	105.9
5	1.2	1.5	2.2	2.1	2.9	3.3	100	125.0	183.3	175.0	241.7	275.0
6	3.1	3.8	2.9	3.1	3.9		100	122.6	93.5	100.0	125.8	0.0
7	5.9	2.7	8.9	5.1	10.9	13.7	100	45.8	150.8	86.4	184.7	232.2
8	1.7	2.2	1.9	1.7	3.3	1.7	100	129.4	111.8	100.0	194.1	100.0
n	**8**	**8**	**8**	**6**	**6**	**7**	**8**	**8**	**8**	**6**	**6**	**8**
mean	**2.82**	**2.11**	**3.55**	**2.57**	**5.10**	**4.08**		**94.89**	**122.09**	**95.85**	**169.46**	**124.83**
SD	**2.19**	**0.92**	**3.05**	**1.52**	**3.72**	**4.78**		**37.28**	**39.25**	**44.30**	**45.56**	**91.37**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	1.1	0.3	0.0	0.6		2.3	100	27.3	3.6	54.5		209.1
2	1.4	1.0	1.6	1.4	1.3	1.3	100	71.4	114.3	100.0	92.9	92.9
3	3.0	2.5	2.8	1.7			100	83.3	93.3	56.7		0.0
4	2.8	1.3	1.8	1.6	1.1	1.0	100	46.4	64.3	57.1	39.3	35.7
5	3.4	2.6	2.2	2.3	3.2	4.4	100	76.5	64.7	67.6	94.1	129.4
6	3.0	1.6	1.7	2.3	3.4		100	53.3	56.7	76.7	113.3	0.0
7	2.9	2.5	2.1	1.9	4.0	3.9	100	86.2	72.4	65.5	137.9	134.5
8	1.3	1.9	1.6		1.9		100	146.2	123.1		146.2	0.0
n	**8**	**8**	**8**	**7**	**6**	**5**	**8**	**8**	**8**	**7**	**6**	**8**
mean	**2.36**	**1.71**	**1.73**	**1.69**	**2.48**	**2.58**		**73.83**	**74.05**	**68.31**	**103.95**	**75.19**
SD	**0.93**	**0.82**	**0.79**	**0.59**	**1.21**	**1.52**		**35.51**	**37.49**	**15.98**	**38.54**	**78.57**

Table A 3.75 Pre-training 20Hz Tetani vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	67	67	76	81	67	67	100	100.0	113.4	120.9	100.0	100.0
2	77	87	85	81	67	66	100	113.0	110.4	105.2	87.0	85.7
3	78	83	89	88	87	85	100	106.4	114.1	112.8	111.5	109.0
4	75	86	89	94	66	63	100	114.7	118.7	125.3	88.0	84.0
5	68	70	79	83	71	69	100	102.9	116.2	122.1	104.4	101.5
6	85	96	87	85	71	73	100	112.9	102.4	100.0	83.5	85.9
7	76	84	93	85	80	66	100	110.5	122.4	111.8	105.3	86.8
8	83	96	96	98	85	83	100	115.7	115.7	118.1	102.4	100.0
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**76.13**	**83.63**	**86.75**	**86.88**	**74.25**	**71.50**		**109.52**	**114.14**	**114.53**	**97.77**	**94.11**
SD	**6.33**	**10.60**	**6.69**	**6.17**	**8.50**	**8.25**		**5.76**	**5.95**	**8.74**	**10.21**	**9.54**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	66	69	75	78	67	66	100	104.5	113.6	118.2	101.5	100.0
2	83	79	70	71	73	82	100	95.2	84.3	85.5	88.0	98.8
3	72	81	86	85	73	74	100	112.5	119.4	118.1	101.4	102.8
4	78	80	86	86	80	70	100	102.6	110.3	110.3	102.6	89.7
5	66	84	88	77	87	79	100	127.3	133.3	116.7	131.8	119.7
6	73	80	82	81	77	74	100	109.6	112.3	111.0	105.5	101.4
7	66	78	88	88	67	69	100	118.2	133.3	133.3	101.5	104.5
8	76	79	82	83	76	79	100	103.9	107.9	109.2	100.0	103.9
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**72.50**	**78.75**	**82.13**	**81.13**	**75.00**	**74.13**		**109.22**	**114.32**	**112.78**	**104.03**	**102.61**
SD	**6.32**	**4.33**	**6.51**	**5.59**	**6.65**	**5.59**		**10.06**	**15.63**	**13.41**	**12.37**	**8.33**

