The Impact of Hypoxia on Growth Hormone Levels in Response to a Maximal Strength Training Session

A thesis submitted in partial fulfilment of the requirements for the award of

MASTER OF EXERCISE SCIENCE (RESEARCH)

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March 2015

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Statement of Sources

"I, Dean Filopoulos, declare that the Master of Exercise Science (Research) thesis entitled "The impact of hypoxia on growth hormone levels in response to a maximal strength training session." is no more than 22,320 words in length including quotes, tables, figures, appendices, excluding list of references. This thesis contains no material published elsewhere or extracted in whole or in part from a thesis by which I have qualified for or been awarded another degree or diploma. No parts of this thesis have been submitted towards the award of any other degree or diploma in any other tertiary institution. No other person's work has been used without due acknowledgment in the main text of the thesis. All research procedures reported in the thesis received the approval of the relevant Ethics/Safety Committees (where required).

Signature: Date:

Acknowledgements

Firstly, I would like to acknowledge the efforts of my supervisor Douglas Whyte for his tireless work over the years, as without his constant guidance and support this project would not have been possible.

Secondly, I would also like to thank my co-supervisor Stuart Cormack for his support and expertise to assist with the completion of this project.

Furthermore, I would like to give a big thank you to my fellow research students at ACU for their endless support over the years. Great friendships have been made. All of you guys and girls are legends.

Finally, thank you to my wife Skye. What an amazing woman. This project would not have been possible without your support and love. Thank you wholeheartedly.

Table of Contents

List of Figures

List of Tables

Abbreviations

1RM	one repetition maximum
ATP	adenosine triphosphate
BFR	blood flow restriction
CSA	cross-sectional area
EMG	electromyography
ES	effect size
F_iO_2	fraction of inspired oxygen
GH	growth hormone
GHRH	growth hormone releasing hormone
h	hours
HR	heart rate
HYP	hypoxic resistance exercise
iEMG	integrated electromyography
IGF-1	insulin-like growth factor 1
MAPK	mitogen-activated protein-kinase
MGF	mechano growth factor
mTOR	mammalian target of rapamycin pathway
min	minutes
MVC	maximal voluntary contraction
NOR	normoxic resistance exercise
p70S6K1	P70 ribosomal protein S6 kinase 1

PI3K	phosphoinositide 3-kinase
PCr	phosphocreatine
Reps	repetitions
RM	repetitions maximum
RPE	rating of perceived exertion
RTH	resistance training in hypoxia
s	seconds
SpO_2	pulse oximetry oxygen saturation
wk	week

Abstract

Background

Performing resistance exercise in a hypoxic environment has been shown to improve gains in muscle strength and hypertrophy, even at low intensities. These adaptations are thought to occur via increases in the accumulation of metabolites and secretion of anabolic hormones, such as growth hormone (GH). The majority of research conducted has assessed these adaptations with the use of low-intensity, high-volume (hypertrophy-type) protocols. However, there is little research investigating the effects of metabolic and hormonal responses to a typical strength training (high-intensity, low-volume) session. Therefore, the purpose of this investigation was to examine whether hypoxia can influence the metabolic stress and GH response during a maximal strength training session.

Methods

Fifteen resistance-trained, male participants (age 25 ± 5 years, height 180 ± 6 cm, mass 83 ± 6 kg), performed high-intensity resistance exercise in normoxic (NOR) and hypoxic (HYP) (12% oxygen) conditions using a randomised, single-blinded, cross-over design. Participants were tested for 1-repetition maximum (1RM) strength in the bench press and leg press exercise. Each participant then completed two experimental trials, consisting of 5 sets of 3 repetitions at 85% of 1RM (leg press and bench press) with 3 min rest between sets and exercises. Serum GH and blood lactate were measured before, and at 5, 15, 30 and 60 min post-exercise. Muscle activity was assessed on the vastus lateralis during the leg press using surface electromyography (EMG). Contraction time was also assessed during each repetition with the use of a goniometer. Differences between HYP and NOR conditions were assessed using effect size (ES) statistics and percent difference ± 90% confidence intervals. Likely differences between the means ≥

75% were classified as *important*, < 75% represented as *trivial*, and when the statistic occurred in both directions > 5%, the effect was reported as *unclear*.

Results

There was an *important* increase in blood lactate area under the curve following resistance exercise in hypoxia (HYP 139.0 ± 34.2 v NOR 106.4 ± 21.4 mmol/L, ES 1.21 ± 0.24). In addition, there was an *important* increase in GH concentrations post-exercise in HYP compared to NOR (Area under the curve; HYP 117.7 ± 86.8 v NOR 72.9 ± 85.3 ng/L, ES 0.56 ± 0.46). While the difference in EMG activity between conditions was *unclear*, there was an *important* increase in total contraction time, with the length of time taken to complete the leg and bench press exercise increasing in the HYP trial (HYP 146 ± 12 v NOR 141 ± 10 s, ES 0.40 ± 0.42). This may be due to an *important* increase in bench press contraction time during the HYP trial, as the difference between HYP and NOR trials during leg press was *unclear*.

Conclusion

The results from this investigation suggest that performing high-intensity, low-volume resistance exercise in a hypoxic environment increases the metabolic and GH response compared to the identical exercise in normoxic conditions, despite inconclusive differences in muscle activity. Therefore, resistance training in systemic hypoxia may have the potential to further enhance hypertrophic adaptations from training traditionally aimed at maximal strength.

Chapter One: Introduction

Resistance training in athletic populations has the ability to improve various athletic qualities such as strength, speed and power [1]. It has become important for athletes to consistently perform resistance exercise to improve these physical qualities in order to maximise performance and decrease the likelihood of injury [1]. Various forms of resistance training programs are currently undertaken by athletes aiming to enhance performance through increases in either neurological or morphological adaptations [2].

There are several factors of the neuromuscular system that have an influence on the overall muscle strength and power of an athlete including; (i) greater recruitment of higher threshold motor units, (ii) improved inter and intra-muscular coordination, (iii) changes in motor unit firing frequency, (iv) reduced neural inhibition, and (v) increased rate of force development [3, 4]. Morphological adaptations, such as an increase in muscle cross sectional area (CSA) and changes in muscle architecture, are also important to promote hypertrophic adaptations, enhance force generating capacity and to improve overall muscle strength [5, 6].

Physiological adaptations to resistance training require the manipulation of exercise training variables (i.e. intensity, volume and rest intervals) to achieve a specific training outcome [7]. Strength-type protocols typically involve low-volume (2-6 sets, $\leq$ 6 repetitions) and high-intensity ($\geq$ 85% of 1RM), combined with a long rest interval (3-5 min), in order to improve neurological adaptations [2]. In contrast, hypertrophy-type protocols involve high-volume (3-6 sets, 6-12 repetitions), moderate-intensity ($\leq$ 85% 1RM), and short rest intervals (30-90 s), with the aim to maximise hypertrophic adaptions [2].

Traditionally, resistance exercise is recommended to be performed at an intensity of $\geq$ 65% 1RM to achieve a substantial effect on muscular hypertrophy [8]. Muscle hypertrophic

responses to resistance exercise occur via a combination of factors, including mechanical and metabolic stress, neural factors and endocrine responses [9].

Anabolic hormones such as GH are thought to play an integral role in promoting muscle hypertrophy [10, 11]. Post-exercise elevations in GH levels have been shown to be highly correlated with the degree of muscle hypertrophy, with hypertrophy-type protocols producing a greater augmentation in GH concentrations compared to traditional strength-type protocols [12].

A novel training method that combines resistance exercise with blood flow restriction (BFR), has shown a correlation between elevations in anabolic hormones, in particular GH, and the promotion of hypertrophy [13]. This training modality generates a localised hypoxic stimulus within the exercised muscle and is typically performed at a low-intensity (20-50% 1RM) [13], which is well below the recommended threshold for hypertrophic adaptations. However, BFR training is limited to exercise of a specific limb, and as a result, training of the whole body musculature is not possible.

Recently, resistance training in hypoxia (RTH) has been proposed as a possible training modality that may overcome this limitation. By inducing hypoxia during resistance exercise, alterations in the muscular environment, similar to those observed during BFR training, can be achieved. The addition of systemic hypoxia to resistance exercise results in similar physiological and morphological responses to that observed following BFR training [14]. Similar to BFR, the potential benefit of performing RTH is to augment the metabolic response to training, which is associated with an increased secretion of GH and may promote hypertrophic adaptation [14]. To date, the majority of studies have performed RTH at a low-intensity and high-volume combined with short rest intervals to maximise muscle hypertrophy. This type of protocol may not be optimal for athletic populations as it eliminates the neural benefits of maximal strength training (high-intensity, low-volume resistance exercise).

However, it is plausible that the addition of hypoxia to maximal strength training may result in an augmented GH response that may provide a supplementary hypertrophic adaptation whilst also maximising neutrally based strength gains.

1.1 Aims

The aim of this investigation was to determine if the use of systemic hypoxia during low-volume, high-intensity resistance exercise is:

(i) Associated with an accentuated metabolic stress response

(ii) Associated with an augmented growth hormone response

It was hypothesised that performing low-volume, high-intensity resistance exercise in a hypoxic environment would result in a greater augmentation in GH and metabolic stress compared to the identical exercise performed in normoxia.

1.2 Limitations

The following may be recognised as limiting factors in the investigation conducted in this thesis:

(i) Nutritional status of each participant prior to the experimental trials.

(ii) Motivational and psychological status of each participant.

(iii) The type of activity the participants performed prior to the 1RM testing and experimental trials.

(iv) Electromyography was only measured during leg press exercise

(v) The design of the study limits the ability to generalise findings to young adult males with a background in resistance training.

1.3 Delimitations

Due to the present limitations, the investigation in this thesis is delimited to:

(i) Male participants aged 18 to 35 years with a background in resistance training of at least 2 x per week for a period of 6 months prior to commencement.

(ii) Participants meeting all the inclusion criterion prior to the recruitment.

Chapter Two: Review of Literature

This review of literature begins with an outline of the importance of resistance training in athletic populations. The difference between strength and hypertrophy-based resistance training protocols and the mechanisms involved in each will be discussed. This will be followed by an examination of the anabolic hormone response and its adaptations to resistance exercise. Then, the potential benefits of BFR resistance exercise on muscle strength and hypertrophy will be explored. Finally, the physiological responses to resistance training in hypoxia will be detailed.

2.1 Importance of Resistance Training In Athletes

Resistance training in athletic populations has the ability to improve various athletic qualities such as strength, speed and power [1]. Resistance training has been associated with superior sprinting and jumping ability in team-sport athletes [15, 16], this can lead to faster sprint times in distances up to 30 m [16, 17]. Resistance training has also been shown to improve maximal strength and running economy in endurance trained athletes [18, 19]. A relationship exists between maximal strength, single sprint performance and repeated-sprint ability (RSA) in team-sport athletes [15, 20]. In support of this, increases in strength following resistance training have been shown to improve RSA, which is a fitness requirement for athletes involved in team-sports [21]. Specific resistance training protocols have the ability to prevent reoccurrences of the same injury, as well as decrease the number of non-contact related injuries [22]. Consequently, it is important for athletes to consistently perform resistance exercise to improve the aforementioned physical qualities in order to maximise their performance [1].

There are various forms of resistance training protocols that athletes currently undertake, which aim to enhance performance through increases in neurological, physiological and morphological adaptations [2]. It is important for the coach and athlete to understand the critical components of a program design for the development of these adaptations. A basic summary

of different types of resistance training programs used to achieve specific training outcomes are outlined in Figure 1.

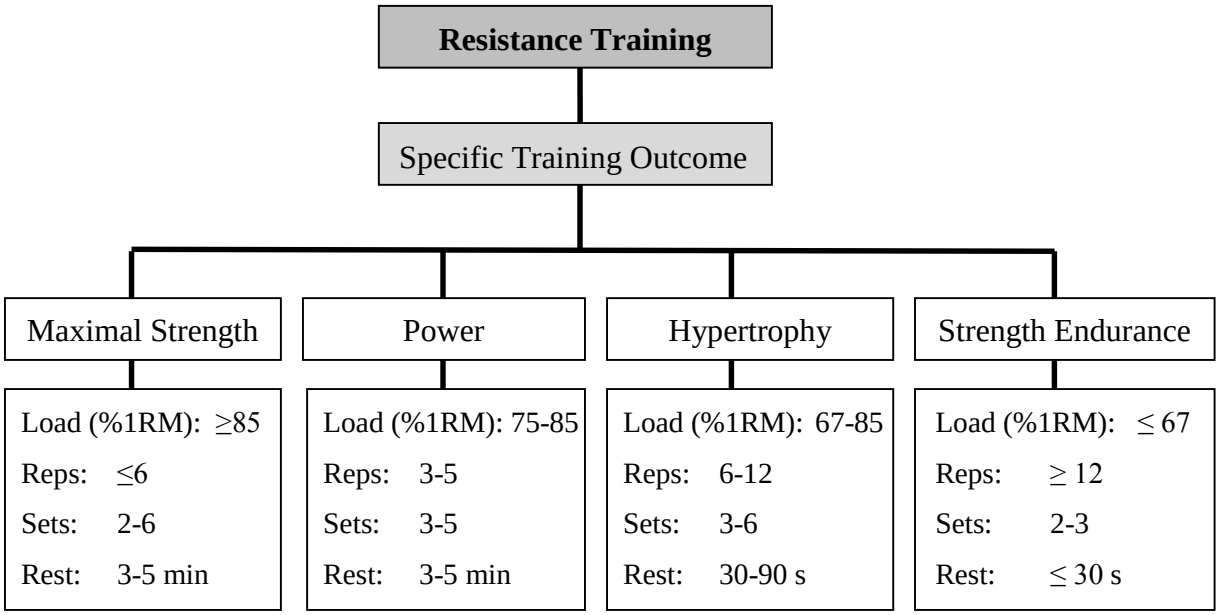


Figure 1. Traditional program design of resistance exercise for specific training outcomes. 1RM: One repetition maximum. Adapted from Bird et al. [23].