Table A 3.76 Post-training 20Hz Tetani vastus medialis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	72	98	98			72	100	136.1	136.1	0.0	0.0	100.0
2	82	79	72	78	71	66	100	96.3	87.8	95.1	86.6	80.5
3	69	69	88			79	100	100.0	127.5	0.0	0.0	114.5
4	76	77	73	74	70	72	100	101.3	96.1	97.4	92.1	94.7
5	82	82	98	98	85	71	100	100.0	119.5	119.5	103.7	86.6
6	80	74	77	74	75		100	92.5	96.3	92.5	93.8	0.0
7	81	62	74	74	75	69	100	76.5	91.4	91.4	92.6	85.2
8	90	73	72	73	79	76	100	81.1	80.0	81.1	87.8	84.4
n	**8**	**8**	**8**	**6**	**6**	**7**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**79.00**	**76.75**	**81.50**	**78.50**	**75.83**	**72.14**		**97.99**	**104.33**	**72.12**	**69.56**	**80.74**
SD	**6.57**	**10.58**	**11.44**	**9.71**	**5.53**	**4.30**		**17.93**	**20.52**	**45.80**	**43.24**	**34.42**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	72	71	82	74	73	72	100	98.6	113.9	102.8	101.4	100.0
2	72	84	75	69	70	76	100	116.7	104.2	95.8	97.2	105.6
3	88	90	91	91			100	102.3	103.4	103.4		
4	70	77	83	85	76	78	100	110.0	118.6	121.4	108.6	111.4
5	83	84	82	82	85	78	100	101.2	98.8	98.8	102.4	94.0
6	82	89	89	87	89		100	108.5	108.5	106.1	108.5	
7	85	72	82	85	70	74	100	84.7	96.5	100.0	82.4	87.1
8	90	72	71		85		100	80.0	78.9		94.4	
n	**8**	**8**	**8**	**7**	**7**	**5**	**8**	**8**	**8**	**7**	**7**	**5**
mean	**80.25**	**79.88**	**81.88**	**81.86**	**78.29**	**75.60**		**100.25**	**102.84**	**104.05**	**99.28**	**99.60**
SD	**7.83**	**7.85**	**6.56**	**7.71**	**7.91**	**2.61**		**12.49**	**12.16**	**8.36**	**9.13**	**9.55**

Table A 3.77 Pre-training 20Hz Tetani vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	21	5	3	4	5	5	100	23.8	14.3	19.0	23.8	23.8
2	147	60	57	24	59	69	100	40.8	38.8	16.3	40.1	46.9
3	71	47	38	39	49	51	100	66.2	53.5	54.9	69.0	71.8
4	10	8	5	6	15	8	100	80.0	50.0	60.0	150.0	80.0
5	108	16	20	21	114	108	100	14.8	18.5	19.4	105.6	100.0
6	145	21	14	21	21	103	100	14.5	9.7	14.5	14.5	71.0
7	99	47	42	13	46	127	100	47.5	42.4	13.1	46.5	128.3
8	41	26	28	22	32	33	100	63.4	68.3	53.7	78.0	80.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**80.25**	**28.75**	**25.88**	**18.75**	**42.63**	**63.00**		**43.88**	**36.93**	**31.38**	**65.94**	**75.30**
SD	**53.24**	**20.24**	**18.95**	**11.16**	**34.17**	**46.58**		**24.84**	**20.90**	**20.74**	**45.13**	**31.51**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	26	7	7	7	9	14	100	26.9	26.9	26.9	34.6	53.8
2	30	27	9	9	27	43	100	90.0	30.0	30.0	90.0	143.3
3	55	77	84	65	52	42	100	140.0	152.7	118.2	94.5	76.4
4	50	18	16	16	12	30	100	36.0	32.0	32.0	24.0	60.0
5	53	38	31	6	34	44	100	71.7	58.5	11.3	64.2	83.0
6	68	44	32	30	32	31	100	64.7	47.1	44.1	47.1	45.6
7	51	65	34	33	54	51	100	127.5	66.7	64.7	105.9	100.0
8	67	47	40	54	27	50	100	70.1	59.7	80.6	40.3	74.6
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**50.00**	**40.38**	**31.63**	**27.50**	**30.88**	**38.13**		**78.37**	**59.20**	**50.98**	**62.57**	**79.60**
SD	**15.23**	**23.31**	**24.44**	**22.37**	**16.29**	**12.41**		**39.79**	**40.68**	**35.01**	**30.84**	**31.01**