2.2 Maximal Strength vs Hypertrophy Resistance Training

Strength training with heavy loads (i.e. ≥ 85% 1RM) has been commonly used to improve the ability of a muscle to exert maximal force at any given velocity [24]. The increase in maximal strength through such training is linked to an improved athletic performance [24, 25]. In particular, improvement in jump height [15, 16, 25, 26], movement velocity [24] and power output [24, 25] occurs after periods of heavy strength training. It is thought that this type of training induces different adaptations to those observed following explosive (power) type training [25, 27]. For example, resistance exercise that focuses on the use of heavy loads has the potential to improve force characteristics of the force-velocity curve, while power-type resistance exercise (≤ 85% 1RM, ≤ 5 repetitions with ≥ 3min rest intervals) alters the velocity

portion of the curve [27]. These two types of resistance training protocols appear to be the most effective in enhancing muscular power and dynamic athletic performance [27].

There are several neuromuscular factors that can influence the overall muscular strength and power output of an athlete. Neural factors include motor unit recruitment, rate coding, synchronisation and inhibition [4]. Motor unit recruitment generally follows the size principle, in which smaller motor units are recruited first, followed by progressively larger motor units [28]. This is known as the Henneman size principle, which suggests that the activation of motor units is dictated by their size [28]. Higher threshold motor units are typically comprised of type II muscle fibres, which are important for muscle force generating characteristics [27]. The greater the external load, the more likely these higher-threshold motor units will be recruited [29]. Motor unit rate coding is associated with motor unit firing frequency. It is suggested that rate coding can play a significant role in the speed of muscle contraction, as high motor unit firing rates contribute to a greater increase in rate of force development (RFD) [30]. As a result, RFD is considered to be an important characteristic in improving muscle actions which require a high power production [29]. Motor unit synchronisation (the simultaneous activation of several motor units) causes an increase in force output [31]. This is supported by that fact that strength trained athletes appear to exhibit greater motor unit synchronisation than untrained individuals [32]. Furthermore, enhanced motor unit synchronisation may play a role in the development of force during rapid muscle contractions [33]. Conversely, neural inhibition can reduce the force production of a muscle [34]. This inhibitory response can occur as a result of neural feedback from various muscle and joint receptors [34]. Heavy resistance exercise can significantly reduce neuromuscular inhibition, which may partly be responsible for the increase in force–generating capacity following strength training [35].

Muscle fibre characteristics may also play a significant role in an athlete's ability to maximise power-generating capacity and muscular strength [36, 37]. Strength and power athletes (i.e. Olympic weightlifters and powerlifters) tend to have a greater percentage of fast twitch (type

II) muscle fibres [36, 38], whereas bodybuilders, generally have a greater percentage of type I (slow twitch) muscle fibres [39].

An increase in muscle size (hypertrophy) has the potential to enhance force-generating capacity [6]. Muscular hypertrophy is the most significant morphological adaptation following resistance exercise [6]. Short-term strength training (≤ 14 wk) has been associated with a significant increase in hypertrophy of type II muscle fibres [5, 40], whereas long-term resistance training studies have demonstrated hypertrophic adaptions of both type I and II muscle fibres [41, 42]. Long-term adaptations have been associated with an increase in muscle cross-sectional area (CSA), which can lead to an increase in contractile material (e.g. number of cross-bridges), and a change in muscle architecture (e.g. pennation angle) [6]. It has been proposed that these two morphological adaptations are important for the gain in enhanced force generating capacity, thus, promoting overall muscle strength [5, 6]. A summary of the neurological and morphological adaptations to resistance training is outline in Figure 2.

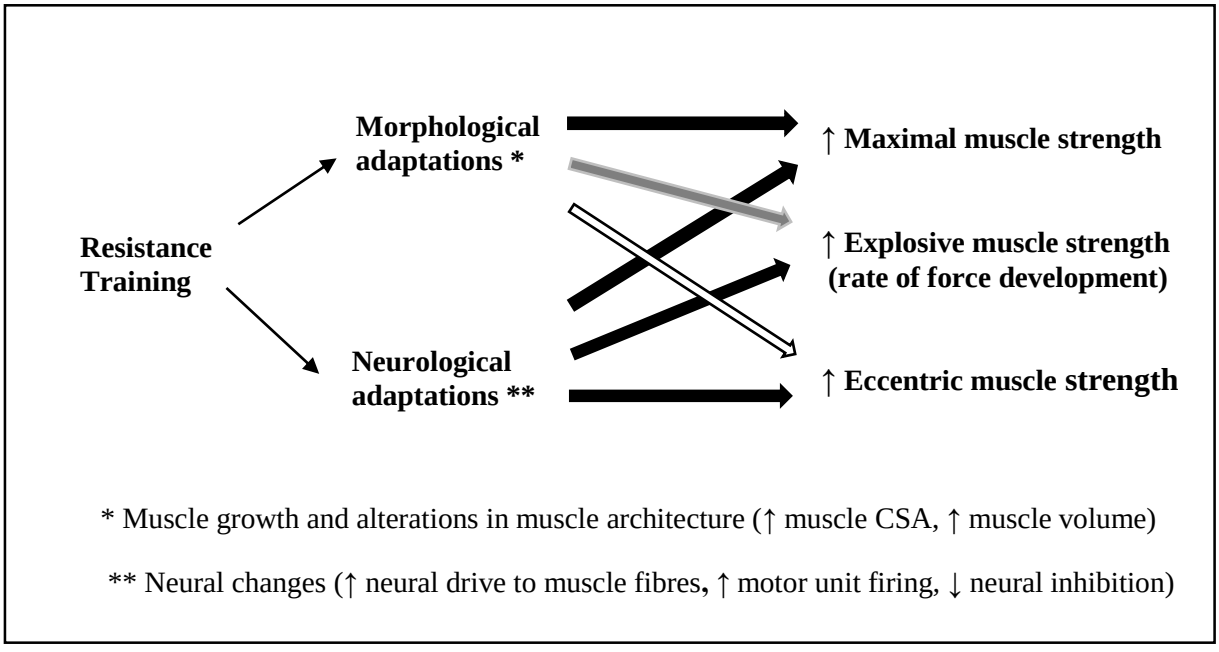


Figure 2. A summary of the neural and muscular adaptations to resistance training. Black arrows: strong influence, Grey arrow: moderate influence, White arrow: low influence. ↑: increase, ↓: decrease. Adapted from Aagaard [3].

The manipulation of exercise training variables (i.e. intensity, volume, and rest intervals) are important during acute resistance exercise to promote the appropriate physiological adaptation [2]. Strength-type protocols typically involve low-volume (2-6 sets, ≤ 6 repetitions), high-intensity (≥ 85% 1RM) exercise, combined with long rest intervals (3-5 min), in order to improve neurological adaptations [2]. Whereas, hypertrophy-type protocols usually involve high-volume (3-6 sets, 6-12 repetitions), moderate-intensity (≤ 85% 1RM) exercise with short rest intervals (30-90 s), and aims to maximise hypertrophic adaptions [2]. It has recently been shown that when resistance exercise is performed at volume-equated loadings between strength (7 x 3RM with 3 min rest intervals) and hypertrophy-type (3 x 10RM with 90 s rest intervals) protocols, similar increases in muscle hypertrophy occur [43]. However, muscle hypertrophy has also been demonstrated when resistance exercise is performed at intensities as low as 20% 1RM when combined with BFR [44-47]. As a result, different loading strategies can have an influence on hypertrophic adaptations.

2.3 Muscle Hypertrophy

Traditionally, it is recommended that resistance exercise be performed at an intensity of ≥ 65% 1RM to promote a substantial hypertrophic effect [8]. The greatest hypertrophic response tends to be produced when the intensity of exercise is supplemented with high-volume (3-6 sets, 6-12 repetitions), short-rest intervals (30-90 s), and multi-joint exercises (that recruit a large amount of muscle mass) [48]. It is hypothesised that the hypertrophic response is driven by the level of mechanical tension, metabolic stress and muscle damage that occurs during the training session [48]. These three factors are thought to be the primary activators of muscle hypertrophy and can be maximised by the manipulation of training variables, in particular intensity, volume, rest intervals and exercise selection [48]. The hypertrophic response is mediated by several anabolic signalling pathways that regulate skeletal muscle growth.

2.4 Anabolic Hormone Response and Adaptations to Resistance Training

Skeletal muscle hypertrophy is thought to be mediated by a number of anabolic and catabolic cell signalling pathways [49]. Activation and interaction of molecular downstream targets regulates muscle growth adaptations by shifting the net protein balance to favour synthesis over degradation [49]. There are several complex anabolic signalling pathways involved, such as Akt/Mammalian target of rapamycin pathway (Akt/mTOR), mitogen-activated protein-kinase (MAPK) and insulin-like growth factor-1 (IGF-1). The IGF-1 signalling pathway is an important contraction and nutrient stimulated pathway that increases protein synthesis in skeletal muscle [50, 51]. The increase in autocrine/paracrine expression of IGF-1 in response to skeletal muscle contraction activates the type I IGF receptor [50, 51]. The subsequent activation of downstream signalling targets including mTOR and P70 ribosomal protein S6 kinase 1 (p70S6K1) through the insulin/IGF-1- phosphatidylinositol 3-kinase (PI3K)-Akt signalling pathway, provides an initial basis for exercise-induced increases in skeletal muscle hypertrophy [50, 51]. Mechanical disruption associated with resistance exercise is also able to activate the mTOR signalling pathway, which plays a significant role in stimulating muscle protein synthesis [52].

While the precise molecular mechanisms involved in the anabolic signalling pathways remain to be elucidated, the endocrine system may play a role in the signalling process. Several hormones have been shown to modify the balance between anabolic and catabolic stimuli in the muscle [53]. Additionally, anabolic hormones have been implicated in the proliferation and differentiation of satellite cells, which may facilitate the repair and subsequent growth of new muscle tissue [54].

Resistance exercise has been shown to augment anabolic hormone secretion in the post-exercise period, which may increase the likelihood of muscle cell receptor interactions and trigger signalling cascades promoting hypertrophic adaptations [55]. Several types of resistance

exercise protocols have been shown to cause acute and chronic alterations in anabolic hormones that may play a role in facilitating a hypertrophic response [12, 55]. A theoretical sequence of events, demonstrating the influence of resistance exercise on hormonal responses, which may lead to an increase in hypertrophy and strength, is shown in Figure 3. The focus of this literature review will be about the hormones most widely studied with a central focus on GH, IGF-1 and testosterone.

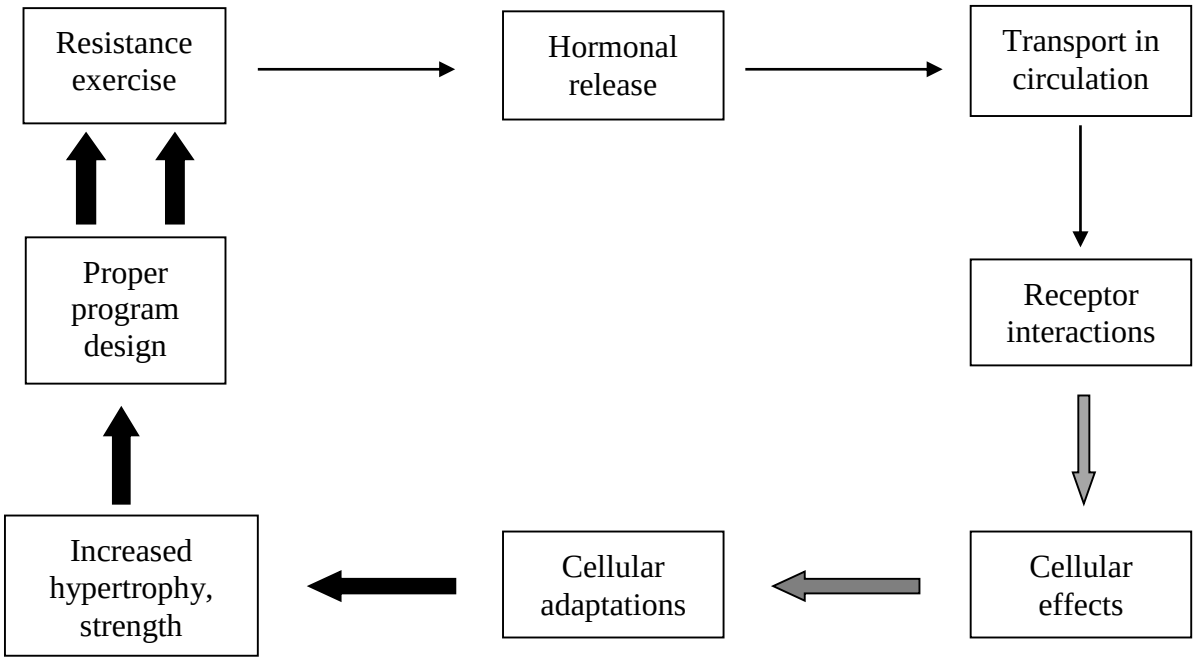


Figure 3. Theoretical sequence of events demonstrating the influence of resistance exercise on hormonal effects leading an increase in hypertrophy and strength. Adapted from Komi [4].

2.5 Growth Hormone

Growth hormone is a peptide hormone that is produced and secreted from the anterior pituitary gland [10, 56]. Growth hormone has many different isoforms circulating in blood, the predominant isoform, 22 kilo Dalton, is known to be the most biologically active and has a half-life of 15-20 min [56, 57]. Growth hormone secretion occurs in a pulsatile fashion that is regulated by two hypothalamic hormones; growth-hormone releasing hormone (GHRH) and somatostatin [58]. GHRH is known to have two specific roles; to stimulate the synthesis and

secretion of GH, whereas, somatostatin inhibits the release of GH [58]. The most important stimuli for GH secretion in humans are exercise, sleep and stress [57]. Once GH is secreted into the circulation its major action is to stimulate protein synthesis either directly, at target tissues, or indirectly, through the actions of IGF-1 [56, 57].

Growth hormone acts directly on target tissues, including fat, muscle, connective tissue, immune and satellite cells to exert its actions and promote physiological adaptations [59]. However, one of its most important actions is to act on the liver to generate IGF-1, which has anabolic effects [57]. The release of IGF-1 by GH is regulated by two negative feedback loops. The first feedback loop directly affects the somatotrope cells in the anterior pituitary, directly inhibiting further release of GH [60], while the second feedback loop affects GHRH and somatostatin release from the hypothalamus, which in turn reduces the secretion of GH [60].

Exercise is postulated to be one of the key regulators of these negative feedback loops, with a net result being increased or maintained GH secretion, by stimulating GHRH and/or decreasing somatostatin release [61]. The magnitude of the GH response to exercise is influenced by several physiological variables such as age [62-64], gender [65-67], body composition [68-70], physical fitness [62, 71], as well as the intensity [72, 73], type [74, 75], and duration of exercise [72]. Resistance exercise is understood to be a potent stimulus of GH [12]. Furthermore, McCall et al. [76] have reported that acute post-resistance exercise elevations in GH concentrations are significantly correlated with the degree of type I and II muscle fibre hypertrophy. The magnitude of the GH response to resistance exercise appears dependant on several factors including; intensity, volume, rest intervals, exercise selection and gender [55]. When high-volume, moderate-intensity resistance exercise is performed with short rest intervals (i.e. hypertrophy-type protocols), a greater GH response occurs compared to that seen in response to high-intensity, low-volume exercise combined with long rest periods (i.e. strength-type protocols) [75, 77-81] (Table 1). For example, Similos et al. [79] compared the acute hormonal response of various strength and hypertrophy resistance exercise protocols. When exercise

volume was manipulated by varying the number of sets and repetitions, they observed different responses in GH concentrations. The hypertrophy-type protocol, consisting of 4 sets of 15 repetitions at 60% 1RM with 1 min rest, demonstrated a 5-fold increased GH response compared with the strength-type protocol (4 sets of 5 repetitions at 88% 1RM with 3 min rest). Furthermore, the hypertrophy-type protocol induced a greater elevation in blood lactate. High correlations have been observed between blood lactate and GH concentrations [77]. The accumulation of hydrogen ions produced by the build-up of lactate may be an important factor influencing the release of GH [82]. Increased hydrogen ions (i.e. a reduction in pH) may potentiate the secretion of GH, through a chemoreceptive reflex mediated by intramuscular metaboreceptors and group III and IV afferent fibres [83, 84]. The localised hypoxic environment associated with BFR training, has been shown to cause an increase in metabolic stress to potentiate the secretion of GH through the aforementioned mechanistic approach [83]. As a result, muscle hypoxia maybe important to facilitate an anabolic response to promote hypertrophic adaptations. However, the relevance of the relationship between lactate and GH has been questioned. Artificial manipulation of blood lactate levels, with the use of sodium lactate, has not shown a link with increased GH secretion [85]. Growth hormone's effect on muscle hypertrophy will be further discussed in section 2.8.

Table 1. Acute growth hormone responses from studies that have directly compared strength and hypertrophy resistance type exercise in men.

Study	Training protocol	Number of exercises (Intensity)	Sets x Reps (rest intervals)	Approx. absolute change in GH from baseline (ng/mL)
Hakkinen and Pakarinen [77]	Strength	One (1RM)	20 x 1 (3 min)	**1**
Goto et al. [86]	Strength	One (90% 1RM)	5 x 5 (3 min)	**1**
Goto et al. [86]	Strength	One (90% 1RM)	5 x 5 (3 min) (extra set at 90% 1RM; 4 reps)	**1**
Walker et al. [80]	Strength	One (100% 1RM) CL	15 x 1 (3 min)	**1**
Kraemer et al. [75]	Strength	Eight (10RM)	5 x 5 (1 min)	**2**
Smilios et al. [79]	Strength	Four (88% 1RM)	2 x 5 (3 min)	**2**
Zafeiridis et al. [81]	Strength	Four (88% 1RM)	4 x 5 (3 min)	**3***
Kraemer et al. [75]	Hypertrophy	Eight (10RM)	3 x 10 (3 min)	**4**
Hoffman et al. [78]	Strength	One (90% 1RM)	4 x 4 (3 min)	**4***
Smilios et al. [79]	Strength	Four (88% 1RM)	4 x 5 (3 min)	**4***
Smilios et al. [79]	Strength	Four (88% 1RM)	6 x 5 (3 min)	**4***
Goto et al. [86]	Strength	One (90% 1RM)	5 x 5 (3 min) (extra set at 70% 1RM; 13 reps)	**4***
Kraemer et al. [75]	Strength	Eight (5RM)	5 x 5 (3 min)	**5***
Walker et al. [80]	Strength	One (100% 1RM) VL	15 x 1 (3 min)	**5***
Smilios et al. [79]	Hypertrophy	Four (75% 1RM)	2 x 10 (2 min)	**5***
Goto et al. [86]	Strength	One (90% 1RM)	5 x 5 (3 min) (extra set at 50% 1RM; 25 reps)	**6***

Study	Training protocol	Number of exercises (Intensity)	Sets x Reps (rest intervals)	Approx. absolute change in GH from baseline (ng/mL)
Kraemer et al. [75]	Strength	Eight (5RM)	5 x 5 (1 min)	**8***
Smilios et al. [79]	Hypertrophy	Four (75% 1RM)	6 x 10 (2 min)	**10***
Hoffman et al. [78]	Hypertrophy	One (60% 1RM)	4 x 15 (3 min)	**12***
Zafeiridis et al. [81]	Hypertrophy	Four (75% 1RM)	4 x 10 (2 min)	**12***
Smilios et al. [79]	Hypertrophy	Four (75% 1RM)	4 x 10 (2 min)	**12***
Smilios et al. [79]	Strength endurance	Four (60% 1RM)	2 x 15 (1 min)	**13***
Walker et al. [80]	Hypertrophy	One (80% 1RM) CL	5 x 10 (3 min)	**13***
Walker et al. [80]	Hypertrophy	One (80% 1RM) VL	5 x 10 (3 min)	**14***
Smilios et al. [79]	Strength endurance	Four (60% 1RM)	4 x 15 (1 min)	**20***
Zafeiridis et al. [81]	Strength endurance	Four (60% 1RM)	4 x 15 (1 min)	**21***
Kraemer et al. [75]	Hypertrophy	Eight (10RM)	3 x 10 (1 min)	**24***
Hakkinen and Pakarinen [77]	Hypertrophy	One (70% 1RM)	10 x 10 (3 min)	**27***

* denotes significant difference ($P < 0.05$) from corresponding resting or pre-exercise value. RM = repetition maximum, CL = constant load, VL = variable load.

2.6 Insulin-like Growth Factor-1

Insulin-like growth factor-1 is a peptide hormone with a purported role in skeletal muscle anabolism [51]. IGF-1 has both autocrine and paracrine functions within skeletal muscle [87]. Three isoforms have been identified in skeletal muscle, IGF-1Ea, IGF-1Eb, and a splice variant, IGF-1Ec with each functioning in a different manner [88, 89]. IGF-1Ea is produced in the liver and muscle. It is the main systemic IGF isoform and acts to stimulate satellite cell activation and proliferation [90]. IGF-1Eb is produced both in the liver and skeletal muscle [89]. Both isoforms act at IGF-1 receptors on target cells to exert its effects on growth promotion with myofibre regeneration and hypertrophy [89, 90]. IGF-1Ec, also known as mechano growth factor (MGF), is expressed in muscle tissue in response to mechanical loading and/or muscle damage [91]. Resistance exercise is understood to be a powerful stimuli for MGF [92]. Moreover, MGF has been shown to activate satellite cell proliferation, which is needed for the repair and subsequent growth of new muscle tissue, thus facilitating muscle hypertrophy [93].

Similar to GH, the performance of hypertrophy-type protocols have been found to produce significantly greater elevations in systemic IGF-1 compared to higher-intensity strength-type protocols [12, 75]. Differences in IGF-1 augmentation may partly be explained by a greater accumulation of metabolites and the secretion of systemic anabolic hormones observed during hypertrophy training [12, 75]. This is further supported by studies in which resistance exercise was performed in combination with BFR [44, 94]. The greater increases in IGF-1 levels observed with BFR post-exercise may partly be due to the higher degree of metabolic stress and systemic GH secretion that occurs during occlusion [44, 94, 95]. While the aforementioned studies demonstrated acute increases in systemic IGF-1, several other studies have shown no augmentation in IGF-1 during or immediately post-exercise [95, 96]. This may be attributed to the delayed secretion of IGF-1, as peak values may not be reached until 16-28 h after GH secretion [12]. Another possibility for the variance in these findings may be due to a difference

in methodological design between these protocols. Takano et al. [94] performed BFR resistance exercise (bilateral leg extension) at 20% 1RM for four sets of maximal repetitions with 20 s rest intervals. While Abe et al. [44] consisted of squat and leg curl exercise with BFR for three sets of 15 repetitions at 20% 1RM with 30 s rest intervals. Alternatively, Fujita et al. [95] performed bilateral leg extension exercise with BFR for a total of 4 sets and 75 repetitions with 30 s rest interval at 20% 1RM. While, Patterson et al. [96] consisted of unilateral knee extension exercise at 20% 1RM until volitional fatigue. A greater total exercise volume observed in the studies by Takano et al. [94] and Abe et al. [44] may have been responsible for the increased IGF-1 response. The effects of IGF-1 on muscle hypertrophy will be further discussed in section 2.8.

2.7 Testosterone

Another well recognised anabolic hormone implicated in muscle hypertrophy is testosterone. Acute post-exercise elevations in testosterone have been significantly correlated with an increase in muscle CSA, thus suggesting testosterone may facilitate muscle hypertrophy [97].

Testosterone is primarily synthesised and secreted from the Leydig cells of the testes through the hypothalamic-pituitary-gonadal axis [98]. However, small amounts of testosterone are derived from the ovaries, adrenals and via conversion of other androgens [98]. Testosterone is secreted into the peripheral circulation to specifically target muscle tissue and binds to its androgen receptor to exert its biological effect [98]. The elevation in testosterone levels post-exercise can increase the interaction with intracellular androgen receptors, initiating gene transcription [11]. While testosterone may directly influence the anabolic process, it may also have an indirect role in stimulating other anabolic hormones such as GH and IGF-1 [55]. Testosterone has been proposed to increase GH secretion by neuroendocrine mechanisms, specifically, increasing GHRH secretion and/or its actions on pituitary, as well as reducing somatostatin's inhibitory effect [61]. Testosterone also mediates the proliferation of satellite cells and inhibits catabolic processes to create a hypertrophic response [99]. Circulating levels

of testosterone have been shown to increase immediately after a bout of resistance exercise, remaining elevated for up to 30 min [98]. The magnitude of the testosterone response following resistance exercise is influenced by several acute training variables such as volume and intensity, exercise selection, and gender [98]. As women do not have Leydig cells, differences in testosterone responses have been observed regardless of the type of resistance exercise protocol performed [55]. This has been further explored with the administration of gonadotropin-releasing hormone analogues, which suppress luteinizing hormone and consequently Leydig cell function [100]. This may prevent an increase in testosterone concentrations, usually seen after acute resistance exercise, and may explain the lack of consistent findings between genders.