Table A 3.78 Post-training 20Hz Tetani vastus medialis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VM

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	21	31	58			19	100	147.6	276.2	0.0	0.0	90.5
2	61	26	62	25	67	20	100	42.6	101.6	41.0	109.8	32.8
3	15	15	19			44	100	100.0	126.7	0.0	0.0	293.3
4	13	10	11	110	21	10	100	76.9	84.6	846.2	161.5	76.9
5	13	15	36	37	26	8	100	115.4	276.9	284.6	200.0	61.5
6	39	40	30	32	38		100	102.6	76.9	82.1	97.4	
7	64	48	134	181	107	107	100	75.0	209.4	282.8	167.2	167.2
8	24	45	42	40	45	23	100	187.5	175.0	166.7	187.5	95.8
n	**8**	**8**	**8**	**6**	**6**	**7**	**8**	**8**	**8**	**8**	**8**	**7**
mean	**31.25**	**28.75**	**49.00**	**70.83**	**50.67**	**33.00**		**105.95**	**165.92**	**212.91**	**115.44**	**116.87**
SD	**21.06**	**14.66**	**38.54**	**62.25**	**32.00**	**34.68**		**45.25**	**81.64**	**280.44**	**79.42**	**88.07**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	12	6	7	6		32	100	50.0	58.3	50.0		266.7
2	12	10	19	18	16	16	100	83.3	158.3	150.0	133.3	133.3
3	58	56	57	49			100	96.6	98.3	84.5		
4	11	20	17	34	14	17	100	181.8	154.5	309.1	127.3	154.5
5	51	53	27	53	45	72	100	103.9	52.9	103.9	88.2	141.2
6	49	17	13	59	56		100	34.7	26.5	120.4	114.3	
7	54	49	46	38	34	42	100	90.7	85.2	70.4	63.0	77.8
8	23	41	39		38		100	178.3	169.6	0.0	165.2	0.0
n	**8**	**8**	**8**	**7**	**6**	**5**	**8**	**8**	**8**	**8**	**6**	**6**
mean	**33.75**	**31.50**	**28.13**	**36.71**	**33.83**	**35.80**		**102.42**	**100.46**	**111.03**	**115.22**	**128.92**
SD	**21.07**	**20.40**	**17.55**	**19.22**	**16.40**	**22.96**		**53.36**	**54.49**	**92.04**	**35.87**	**88.36**

Table A 3.79 Pre-training 20Hz Tetani vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Pre-Training
VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	1.6	0.9	0.6	0.3	0.4	1.1	100	60.6	36.8	20.6	23.2	73.5
2	5.2	4.4	2.7	2.7	3.1	4.7	100	84.0	51.9	51.9	59.1	90.8
3	4.8	3.0	2.7	1.1	2.1	3.7	100	61.5	56.6	22.9	44.3	76.3
4	5.5	2.7	2.1	2.8	4.4	3.4	100	49.8	37.6	50.5	79.8	61.8
5	5.9	4.2	3.4	2.7	3.6	5.1	100	71.2	57.6	45.8	61.0	86.4
6	5.9	5.2	4.6	4.0	4.8	4.7	100	88.1	78.0	67.5	81.4	79.7
7	8.9	5.9	6.0	6.1	7.2	7.4	100	66.3	67.4	68.5	80.9	83.1
8	2.7	2.3	1.7	1.9	2.6	2.2	100	85.2	63.0	70.4	96.3	81.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**5.06**	**3.58**	**2.97**	**2.70**	**3.52**	**4.30**		**70.85**	**56.11**	**49.76**	**65.75**	**79.15**
SD	**2.21**	**1.64**	**1.70**	**1.78**	**2.03**	**1.91**		**13.80**	**14.08**	**19.58**	**23.72**	**8.88**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	3.5	2.8	2.4	1.2	2.7	5.4	100	80.0	68.6	34.3	77.1	154.3
2	4.3	3.5	2.1	2.1	2.9	3.2	100	81.4	48.8	48.8	67.4	74.4
3	2.2	1.7	1.7	1.6	1.9	3.1	100	77.3	77.3	72.7	86.4	140.9
4	3.4	2.7	2.6	1.5	2.5	2.5	100	79.4	76.5	44.1	73.5	73.5
5	4.2	3.4	3.8	2.0	3.2	5.1	100	81.0	90.5	47.6	76.2	121.4
6	3.7	3.0	2.7	2.1	2.6	3.0	100	80.7	74.2	58.1	71.0	80.7
7	4.1	3.8	2.6	2.7	2.9	3.4	100	92.7	63.4	65.9	70.7	82.9
8	4.4	3.5	2.0	2.0	2.4	2.6	100	80.0	45.6	46.1	54.2	58.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**3.72**	**3.05**	**2.49**	**1.91**	**2.64**	**3.66**		**81.55**	**68.11**	**52.20**	**72.08**	**98.33**
SD	**0.72**	**0.67**	**0.63**	**0.46**	**0.39**	**1.12**		**4.67**	**15.08**	**12.52**	**9.21**	**35.46**

Table A 3.80 Post-training 20Hz Tetani vastus lateralis muscle M-wave amplitude evoked via magnetic stimulation and expressed as a percentage of pre-exercise

Post-Training
VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	1.7	1.9	2.3	1.7	1.8	1.8	100	111.8	135.3	100.0	105.9	105.9
2	4.2	4.2	5.4	4.5	4.3	4.2	100	100.0	128.6	107.1	102.4	100.0
3	2.1	2.1	3.7			4.1	100	100.0	176.2			195.2
4	1.5	1.5	1.2	1.2	1.3	1.4	100	100.0	80.0	80.0	86.7	93.3
5	3.9	1.4	2.1	2.2	3.8	4.6	100	35.9	53.8	56.4	97.4	117.9
6	4.0	4.6	5.6	3.8	3.9		100	115.0	140.0	95.0	97.5	0.0
7	7.8	5.5	10.3	9.7	8.6	9.7	100	70.5	132.1	124.4	110.3	124.4
8	3.3	2.1	1.9	1.6	4.2	2.4	100	63.6	57.6	48.5	127.3	72.7
n	**8**	**8**	**8**	**7**	**7**	**7**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**3.56**	**2.91**	**4.06**	**3.53**	**3.99**	**4.30**		**87.10**	**112.94**	**87.34**	**103.91**	**101.19**
SD	**2.02**	**1.60**	**3.00**	**2.98**	**2.36**	**2.97**		**27.60**	**43.89**	**27.39**	**12.73**	**54.51**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Amplitude (mV)						Amplitude (%)					
1	3.9	1.3	0.3		1.3	2.2	100	33.3	7.7		33.3	56.4
2	1.4	1.8	1.6	2.5	2.3	2.3	100	128.6	114.3	178.6	164.3	164.3
3	3.9	2.8	2.8	1.8			100	71.8	71.8	46.2	0.0	0.0
4	2.2	2.3	1.7	1.6	2.4	1.8	100	104.5	77.3	72.7	109.1	81.8
5	2	2.1	2.1	2.3	2.1	1.6	100	105.0	105.0	115.0	105.0	80.0
6	3.8	4.4	4.6	2.2	3.5		100	115.8	121.1	57.9	92.1	0.0
7	3.6	2.3	4.2	3.4	2.8	2	100	63.9	116.7	94.4	77.8	55.6
8	2.9	1.9	1.7		3.4		100	65.5	58.6		117.2	0.0
n	**8**	**8**	**8**	**6**	**7**	**5**	**8**	**8**	**8**	**6**	**8**	**8**
mean	**2.96**	**2.36**	**2.38**	**2.30**	**2.54**	**1.98**		**86.06**	**84.05**	**94.13**	**87.35**	**54.76**
SD	**0.99**	**0.93**	**1.43**	**0.63**	**0.77**	**0.29**		**32.27**	**38.65**	**48.25**	**51.07**	**56.52**