Similar to GH, hypertrophy-type protocols have been shown to produce the greatest testosterone response compared to conventional strength-type protocols [75, 77, 79, 80]. For example, Kraemer et al. [101], compared the hormonal response to two different resistance exercise protocols that used the same eight exercises; (i) strength protocol; 3-5 sets of 5RM with 3 min rest and (ii) hypertrophy protocol; 3 x 10 RM with 1 min rest. The results from this study showed that increases in testosterone were ~3 fold higher in the hypertrophy protocol compared to the strength protocol. The hypertrophy protocol employed in the aforementioned study demonstrated a greater increase in metabolic stress, which may play a role in elevations in testosterone concentrations post-resistance exercise [101]. As a result, increases in post-exercise circulating testosterone may contribute to the anabolic response promoting hypertrophic adaptations. The relevance of the elevations in testosterone post-exercise stimulating muscle hypertrophy is further discussed in section 2.8.

2.8 Relevance of Acute Hormonal Responses to Hypertrophic Adaptations

Recently, the role of acute, post-resistance exercise elevations in anabolic hormones in skeletal muscle anabolism and hypertrophy has been questioned [102-105]. Wilkinson et al. [105]

employed a unilateral training model where participants performed lower-body resistance exercise (knee extension and leg press) for 8 wk at 3 days per wk. The participants performed a hypertrophy-type protocol consisting of 3 sets at 10-6 RM, 80-90% 1RM with 3 min rest intervals. Following training, muscle CSA of the vastus lateralis had increased, despite no significant acute elevations of serum GH, testosterone and IGF-1 being observed. These findings suggest that resistance exercise can result in muscle hypertrophy in the absence of alterations in systemic hormones. In another study, West et al. [104] employed a unique methodological design, where participants performed acute resistance exercise to elicit low or high hormone concentrations to assess the role of changes in endogenous hormone concentrations on muscle hypertrophy. Participants performed two resistance exercise trials consisting of (i) unilateral arm curl (low hormone) and (ii) the same single arm exercise with the contralateral arm followed by high-volume leg exercise (high hormone). The low hormone resistance exercise protocol consisted of 4 sets of 10 repetitions at a load that was 95% of 10 RM (with 2 min rest intervals), while the high hormone protocol comprised the same arm exercise intensity followed by 5 sets of 10 repetitions of leg press and 3 sets of 12 repetitions of leg extension/leg curl supersets (with 1 min inter set rest intervals between leg exercises). Despite greater elevations in serum GH, testosterone and IGF-1 concentrations, similar increases in myofibrillar protein synthesis of the biceps brachii was observed. Therefore, circulating hormones may not be necessary to initiate acute skeletal muscle protein synthesis and the adaptations observed may be mediated instead by an intrinsic, intramuscular process. Furthermore, West et al. [103] employed the same unique methodological design over a prolonged training period of 15 wk. No difference in muscle CSA of the elbow flexors and 1RM strength was observed between the low and high hormone training conditions. These findings are in agreement with their previous work suggesting the elevations in endogenous anabolic hormones may not be necessary for promoting hypertrophic adaptations.

In contrast, Ronnestad et al. [106] set out to challenge the evidence provided by West et al. [103]. In their study participants performed resistance exercise 4 x per wk over an 11 wk period and consisted of a high and low hormone condition, similar to the methods employed by West et al. [103]. However, high hormone training consisted of three leg exercises (leg press, knee extension and flexion) performed at 3 sets of 10 RM with 60 s rest followed by arm curl exercise (2 sets at 6-10 RM). The low hormone training comprised only of the arm exercise. It was reported that elevations in anabolic hormones such as GH and testosterone post-exercise contributed to superior 1RM strength and muscle CSA of the elbow flexors. Although, differences lie in the methodological design of these studies (i.e. training duration, volume and frequency), Ronnestad et al. [106] suggested that the reason for the non-significant difference observed in muscle CSA of the elbow flexors between the high vs low hormone training groups may be due to the exercise order. In the study by West et al. [103] the high hormone group performed arm curl exercise prior to the leg exercises, while Ronnestad et al. [106] high hormone group performed resistance exercise in the reverse order (i.e. the leg exercises before arm exercise). It was speculated that the exercise order employed by West et al. [103] may have redistributed the hormone-rich blood, from the arms to the legs, thus limiting the potential hypertrophic adaptions of the elbow flexors [107]. Considering the inconsistent evidence, it is difficult to draw definitive conclusions as to whether or not acute post-exercise elevations in anabolic hormones contribute to muscle protein synthesis over an acute or prolonged training period.

2.9 Resistance Exercise Combined With Blood Flow Restriction (BFR)

Over the last decade BFR, also known as occlusion or KAATSU training, has received a significant amount of attention due to the potential gains in hypertrophy and strength [13, 83]. The American College of Sports Medicine recommends resistance training should be performed at an intensity of ≥ 65% of 1RM to promote a substantial hypertrophic effect [108]. However,

BFR training has demonstrated significant increases in muscle strength and hypertrophy at training intensities as low as 20% 1RM [44-47].

The BFR technique involves creating a localised hypoxic environment during exercise by applying a pressure cuff to the proximal end of a limb, to partially occlude distal arterial blood flow and prevent venous outflow [13]. BFR training is typically performed at low-intensity (≤ 50% 1RM), with a set range of 3-5 and at ≥ 15 repetitions (or to volitional fatigue), combined with short rest periods (≤ 60 s) [13]. This training method has been suggested to be an effective training modality for athletes [46], injury rehabilitation patients, and the elderly [94, 109]. The hypertrophic and strength adaptations from BFR training are thought to be due to an increase in metabolic stress, which subsequently leads to an augmented anabolic hormone secretion, motor unit recruitment and intramuscular cell signalling [83].

2.10 Mechanisms of Muscle Hypertrophy and Strength adaptations from BFR training

2.10.1 Metabolic Stress and Hormonal Responses

Metabolic stress may contribute to skeletal muscle hypertrophic adaptations [110]. Resistance exercise combined with BFR has demonstrated significant elevations in the accumulation of metabolites, in particular, increased lactate production and decreased pH [94, 95, 111-113]. Takarada et al. [113] investigated the effects of 5 sets of ~14 repetitions of bilateral knee extension exercise at 20% 1RM, combined with or without BFR on several physiological responses. The increase in blood lactate doubled in the BFR group compared to control immediately post-exercise. The localised hypoxic environment created with BFR training increases dependence on anaerobic metabolism and also restricts the ability for lactate clearance by limiting venous return [114]. A greater augmentation in metabolic stress may play a role in the increase in anabolic hormone secretion [110]. It has been postulated that acute elevations in

GH concentrations in response to BFR training are associated with the accumulation of lactate and/or hydrogen ions within the muscle [77, 115]. The reduction in pH, may then potentiate the secretion of GH, through a chemoreceptive reflex mediated by intramuscular metaboreceptors and group III and IV afferent fibres [83, 84]. In the aforementioned study by Takarada et al. [113], GH concentrations rapidly increased ~290 times more than resting levels following BFR training. There are several other studies that have employed BFR training and have shown a significantly greater GH response in comparison to the identical resistance training without BFR [47, 94, 96, 111-113].

Other anabolic hormonal responses that have been measured following BFR training include IGF-1 and testosterone. Several studies have demonstrated an increase in circulating IGF-1 levels with BFR training [44, 94], while other studies have found no significant increase [95, 96]. Interestingly, while no difference in IGF-1 was observed, these studies reported a significant increase in GH concentrations following BFR training [95, 96]. One of the proposed functions of GH is to stimulate the secretion of circulating IGF-1 [56, 57]. The acute increases in GH, seen in the aforementioned studies, may not have had an impact on systemic IGF-1. It is proposed that the IGF-1 response to GH secretion may be delayed by 3-9 h, and peak IGF-1 levels until 16-28 h following resistance exercise [12]. The discrepancies between these studies may also be due to methodological variations. While all studies performed BFR resistance exercise at the same intensity, Takano et al. [94] and Abe et al. [44] protocols consisted of greater volume, which may have stimulated a greater IGF-1 response.

Conversely, BFR training has not yet shown to be a greater stimulator of testosterone responses than training without BFR [95, 112]. Despite observing high levels of blood lactate, BFR failed to generate a testosterone response. This leaves in doubt the association of metabolic stress and the secretion of testosterone. The difference in methodological design of these studies, in particular the intensity ($\leq$ 30% 1RM), volume, and exercise selection (bilateral knee extension [95], and single arm bicep curl combine with single leg calf raise [112]) may have led to this

result, as higher intensity, greater volume and large muscle mass exercises have been shown to promote greater increases in metabolic stress [12]. Furthermore, several other factors such as training experience, age, and gender can also affect the release of testosterone [12], which may have influenced the results. While varying responses in anabolic hormones have been observed following BFR training, its effects on hypertrophic adaptations may be associated with an increase in motor unit recruitment, as a result of increased metabolic stress.

2.10.2 Recruitment of Muscle Fibres

Blood flow restriction training creates a localised hypoxic environment by reducing the supply of oxygenated arterial blood to the muscle. By lowering the oxygen supply, it has been theorised that the lower threshold type I motor units fatigue more rapidly, which then requires the activation of type II motor units to maintain the same level of force production [116]. As a result, the recruitment of type II muscle fibres has been proposed to be an important mechanism to promote hypertrophic adaptions following BFR resistance exercise [117]. Several studies have assessed motor unit activity during BFR resistance exercise with surface electromyography (EMG) with varying outcomes. Following low-intensity BFR resistance exercise (≤ 50% 1RM), greater increases in EMG activity have been observed compared to the identical exercise without BFR [113, 118, 119]. In contrast, Wernborn et al. [120] reported no significant difference in muscle activity of the quadriceps following 3 sets of knee extension exercise at 30% 1RM to failure with BFR compared to without. Furthermore, low-intensity (≤ 20% 1RM) BFR training does not necessarily recruit the same amount of motor units compared to traditional high-intensity (≥ 80% 1RM) resistance exercise without BFR [121, 122]. While conflicting results have been reported, it is theorised that the build-up of metabolic stress can mediate muscle hypertrophy through an increase in fibre recruitment, which is associated with enhanced systemic and local growth factors [110].

2.10.3 Cell Signalling

Two studies have demonstrated increased phosphorylation of S6K1 following a bout of low-intensity resistance exercise with BFR and subsequently reported a greater increase in muscle protein synthesis at 3 h post-exercise [95, 123]. Furthermore, Werborn et al. [124] found a significant increase in mTOR signalling 1 h post low-intensity BFR training, while no changes were observed following the identical training without BFR. However, at 24 h post-exercise, there was no difference in mTOR signalling between the BFR and control groups, which is likely due to the acute (ie. 1-4 h) post-exercise time course for mTOR activation [125]. Therefore, BFR training, even at low-intensity (20% 1RM) is able to upregulate local anabolic signalling pathways and subsequently initiate muscle protein synthesis.

2.11 Physiological Responses to Resistance Training In Hypoxia

2.11.1 Differences between Blood Flow Restriction and Systemic Hypoxic Resistance Training Methods

Low-intensity BFR training can lead to significant morphological adaptations compared with traditional resistance exercise at higher intensities (i.e. ≥ 65% 1RM) [126]. The benefit of using this type of training modality is to allow diverse populations, such as the elderly or rehabilitation patients, to develop muscular strength and hypertrophic adaptations. BFR training is known to limit potential joint and muscle injury due to the associated low mechanical stress, reduced muscle damage and inflammation [113]. However, BFR training is not without its potential physiological risks, including dizziness, paraesthesia, chills and subcutaneous petechial haemorrhage [127]. Therefore, it is important to have an experienced individual apply the pressure cuff and use the appropriate equipment to monitor the occlusive pressure whilst undertaking BFR training. Elastic wraps can be used as an alternative method, however, caution

needs to be taken when applying and monitoring the occlusive pressure, which can be difficult without protocols and equipment that provide feedback [13].

While strength and hypertrophic adaptations have been reported following low-intensity resistance training with BFR (REF), it may be difficult to transfer this type of training modality to athletic populations due to some of the aforementioned limitations. For example, it may be difficult to supervise a group of athletes, as each individual may require the application of multiple pressure cuffs, and this may need to be closely monitored throughout the training session. Furthermore, training at these low-intensities (aiming to reduce mechanical stress), avoids training at high-intensity (i.e. > 80% 1RM), which has been shown to increase connective tissue strength [48] and neurological adaptations [4]; subsequently risking the loss of these benefits. Moreover, BFR training requires the application of the cuff to the proximal ends of the joints, consequently limiting exercise to specific limbs, and as a result, training of the whole body musculature is eliminated.

To overcome these limitations, the use of systemic hypoxia, instead of BFR, offers an alternative training modality appealing to individuals who want to promote strength and hypertrophic adaptations. Both of these training interventions are mediated by the hypoxic stimulus. However, RTH may be more beneficial for athletic populations, as it allows individuals to train at higher intensities and perform multi-joint exercise while under hypoxic conditions. As such, RTH has the potential to maximise both morphological and neurological adaptions and subsequently enhancing performance. A summary of the studies examining the physiological and morphological responses to RTH is outlined in Table 2.

Table 2. Summary of research examining the acute and chronic responses to resistance training combined with systemic hypoxia.

Study	Subjects	Training Protocol/ Conditions	Exercise (Intensity)	Sets x Reps (rest intervals)	Significant Outcomes
Etheridge et al. [128]	Healthy males (n = 7)	Acute H; F_iO_2 = 0.12 N; F_iO_2 = 0.21	Isometric knee extension (70% MVC)	8 x 6 (2 min)	↑ MPS in N but not H ↔ peak MVC in H and N
Kon et al. [129]	Healthy males (n = 14)	Acute H; F_iO_2 = 0.13 N; F_iO_2 = 0.21	Bench and leg press (70% 1RM)	5 x 10 (1 min)	↓ SpO_2 in H Greater ↑ [BLa^-] after H ↑ GH after H only
Kon et al. [130]	Healthy males (n = 8)	Acute H; F_iO_2 = 0.13 N; F_iO_2 = 0.21	Bench and leg press (70% 1RM)	5 x 14 (1 min)	↓ SpO_2 in H Greater ↑ [BLa^-] after H ↑ GH after H only ↔ subjective fatigue between H and N
Ho et al. [131]	Healthy males (n = 10)	Acute H; F_iO_2 = 0.15 N; F_iO_2 = 0.21	Squat (30% 1RM)	5 x 15 (90 s)	↓ SpO_2 in H ↑ [BLa^-] after H and N (no difference between conditions) ↑ GH and T after H and N (no difference between conditions)
Scott et al. [132]	Healthy males (n = 12)	Acute HH; F_iO_2 = 0.13 MH; F_iO_2 = 0.16 N; F_iO_2 = 0.21	Squat and deadlifts (80% 1RM)	5 x 5 (3 min)	↓ SpO_2 in H (greater in HH) ↔ force and power in H and N ↑ HR in H (greater in HH) ↔ subjective fatigue between H and N

Study	Subjects	Training Protocol/ Conditions	Exercise (Intensity)	Sets x Reps (rest intervals)	Significant Outcomes
Friedman et al. [133]	Untrained males (n = 10)	Chronic 3 pw x 4 wk H; F_iO_2 = 0.12 N; F_iO_2 = 0.21	Unilateral knee extension (30% 1RM)	6 x 25 (1 min)	↔ maximal isokinetic strength between H and N ↔ muscle CSA between H and N ↑ strength endurance (no difference between conditions)
Nishimura et al. [134]	Untrained males (n = 10)	Chronic 2 pw x 6 wk H; F_iO_2 = 0.16 N; F_iO_2 = 0.21	Bilateral elbow extension and flexion (70% 1RM)	4 x 10 (1 min)	↑ muscle CSA after H only ↑ 1RM strength 3 wk after H ↑ 1RM strength 6 wk after in H and N
Manimmanakorn et al. [135]	Female netball athletes (n = 30)	Chronic 2 pw x 5 wk H; SpO_2 maintained at ~80% BFR (160-230 mmHg) N: ambient air	Bilateral knee extension and flexion (20% 1RM)	6 x ~28 (30 s)	Greater ↑ MVC_3 after H than N Greater ↑ MVC_{30} after H than N Greater ↑ strength endurance after H and BFR than N ↑ perceived muscle pain in H than BFR and N Greater ↑ sport-specific performance after H and BFR than N

Study	Subjects	Training Protocol/ Conditions	Exercise (Intensity)	Sets x Reps (rest intervals)	Significant Outcomes
Manimmanakorn et al. [136]	Female netball athletes (n = 30)	Chronic 3 pw x 5 wk H; SpO_2 maintained at ~80% BFR (160-230 mmHg) N: ambient air	Bilateral knee extension and flexion (20% 1RM)	6 x ~28 (30 s)	↑ RMS during MVC_3 with BFR than H and N ↑ RMS during MVC_{30} with BFR than H and N ↑ RMS during strength endurance with BFR than H and N
Kon et al. [137]	Healthy males (n = 16)	Chronic 2 pw x 8 wk H; $F_iO_2 = 0.14$ N; $F_iO_2 = 0.21$	Bench and leg press (70% 1RM)	5 x 10 (90 s)	↑ body composition (no difference between conditions) ↑ muscle CSA (no difference between conditions) ↑ 1RM strength (no difference between conditions) Greater ↑ strength endurance after H than N ↑ GH after H than N (in the first and last session)
Kurobe et al. [138]	Healthy males (n = 13)	Chronic 3 pw x 8 wk H; $F_iO_2 = 0.13$ N; $F_iO_2 = 0.21$	Unilateral elbow extension (10RM load)	3 x 10 (1 min)	↑ muscle strength (no difference between conditions) Greater ↑ muscle thickness after H than N ↑ GH after H than N (in the first and last session)

Study	Subjects	Training Protocol/ Conditions	Exercise (Intensity)	Sets x Reps (rest intervals)	Significant Outcomes
Ho et al. [139]	Healthy males (n = 18)	Chronic 3 pw x 6 wk H; F_iO_2 = 0.15 N; F_iO_2 = 0.21	Squat (10RM load)	3 x 10 (2 min)	↑ 1RM strength (no difference between conditions) ↔ maximal isometric and isokinetic strength between H and N
Yan et al. [140]	Healthy males (n = 25)	Chronic 2 pw x 5 wk HH; F_iO_2 = 0.13 MH; F_iO_2 = 0.16 N; F_iO_2 = 0.21	Squat (70% 1RM)	5 x 10 (1 min)	Greater ↑ GH after HH than MH and N (in the first and last session) ↑ 1RM strength (no difference between conditions) ↑ maximal isokinetic strength (HH greater than N) ↑ body composition (no difference between conditions)

Reps: repetitions, pw: per week, wk: weeks, H: hypoxia, N: normoxia, F_iO_2: fraction of inspired oxygen, HH: high level hypoxia, MH: moderate level hypoxia, BFR: blood flow restriction, MVC: maximal voluntary contraction, 1RM: one repetition maximum, RM: repetition maximum, min: muntes, s: seconds, MPS: muscle protein synthesis, SpO_2: oxygen saturation, GH: growth hormone, [BLa^-]: blood lactate, CSA: cross-sectional area, MVC_3: 3 second maximal voluntary contraction, MVC_{30}: 30 second maximal voluntary contraction, RMS: root mean square of electromyography, ↑: increase, ↓: decrease, ↔: no significant change.

2.11.2 Morphological and Strength Adaptations

There are conflicting results regarding RTH and its effect on morphological adaptations [134, 135, 137, 138]. Manimmanakorn et al. [135] reported a greater increase in muscle CSA of the knee extensors and flexors, when resistance exercise was performed at 20% 1RM (3 sets of repetitions to failure), 3 x per wk for 5 wk in a hypoxic environment (arterial oxygen saturation [SpO_2] 80%), compared with identical exercise in normoxia. Additionally, following RTH (fraction of inspired oxygen [F_iO_2] = 0.16) at 70% 1RM (4 sets of 10RM), 2 x per wk over 6 wk, an increase in muscle CSA of the elbow flexors and extensors has been observed [134]. More recently, Kurobe et al. [138] also demonstrated an increase in muscle thickness of the elbow extensors following RTH (F_iO_2 = 0.13), at 4 sets of 10RM, 3 x per wk over an 8 wk period. While all three studies observed a significant increase in morphological adaptations, it was also reported that RTH resulted in significant increases in muscle strength compared with the equivalent training in normoxia [134, 135, 138] (Table 2). Further to this, Manimmanakorn et al. [135] showed RTH improved sport-specific fitness tests in female netball players and this may have be attributed to enhanced training adaptations.

In contrast, three separate studies have reported no difference in morphological adaptations following RTH when compared with the equivalent exercise in normoxia [133, 137, 139]. The discrepancies between the results of these studies may be attributed to the methodological design. For example, increases in the level of hypoxia, training frequency and duration, exercise intensity and volume, individually or combined can have an impact on promoting morphological adaptations (Table 2). Interestingly, in these studies [133, 137, 139], resistance exercise in either hypoxic or normoxic conditions produced similar increases in 1RM strength, suggesting that hypoxia provided no additional benefit on these physiological adaptations.

A more recent study by Scott et al. [132] assessed whether physical performance during high-intensity resistance exercise (two exercises, 5 sets of 5 at 80% 1RM with 3 min rest) is effected

by high (F_iO_2 = 0.13) or moderate (F_iO_2 = 0.16) levels of hypoxia. It was determined that the hypoxic stimulus did not alter physical performance which was measured by concentric force and power variables of the squat and deadlift exercises. Although the results from this acute study indicate hypoxia does not impact physical performance, there is conflicting evidence in the literature regarding RTH and its effect on morphological and strength adaptations, therefore further investigation is warranted.

2.11.3 Hormonal and Metabolic Responses

Few studies have investigated the effects of metabolic and hormonal responses to RTH. Kon et al. [130] and [129] investigated acute hormonal responses in hypoxia (F_iO_2 = 0.13) and normoxia during leg and bench press exercise at 50% and 70% 1RM, consisting of 5 sets of 14 repetitions and 5 sets of 10 repetitions (with 1 min rest intervals), respectively. Both studies reported RTH accentuated the secretion of GH and the accumulation of metabolic stress to a greater extent compared to the equivalent exercise in normoxia. In contrast, Ho et al. [131] asked participants to perform 5 sets of 15 repetitions at 30% 1RM (90 s rest intervals) of the squat exercise only in hypoxia (F_iO_2 = 0.15), and reported no significant difference in GH concentrations or blood lactate levels post-exercise. Discrepancies in the results observed in these studies may be due to a combination of the exercise training variables of volume, intensity and rest intervals between sets, as the appropriate manipulation of these variables is likely to alter the degree of hypoxia experienced by the muscle, therefore altering the response (Table 2). The aforementioned studies by Kon et al. [129, 130] also found no significant difference in serum testosterone or IGF-1 levels following the same low-intensity resistance exercise performed in hypoxia and normoxia, which is similar to the observed responses following BFR training.

More recently, two studies have investigated the effects of moderate-intensity RTH over a six to eight week duration. Both Kurobe et al. [138] (one exercise, 3 sets of 10RM with 60 s rest

intervals, F_iO_2 = 0.13%) and Kon et al. [137] (two exercises, 5 sets of 10 at 70% 1RM with 60 s rest intervals, F_iO_2 = 0.14) assessed the acute GH response on the first and last resistance exercise session. The hypoxic group observed a significantly greater increase in GH concentrations compared to the identical training completed in normoxia. Further to this, peak GH levels were similar in both the first and last session following RTH, while no such GH response was observed in normoxia. More recently, Yan et al. [140] investigated the effects of different levels of systemic hypoxia on hormonal responses following 5 weeks of resistance training (one exercise, 5 sets of 10 at 70% 1RM with 60 s rest intervals, F_iO_2 = 0.13 and 0.16). Similar to the aforementioned studies, acute GH concentrations were measured during the first and last training sessions. The greatest GH response was observed following exposure to high levels of hypoxia (F_iO_2 = 0.13), compared to moderate hypoxia (F_iO_2 = 0.16) and normoxia. These findings suggested that repeated bouts of the same resistance exercise protocol, combined with a hypoxic stimulus, may have a greater influence on hormonal responses and that this response is not altered through adaptation to the stimulus.

2.11.4 Cell Signalling

Currently, only one study has investigated the effects of RTH on muscle protein synthesis and anabolic cell signalling [128]. In this study, participants performed moderate-intensity 70% 1RM resistance exercise (6 sets of 8 repetitions) with 2 min rest intervals in a hypoxic environment (F_iO_2 = 0.12). They found an increase in S6K1 phosphorylation but observed no significant increase in muscle protein synthesis. However, it must be noted that increases in S6K1 phosphorylation and other anabolic cell signalling markers do not always correlate with muscle protein synthesis responses post-exercise [141]. A simplified flowchart of the proposed mechanisms that may affect hypertrophic and strength adaptions to BFR and RTH training modalities are displayed in Figure 4.