Table A 3.81 Pre-training 20Hz Tetani vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	67	79	88	85	67	69	100	117.9	131.3	126.9	100.0	103.0
2	75	81	85	86	76	76	100	108.0	113.3	114.7	101.3	101.3
3	78	82	85	85	77	76	100	105.6	109.0	109.0	98.7	97.4
4	84	87	82	82	76	71	100	103.6	97.6	97.6	90.5	84.5
5	58	70	72	82	65	69	100	120.7	124.1	141.4	112.1	119.0
6	86	90	92	94	76	76	100	104.7	107.0	109.3	88.4	88.4
7	75	86	98	89	81	70	100	114.7	130.7	118.7	108.0	93.3
8	80	98	87	87	78	70	100	122.5	108.8	108.8	97.5	87.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**75.38**	**84.17**	**86.13**	**86.25**	**74.50**	**72.13**		**112.19**	**115.23**	**115.78**	**99.56**	**96.81**
SD	**9.16**	**8.26**	**7.55**	**3.92**	**5.53**	**3.27**		**7.65**	**12.19**	**13.39**	**7.96**	**11.15**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	98	71	72	73	81	82	100	72.4	73.5	74.5	82.7	83.7
2	77	78	81	85	77	74	100	101.3	105.2	110.4	100.0	96.1
3	83	87	88	89	80	73	100	104.8	106.0	107.2	96.4	88.0
4	79	87	76	75	74	69	100	110.1	96.2	94.9	93.7	87.3
5	76	79	87	81	84	71	100	103.9	114.5	106.6	110.5	93.4
6	69	75	75	79	71	67	100	108.2	108.2	113.5	102.9	97.1
7	65	75	75	87	81	69	100	114.8	114.8	133.2	124.5	106.1
8	76	82	80	88	75	74	100	107.5	104.8	115.4	98.2	96.9
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**77.96**	**79.21**	**79.21**	**82.04**	**77.92**	**72.42**		**102.88**	**102.89**	**106.95**	**101.11**	**93.58**
SD	**9.79**	**5.75**	**5.84**	**6.06**	**4.35**	**4.56**		**12.97**	**13.27**	**16.95**	**12.34**	**7.13**

Table A 3.82 Post-training 20Hz Tetani vastus lateralis muscle M-wave duration evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	72	98	98	71	71	72	100	136.1	136.1	98.6	98.6	100.0
2	78	98	80	80	76	71	100	125.6	102.6	102.6	97.4	91.0
3	81	82	81			73	100	101.2	100.0			90.1
4	69	70	72	70	69	69	100	101.4	104.3	101.4	100.0	100.0
5	75	82	98	93	86	78	100	109.3	130.7	124.0	114.7	104.0
6	81	74	80	77	80		100	91.4	98.8	95.1	98.8	0.0
7	96	83	81	90	91	74	100	86.5	84.4	93.8	94.8	77.1
8	83	73	72	73	75	71	100	88.0	86.7	88.0	90.4	85.5
n	**8**	**8**	**8**	**7**	**7**	**7**	**8**	**8**	**8**	**7**	**7**	**8**
mean	**79.38**	**82.50**	**82.75**	**79.14**	**78.29**	**72.57**		**104.94**	**105.45**	**100.48**	**99.23**	**80.97**
SD	**8.26**	**10.69**	**10.12**	**9.15**	**7.95**	**2.88**		**17.97**	**18.72**	**11.50**	**7.54**	**33.87**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Duration (ms)						Duration (%)					
1	72	98	85	74	77	81	100	136.1	118.1	102.8	106.9	112.5
2	71	75	75	75	72	74	100	105.6	105.6	105.6	101.4	104.2
3	89	90	91	93			100	101.1	102.2	104.5		
4	75	81	76	74	75	76	100	108.0	101.3	98.7	100.0	101.3
5	89	84	85	85	81	79	100	94.4	95.5	95.5	91.0	88.8
6	82	98	98	98	98		100	119.5	119.5	119.5	119.5	
7	92	71	82	98	79	73	100	77.2	89.1	106.5	85.9	79.3
8	83	71	71		83		100	85.5	85.5		100.0	0.0
n	**8**	**8**	**8**	**7**	**7**	**5**	**8**	**8**	**8**	**7**	**7**	**6**
mean	**81.63**	**83.50**	**82.88**	**85.29**	**80.71**	**76.60**		**103.43**	**102.12**	**104.73**	**100.68**	**81.03**
SD	**8.18**	**11.05**	**8.90**	**11.13**	**8.46**	**3.36**		**18.70**	**12.29**	**7.62**	**10.86**	**41.40**