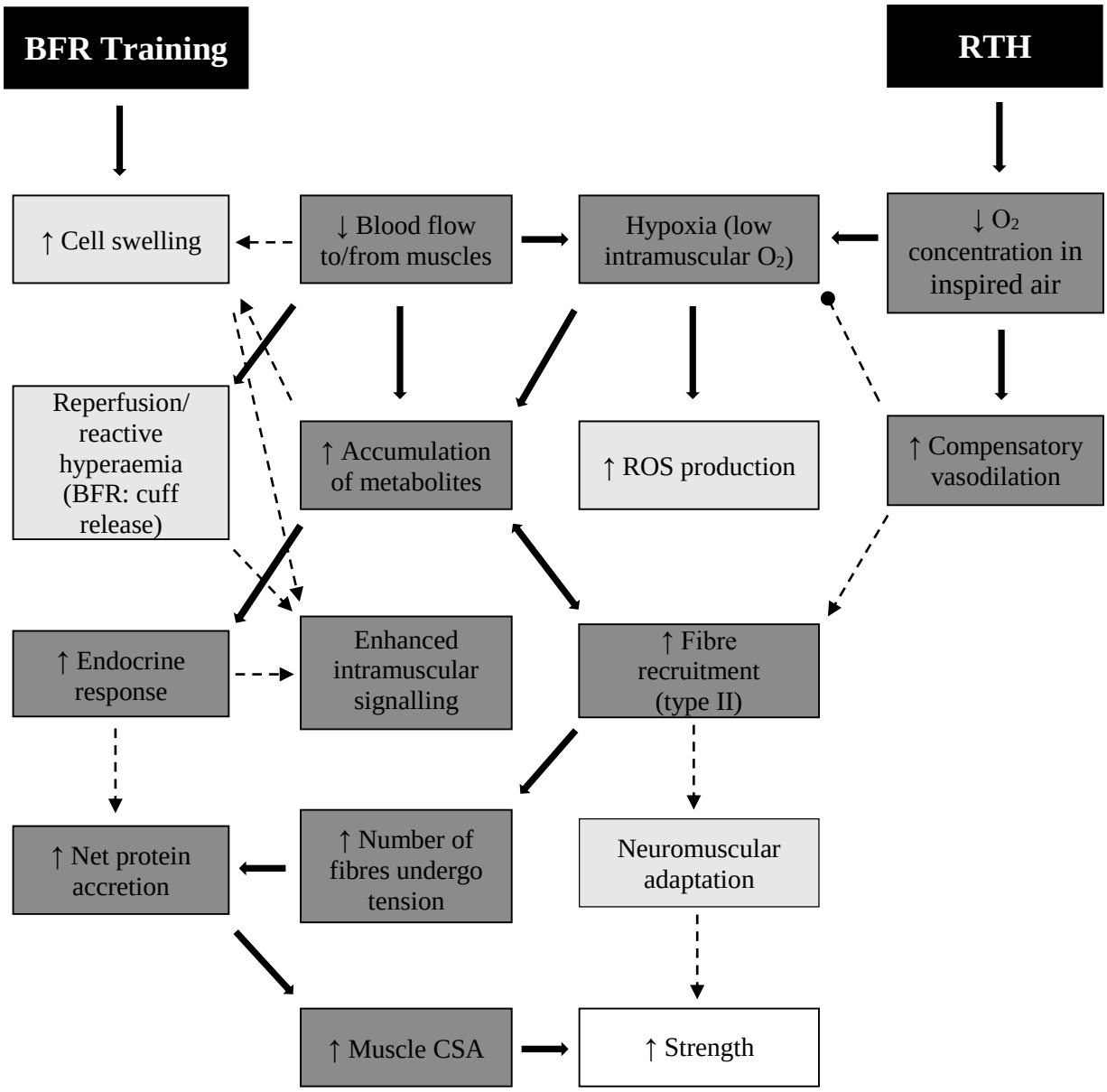


Figure 4. A schematic of the proposed mechanisms by which blood flow restriction (BFR) and resistance training in systemic hypoxia (RTH) may facilitate muscle hypertrophy and strength. *Dark grey boxes* represents likely mechanisms, *light grey boxes* denotes mechanisms that require further research, *white boxes* signifies outcomes of training. *Bold arrows* indicate likely link between proposed mechanisms, while *dotted arrows* imply a possible link requiring further investigation. *Circle arrow heads* indicate an inhibitory effect. O_2: oxygen, ROS: reactive oxygen species, CSA: cross-sectional area, ↑: increase, ↓: decrease. Adapted from Scott et al. [14].

2.12 Chapter Summary

Resistance training is known to improve various athletic qualities (i.e. strength, power and speed) [1]. Therefore, it is necessary for athletes to consistently perform resistance exercise in order to improve their performance. There are various forms of resistance exercise protocols that athletes currently undertake aiming to enhance performance through increases in neurological and morphological adaptations [2]. These physiological adaptations to resistance training require the appropriate manipulation of exercise training variables to achieve a specific training outcome. Strength-type protocols aim to improve neurological adaptations, whereas, the aim of hypertrophy-type protocols is to maximise morphological responses [2].

Traditionally, it is recommended that resistance exercise be performed at an intensity of ≥ 65% 1RM to achieve a substantial effect for muscular hypertrophy [8]. Muscle hypertrophic adaptations to resistance exercise occur via a combination of multiple factors which include; mechanical and metabolic stress, neural factors and endocrine responses [9].

Anabolic hormones are thought to play an integral role in promoting muscle hypertrophy [10, 11]. The augmentation of these systemic hormones appears to be strongly related to significant increases in muscle hypertrophy, with hypertrophy-type protocols producing greater augmentation in anabolic hormones than traditional strength-type protocols [12].

A novel training modality that combines low-intensity resistance exercise with BFR has been shown to facilitate muscular strength and hypertrophic adaptions through multiple factors which include; enhanced metabolic stress, motor unit recruitment, intramuscular cell signalling, and elevated hormonal production [13]. This training modality is predominately mediated by a localised hypoxic stimulus and is typically performed at a low-intensity (≤ 50% 1RM) [13], which is well below the recommended threshold for strength and hypertrophic adaptations. However, BFR training is limited to exercising isolated limbs, and as a result, training of the whole body musculature is eliminated.

Resistance training in hypoxia can overcome these limitations and produce similar physiological responses to those observed following BFR training. The potential benefit of performing RTH is to augment the metabolic stress response and associated increase in GH secretion to promote a hypertrophic adaptation [14]. The majority of studies have performed RTH at low-intensity levels, aiming to maximise muscle hypertrophy. However, this type of protocol may not be optimal for athletic populations as it eliminates the benefits of maximal strength. As a result, it may be more beneficial for athletes to perform RTH during maximal strength training to get a supplementary benefit of hypertrophy instead. Therefore, the aim of this investigation was to determine if the use of systemic hypoxia can increase the GH response to a strength training protocol to within the levels previously reported using hypertrophy-type protocols.

Chapter Three: Methods

3.1 Participants

Sixteen resistance trained males (age 24 ± 5 years, height 180 ± 6 cm, mass 82 ± 8 kg) were recruited to participate in this investigation. Participants were recruited from the local University community via notices posted on University bulletin boards, and announcements at lecture and laboratory classes. Females were excluded from participation due to the variable hormonal responses observed following resistance exercise in this population [101].

In order to be eligible for the study, participants were required to meet all of the following inclusion criteria:

(i) Males aged between 18-35 years;

(ii) Currently involved in resistance training (minimum 2 x per wk for 6 months);

(iii) Injury-free at the time of testing;

(iv) No exposure to > 3000 m altitude in the preceding 6 months;

(v) No history of severe mountain sickness, cardiovascular or respiratory conditions;

(vi) No current history of taking medications, such as anabolic supplements and anti-inflammatory agents;

(vii) Agreed to abstain from resistance exercise 48 hours prior to all experimental trials.

(viii) Agreed to perform the experimental trials in a fasted state.

This investigation was approved by the Human Research Ethics Committee of the Australian Catholic University (review number 2014 197V). All participants provided informed written consent prior to participating in the study (Appendix B).

3.2 Methods and Procedures

This investigation was conducted using a single-blinded, counterbalanced crossover-design. Participants attended the Exercise Science clinical gym at the Australian Catholic University on three occasions over a two week period. The first session involved the participants performing a 1RM strength test for bench press and leg press exercises, followed by a familiarisation with the isometric maximal voluntary contraction (MVC) procedure. The following two sessions comprised the experimental trials in which the participants randomly performed the resistance exercise protocol in either hypoxia or normoxia. Each participant performed the experimental trials in in a random order, separated by seven days.

3.2.1 One Repetition Maximum (1RM) Testing

Maximum strength levels were assessed for 45° leg press and bench press exercises using the recognised guidelines established by the National Strength and Conditioning Association [7]. Participants performed a warm-up with a light resistance (~50% of their perceived 1RM) for 10 repetitions, followed by one set of 4 repetitions at a load corresponding to ~60-80% of their perceived 1RM. A last warm-up set of 2 repetitions was performed prior to their first 1RM attempt. Following this, sets of one repetition of increasing weight (5-10% for upper-body exercise and 10-20% for lower-body exercise) were then performed until their 1RM was determined. Three minutes rest was provided between each successive lift attempt. Using this protocol, 1RM was determined within five trials (leg press 5 ± 1 and bench press 4 ± 1 trials). The participants were instructed to maintain proper technique during each lift in order for the lift to be considered a successful 1RM attempt. A successful 1RM leg press lift required the participants to lower the weight to a knee angle of 90° flexion during the eccentric phase and to fully extent the knee (180°) at the end of the concentric phase. Successful bench press 1RM required the participants to maintain five-point body contact position (head, upper back, and

buttocks on the bench with both feet on the floor), and to lift the weight from the chest to full elbow extension (180°) during each lift.

3.2.2 Experimental Trials Including Resistance Exercise Protocol

Experimental trials were conducted at the same time of day for each participant between 0700 and 1100 to minimise any diurnal variations in metabolism and hormonal responses [142]. Participants arrived at the gym in a fasted state **(**11 ± 2 h**)** and immediately provided a venous blood sample to determine baseline GH and blood lactate levels. At this time, participants were also prepared for surface EMG assessment. Prior to the commencement of the resistance exercise protocol, participants performed two isometric MVC to allow normalisation of surface EMG recordings between trials. Following this, the participants performed the resistance exercise protocol, which consisted of two consecutive exercises (leg press and bench press). Each exercise involved a two set warm-up at 50% (five repetitions) and 75% of 1RM (three repetitions), respectively, followed by 5 sets of 3 repetitions at 85% of 1RM. A 3 min rest was allowed between all sets and exercises. For both lifts, participants were instructed to lower the load at a constant velocity over 2 s and lift the load as explosively as possible for each repetition. Participants were assisted on proper lifting cadence using verbal cues and a metronome to maintain the appropriate timing. The participants performed the resistance exercise protocol in both normobaric normoxia (21% oxygen [NOR]), and normobaric hypoxia (12% oxygen, [HYP]). After the completion of the resistance exercise protocol, further venous blood samples were collected for GH and lactate, at 5, 15, 30, and 60 min (Figure 5). In addition, arterial oxygen saturation (SpO_2), heart rate (HR) and rating of perceived exertion (RPE) were collected throughout the experimental trials.

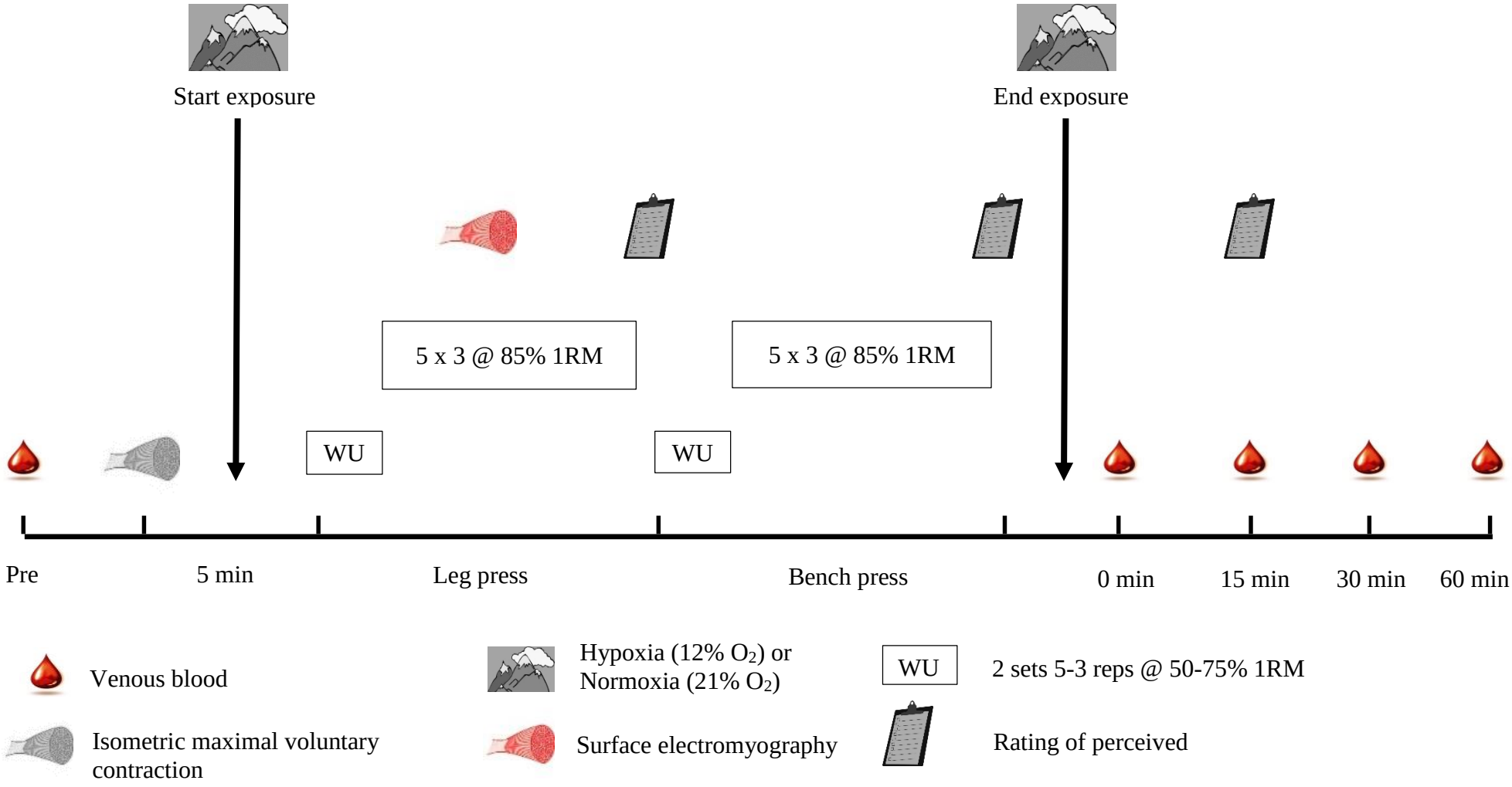


Figure 5. The experimental trial. Note: Exposure to hypoxia (12% O_2) occurs only in one trial, while normoxia is used in the alternate trial.

3.2.3 Surface Electromyography

Muscle activation of the right vastus lateralis was recorded using surface EMG during the leg press component of the resistance exercise protocol. The muscle site was located at the lower third on the line from the anterior superior iliac spine to the lateral side of the patella, as outlined by SENIAM [143]. After locating the site, the participant's skin was shaved, lightly abraded and cleaned with alcohol to improve the electrode-skin contact. Bipolar electrodes (12.5mm in diameter, 19mm inter-electrode distance; Duotrode Electrodes, Myotronics, USA) were placed on the muscle belly, and correct placement confirmed via palpation of the quadriceps during an isometric contraction.

3.2.4 Isometric Maximal Voluntary Contraction

Surface EMG signals were normalised between the two experimental sessions using an isometric MVC on the 45° leg press apparatus. A force plate (9286AA, Kistler, Switzerland) was secured to the leg press platform by ratchet tie down straps. The leg press was customised to allow each participant to perform the isometric MVC at a knee angle of 60°. Previous research has demonstrated that the quadriceps can produce the greatest amount of force at long to moderate muscle lengths [144]. Therefore, the functionality of the apparatus allowed the assessment of optimal force at muscle lengths relative to 60° knee joint angle. The appropriate angle was determined using a goniometer and the leg press platform immobilised by two ratchet tie down straps on either side to a 2 m plank of timber, placed underneath the seat of the apparatus (Figure 6). The isometric MVC was performed on the right leg only with the foot positioned wholly on the force platform. A grid was drawn up on the force plate to ensure the participant performed this task in the same foot position both within and between trials. This foot position was identical to the position used during the 1RM leg press test and was maintained throughout the experimental trials. During the performance of the isometric MVC

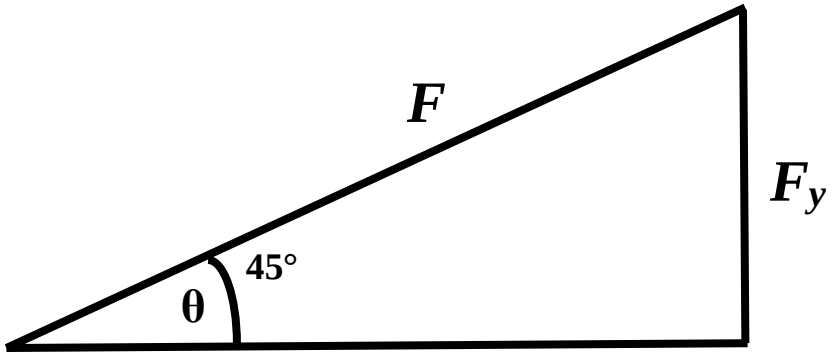
the participants were instructed to place their right foot on the force plate and on the verbal command “go”, push as hard and fast as possible for 3 s. The testing protocol consisted of the participant performing two warm-up sets at 50% and 75% of their perceived isometric MVC for 3 s, respectively. Two isometric MVC of 3 s duration were then performed separated by a 3 min rest period. Mean force was calculated for each trial, with the participants required to perform the two trials with < 5% difference in mean force. If the mean force was > 5% between trials, additional trials were performed until the criterion was met. To minimise the risk of performing multiple trials, the participants performed familiarisations trials of the isometric MVC during the 1RM strength testing session.

As a result of equipment limitations, we were unable to perform an isometric MVC of the bench press at the same relative elbow joint angle (e.g. 90 degrees). Given the performance of an isometric MVC is critical for the normalisation of the EMG signal between experimental sessions, this limitation meant the collection of meaningful EMG data during the bench press portion of the experiment was not possible.

Figure 6. The customised leg press. The platform is locked in place by the ratchet tie down straps, so that the contraction is isometric. Each participant was seated at a knee angle of 60° flexion when performing the MVC.

3.2.5 Quantification of Force on the Leg Press Apparatus

To confirm the accuracy of force produced during the performance of the isometric MVC, trigonometry was used to solve and correct for any effect of securing the force plate to the 45° leg press apparatus (Figure 7). To clarify the force plate output a strain gauge was attached between the steel frame (immovable) and the leg-press sled (moveable), which was immobilised by a ratchet tie down strap. With the strain gauge attached, a range of loads (i.e. 5, 10, 20, 40 kg) was added to the leg-press sled to calibrate the force produced at sin (45°) and compare this resultant force to the equivalent vertical ground reaction force. Strapping of the force plate to the 45° leg-press sled had no impact on the accuracy of force produced during the isometric MVC. Throughout the duration of the study, calibration of the force plate was frequently performed to ensure the accuracy of force measured during the experimental trials.



F= force produced in Newtons

F_y = sinθ x F

Θ= angle of the leg press platform (45°)

***Figure* 7**. Trigonometry calculation of force produced during the isometric MVC on the leg press apparatus.

3.2.6 Hypoxic and Normoxic Exposure

During the performance of the experimental trials the participants wore a facemask (7450 V2, Hans Rudolph, USA) combined with a two way non-rebreathing respiratory valve (2700 Series, Hans Rudolph, USA). The facemask was connected to a hypoxic generator (HYP123, Hypoxico Inc, USA) via a series of Douglas bags to create a reservoir from which the participants could breathe (Figure 8). The hypoxic generator was used to fill and maintain the Douglas bags in both normoxic (21% oxygen) and hypoxic (12% oxygen) conditions to ensure the participants were blinded to the condition they were experiencing in each of the trials. The mask was fitted to the participants immediately after the completion of the isometric MVC and 5 min prior to starting the resistance exercise protocol. Exposure ceased immediately after exercise (~50 min) (Figure 5). Given that previous studies have shown no change in basal levels in GH after 15 min exposure to hypoxia, we elected to provide 5 min of acclimation to the different environmental conditions [129, 130]. This provided adequate time for SpO_2 to decrease and

reflected a more ecologically valid approach to this type of training. The level of hypoxia (12% oxygen) was chosen as Kon et al. [129, 130] demonstrated significant increases in GH concentrations using a similar level of hypoxia during resistance exercise.

Figure 8. Hypoxic environment. The hypoxic generator was connected to a series of Douglas bags and further on the participant with the Hans Rudolf two-way valve facemask.

3.2.7 Rating of Perceived Exertion (RPE)

The Borg RPE scale [145] was used to measure the perceived difficulty of each specific exercise and the overall session. Using a chart, the participants were instructed to select a number from 0-10, where 0 represented "rest" and 10 "maximal" to rate the difficulty of exercise (Appendix C). The participants provided an RPE score at three time points; immediately post leg press, immediately post bench press and a sessional RPE, 15 min after the completion of the resistance exercise protocol.

3.2.8 Heart Rate (HR) and Oxygen Saturation (SpO_2)

Throughout the experimental trials HR was measured using a standard chest strap heart rate monitor (FT1, Polar, Finland), and SpO_2 by pulse oximetry from the index finger (Oxi-Go QuickCheck Pro, Oximeter Plus, Inc., USA). These two measures were collected prior to the performance of each set (in the last 30 s of the rest period) to ensure consistent readings and reduce any variability when collecting these measurements, with the participants being blinded during the collection. The data were then averaged and presented as an average HR and SpO_2 for leg press and bench press exercises.

3.2.9 Blood Sampling and Analysis

Venous blood samples (5 mL) were obtained from a forearm vein before normoxia and hypoxia exposures (pre), and 5, 15, 30 and 60 min after exercise. Pre samples were collected into a serum separator tube (Greiner Vacuette Z Serum Sep Clot Activator, Grenier Bio-One, Thailand) via a 21 gauge needle inserted into a medial forearm vein. Post-exercise blood samples were collected via cannulation of a medial forearm vein with the participants lying in a supine position. Serum samples were allowed to clot for 30 min before centrifugation (K241R, Thermoline Scientific, Australia) at 4°C and 4000 rpm for 10 min. Serum was aliquoted and stored at -80° for later analysis.

Serum GH concentrations were measured using an ELISA assay kit (DGH100 Quantikine ELISA Kit, R&D Systems, USA). The assay had a reported minimum detectable dose of 2.1 pg/mL and an intra and inter-assay CV of 4.1 and 9.4%, respectively. Blood lactate concentrations were analysed from the same venous blood samples immediately after blood collection at each of the equivalent time points. Blood lactate was measured using a portable lactate analyser (Lactate Pro 2, Arkray Inc, Japan).

3.2.10 Data Collection and Analysis

A mechanical goniometer (DTS Mechanical Goniometer 504, Noraxon, USA) was positioned on the right leg on the lateral side of the knee joint between femur and tibia articulations, which was placed in line with the greater trochanter and lateral malleolus. A second goniometer was positioned on the right arm on the lateral side of the elbow joint (lateral epicondyle), and placed in line with the humeral and ulna shafts. The time derivative of the flexion angle was used to identify the concentric, isometric and eccentric phases of each repetition. Surface EMG data was collected from the vastus lateralis only and was sampled at 1000 Hz with all channels having a low pass anti-alias filter set to 500 Hz using an EMG feedback unit (Myotrace 400, Noraxon, USA). The data were transferred to a laptop where it was then full wave rectified using the root-mean-square method across a 200 ms window. Myoelectrical activity was defined as the area under the rectified EMG-time trace, commonly referred to as integrated EMG that was measured after the onset on contraction. All myoelectrical data is expressed as normalised mean and integrated EMG in arbitrary units.

The onset of contraction for the 2 s mean EMG during the isometric MVC was determined when the smoothed rectified signal rose above 10% of the maximal signal reached during the isometric MVC. For each repetition (both eccentric and concentric contraction), EMG data for the vastus lateralis was normalised to the best of the two isometric MVC. The onset of contraction for each repetition during the performance of the leg press was determined when knee joint angle deviated 2° off baseline knee joint angle. Baseline joint angle is referred to the knee being fully extended prior to the start of the eccentric contraction phase (~180°). The same determination for the onset of contraction (2° off baseline elbow joint angle) for each repetition of the bench press was also used. All analysis was performed using LabChart 7.3 (ADInstruments, Australia).

Vertical ground reaction force was recorded using a force plate (9286AA, Kistler, Switzerland), with data sampling at 1000 Hz through a low pass Butterworth filter of a 100 Hz using Bioware software 5.03 (2812A-05, Kistler Bioware, Switzerland). During each isometric MVC, force-time data was immediately transferred from the Bioware software onto a customised spreadsheet in Microsoft Excel, where mean force was calculated over a 2 s window. The onset of contraction during each trial was determined when the force exceeded 25% of baseline force (1 s average) prior to the commencement of the isometric MVC (command "go").

3.3 Statistical Analysis

A contemporary analytical approach involving magnitude-based inferences was used to detect small but important effects between HYP and NOR trials [146]. All data was log-transformed to account for non-uniformity of error. Differences between conditions were assessed using the effect size (ES) statistic with 90% confidence intervals and percent difference to determine the magnitude of effect using a customised spreadsheet [147]. The magnitude of difference (increase or decrease) between the means were classified as '*important*' when there was a ≥75% likelihood that the true value of the statistic was practically or mechanistically important, and when there was a <5% chance that the statistic would occur in the opposite direction [146]. Likely differences between the means that were <75% were classified as '*trivial*', and when the likelihood of the statistics could occur >5% in both directions, the effect was reported as '*unclear*'[146]. Area under the curve (AUC) analysis for GH and lactate in the post-exercise period were calculated using a standard trapezoidal technique in Microsoft Excel. The magnitude of effect was classified as small (0.2-0.5), moderate (0.6-1.1), large (1.2-1.9), and very large (≥ 2.0) [148]. All descriptive data are expressed as mean ± standard deviation. Post-hoc analysis comparing the difference in the means of GH from pre to 5 min post-exercise, power was calculated as 0.84 (input parameters, effect size = 0.82; alpha = 0.05, sample = 15), using G*Power (version 3.1.7).

Chapter Four: Results

4.1 Participants

All sixteen participants successfully completed both experimental trials; however, due to equipment malfunction, the blood samples of one of the one participants were compromised. Consequently, data is reported for an N=15. Following the completion of each experimental trial, participants described whether they were in HYP or NOR conditions. Twenty-nine out of thirty-two trials assumed the correct condition. The anthropometric and strength measures are reported in Table 3.

Table 3. Participants' physical and strength characteristics

Age (years)	Height (cm)	Mass (kg)	Leg press 1RM (kg)	Bench press 1RM (kg)	Leg press 85% load (kg)	Bench press 85% load (kg)
25 ± 5	180 ± 6	83 ± 6	336 ± 43	103 ± 16	291 ± 36	88 ± 13

Values are expressed as mean ± SD (n=15)

4.2 Pulse Oximetry

Using magnitude-based analysis, an *important* decrease in SpO_2 during exposure to the hypoxic trial was observed (Figure 9. A). SpO_2 in the HYP trial was *importantly* lower than baseline levels at all-time points after hypoxic exposure (post-exposure ES -1.81 ± 0.14, leg press ES -2.45 ± 0.15, bench press ES -2.25 ± 0.15).