Table A 3.83 Pre-training 20Hz Tetani vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	5	3	4	3	1	4	100	60.0	80.0	60.0	20.0	80.0
2	101	27	24	19	60	59	100	26.7	23.8	18.8	59.4	58.4
3	71	38	39	34	51	49	100	53.5	54.9	47.9	71.8	69.0
4	74	53	43	50	75	72	100	71.6	58.1	67.6	101.4	97.3
5	99	68	58	57	65	99	100	68.7	58.6	57.6	65.7	100.0
6	83	64	38	40	67	56	100	77.1	45.8	48.2	80.7	67.5
7	149	99	83	54	111	122	100	66.4	55.7	36.2	74.5	81.9
8	39	36	24	29	29	24	100	92.3	61.5	74.4	74.4	61.5
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**77.63**	**48.50**	**39.13**	**35.75**	**57.38**	**60.63**		**64.55**	**54.80**	**51.33**	**68.48**	**76.95**
SD	**43.01**	**29.25**	**23.87**	**18.55**	**32.44**	**37.94**		**19.17**	**15.82**	**17.79**	**23.15**	**15.64**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	38	20	14	16	23	20	100	52.6	36.8	42.1	60.5	52.6
2	45	37	25	27	35	39	100	82.2	55.6	60.0	77.8	86.7
3	30	28	34	20	36	33	100	93.3	113.3	66.7	120.0	110.0
4	32	34	35	29	30	29	100	106.3	109.4	90.6	93.8	90.6
5	43	50	59	54	57	49	100	116.3	137.2	125.6	132.6	114.0
6	49	39	28	25	37	38	100	79.6	57.1	51.0	75.5	77.6
7	69	80	59	65	66	70	100	115.9	85.5	94.2	95.7	101.4
8	42	46	41	41	42	42	100	109.5	97.6	97.6	100.0	100.0
n	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
mean	**43.50**	**41.75**	**36.88**	**34.63**	**40.75**	**40.00**		**94.47**	**86.57**	**78.48**	**94.47**	**91.61**
SD	**12.13**	**18.13**	**15.82**	**17.25**	**14.16**	**14.93**		**22.12**	**34.28**	**28.13**	**23.68**	**19.81**

Table A 3.84 Post-training 20Hz Tetani vastus lateralis muscle M-wave area evoked via magnetic stimulation and expressed as a percentage of pre-exercise

VL

Train	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	21	31	59	21	21	19	100	147.6	281.0	100.0	100.0	90.5
2	47	58	70	60	48	44	100	123.4	148.9	127.7	102.1	93.6
3	26	26	38			47	100	100.0	146.2			180.8
4	26	26	22	21	20	22	100	100.0	84.6	80.8	76.9	84.6
5	62	24	27	28	62	61	100	38.7	43.5	45.2	100.0	98.4
6	55	52	51	51	54		100	94.5	92.7	92.7	98.2	
7	98	75	138	136	83	108	100	76.5	140.8	138.8	84.7	110.2
8	53	45	41	39	58	44	100	84.9	77.4	73.6	109.4	83.0
n	**8**	**8**	**8**	**7**	**7**	**7**	**8**	**8**	**8**	**7**	**7**	**7**
mean	**48.50**	**42.13**	**55.75**	**50.86**	**49.43**	**49.29**		**95.71**	**126.89**	**94.10**	**95.91**	**105.87**
SD	**25.26**	**18.56**	**36.84**	**40.37**	**22.57**	**29.74**		**32.15**	**72.84**	**32.02**	**11.15**	**34.27**

Control	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min	pre-exercise	4min	Wingate 1	Wingate 2	+10 min	+30 min
Subject	Area (uV.s)						Area (%)					
1	41	15	8		15	36	100	36.6	19.5		36.6	87.8
2	26	24	19	32	27	25	100	92.3	73.1	123.1	103.8	96.2
3	58	57	59	51			100	98.3	101.7	87.9		
4	27	32	27	23	27	27	100	118.5	100.0	85.2	100.0	100.0
5	42	39	41	42	38	12	100	92.9	97.6	100.0	90.5	28.6
6	52	63	63	43	60		100	121.2	121.2	82.7	115.4	
7	80	17	66	61	41	32	100	21.3	82.5	76.3	51.3	40.0
8	53	42	39		61		100	79.2	73.6		115.1	
n	**8**	**8**	**8**	**6**	**7**	**5**	**8**	**8**	**8**	**6**	**7**	**5**
mean	**47.38**	**36.13**	**40.25**	**42.00**	**38.43**	**26.40**		**82.52**	**83.65**	**92.52**	**87.52**	**70.51**
SD	**17.61**	**17.63**	**21.39**	**13.45**	**17.28**	**9.13**		**36.08**	**30.53**	**16.89**	**31.30**	**33.60**