4.3 Heart Rate

There was an *important* increase in HR from baseline to post-exposure in the HYP trial ES (1.17 ± 0.41) (Figure 9. B). Similarly, an *important* increase was also observed during leg press (ES 1.33 ± 0.37) and bench press (ES 1.37 ± 0.31) exercise compared to baseline in the HYP trial (Figure 9. B). However, participants appeared to recover similarly between trials as *trivial* differences were observed in HR between conditions when comparing leg and bench press to post-exposure (ES 0.04 ± 0.19).

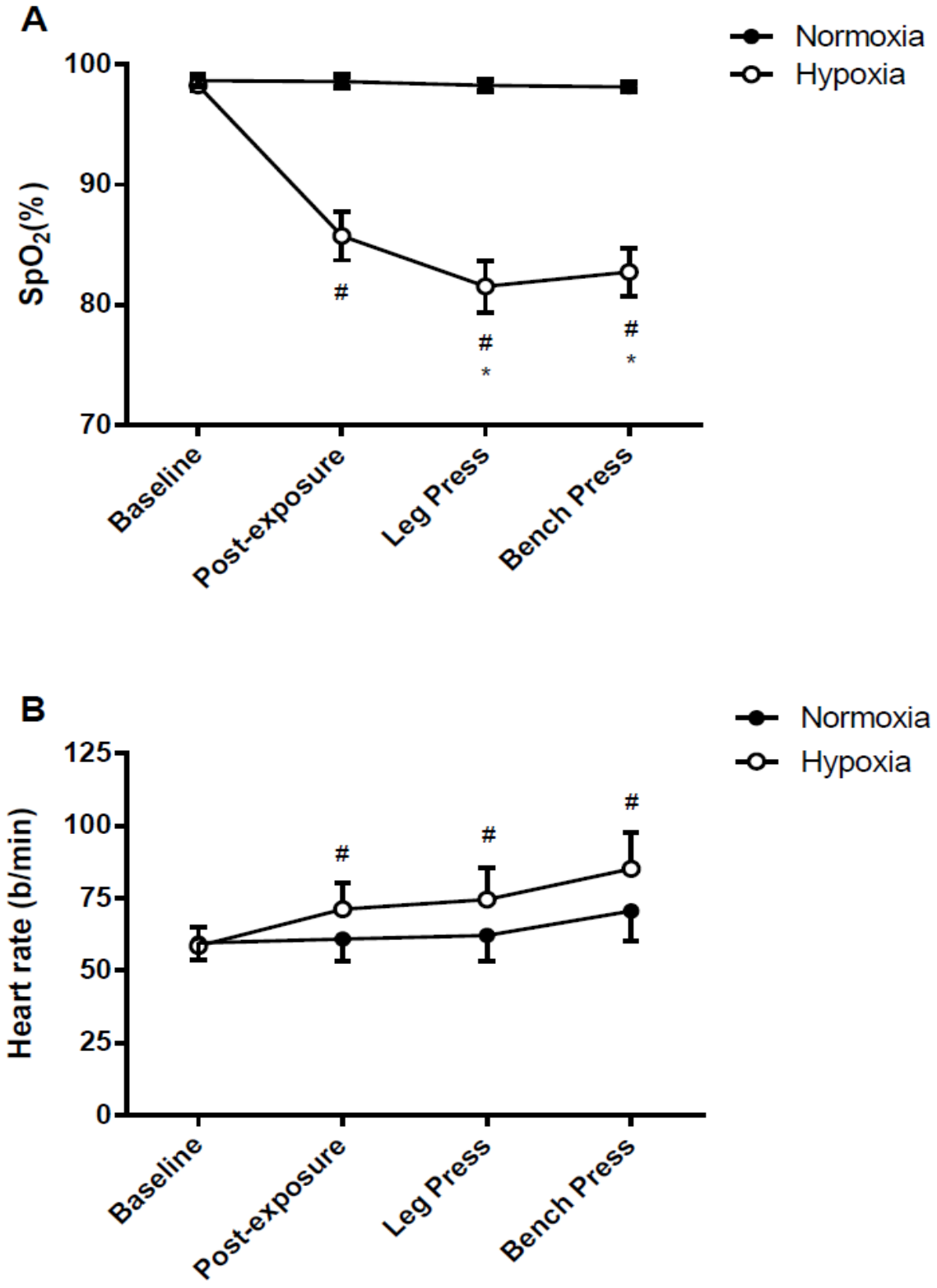


Figure 9. (A) Mean oxygen saturation (SpO_2), and (B) heart rate (b/min) during resistance exercise in normoxia and hypoxia. # *Important* difference between trials compared to baseline. * *Important* difference between trials compared to post-exposure. Baseline = before normoxia and hypoxia exposures. Post-exposure = 5 minutes after normoxia and hypoxia exposures. Leg and bench press SpO_2 and heart rate = mean values during that specific exercise. Values are means ± SD (n=15).

4.3 Blood Lactate

Blood lactate showed an *important* increase from baseline values at 5 (ES 1.49 ± 0.51), 15 (ES 1.30 ± 0.63), 30 (ES 0.92 ± 0.76), and 60 min (ES 0.57 ± 0.64) post-exercise in HYP compared with NOR. Additionally, AUC analysis for blood lactate following the resistance exercise protocol reported an *important* increase in HYP compared with NOR (HYP 139.0 ± 34.2 v NOR 106.4 ± 21.4 mmol/L, ES 1.21 ± 0.24) (Figure 10. A).

4.4 Growth Hormone

There was an *important* increase in GH concentrations from baseline values at 5 (ES 1.24 ± 0.75), 15 (ES 1.02 ± 0.71), 30 (ES 0.94 ± 0.74), and 60 min (ES 0.60 ± 0.56) post-exercise in HYP compared with NOR. Similar to blood lactate, the AUC analysis for GH following the resistance exercise protocol reported an *important* increase in HYP compared with NOR (HYP 117.7 ± 86.8 v NOR 72.9 ± 85.3 ng/mL, ES 0.56 ± 0.46) (Figure 10. B)

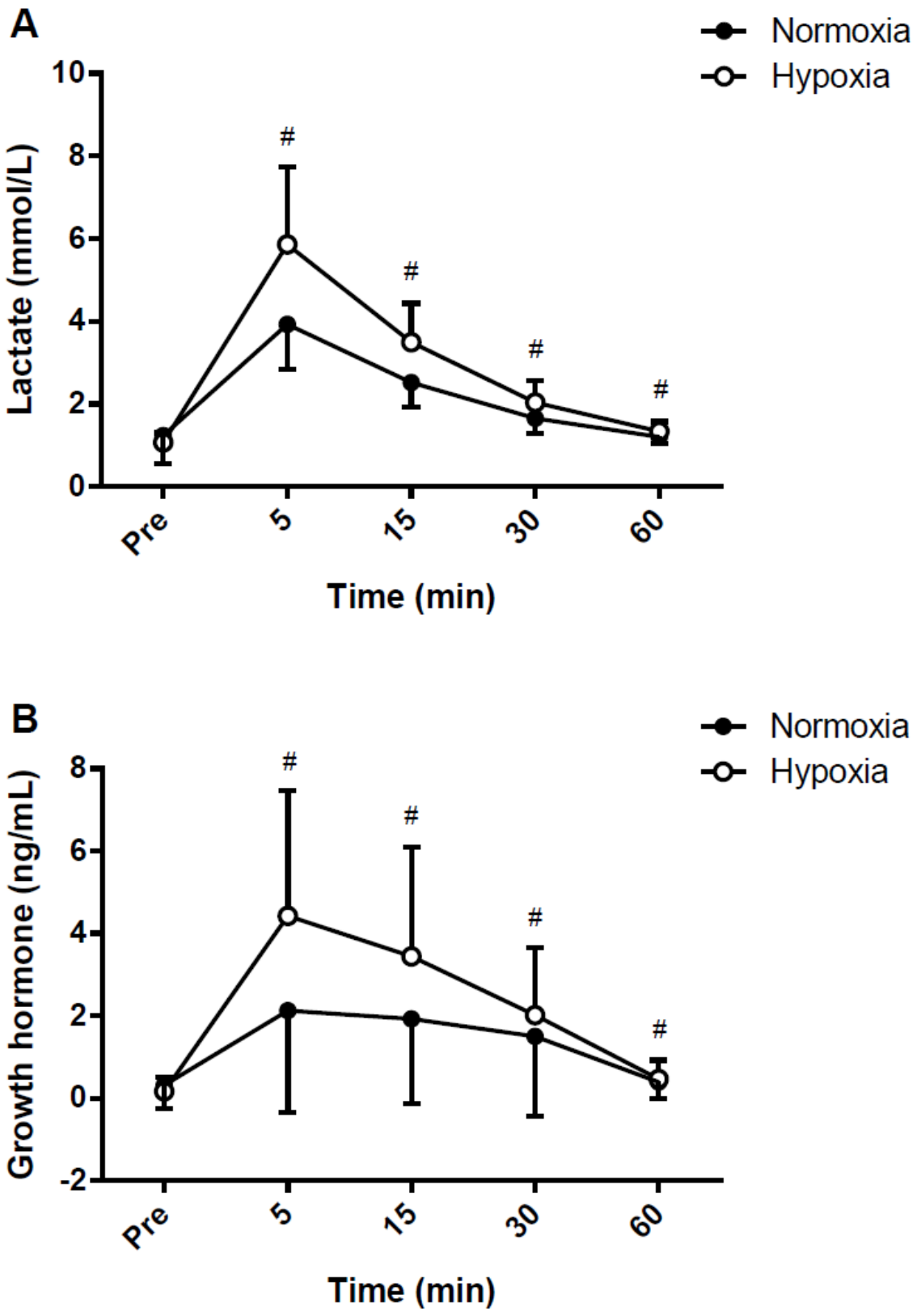


Figure 10. (A) Blood lactate concentrations (mmol/L) and (B) serum growth hormone concentrations (ng/mL) before and after exercise. # *Important* difference between trials compared to Pre. 5 min = 5 minute after exercise, 15 min = 15 minute after exercise, 30 min = 30 minute after exercise, 60 min = 60 minute after exercise. Values are means ± SD (n = 15).

4.5 Total Contraction Time

There was an *important* increase in total contraction time, with the length of time taken to complete the leg and bench press exercise increasing in the HYP trial (ES 0.40 ± 0.42) (Figure 11).

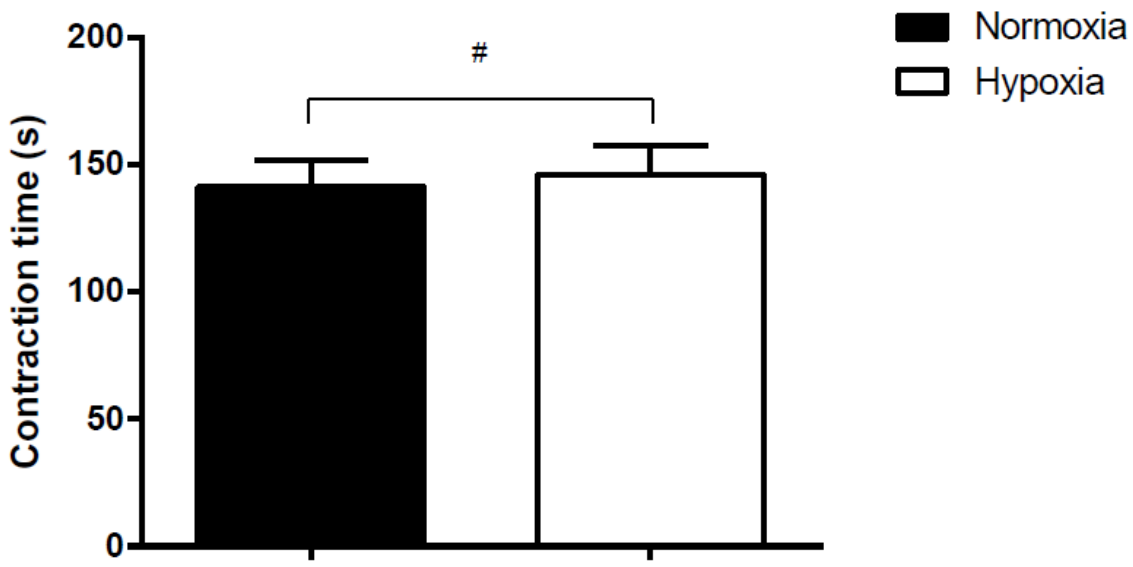


Figure 11. Total contraction time (seconds) for both leg and bench press exercise in normoxia and hypoxia. # *Important* difference between trials. Values are means ± SD (n = 15).

4.6 Overall Mean and Integrated EMG

Activation of the vastus lateralis during the leg press was inconclusive as the difference between mean (ES 0.18 ± 0.60) or integrated EMG (ES 0.20 ± 0.54) activity between conditions was *unclear* (Figure 12. A and B). Similarly, the difference in leg press contraction time between HYP and NOR trials were also *unclear* (ES 0.15 ± 0.39) (Figure 12. C).

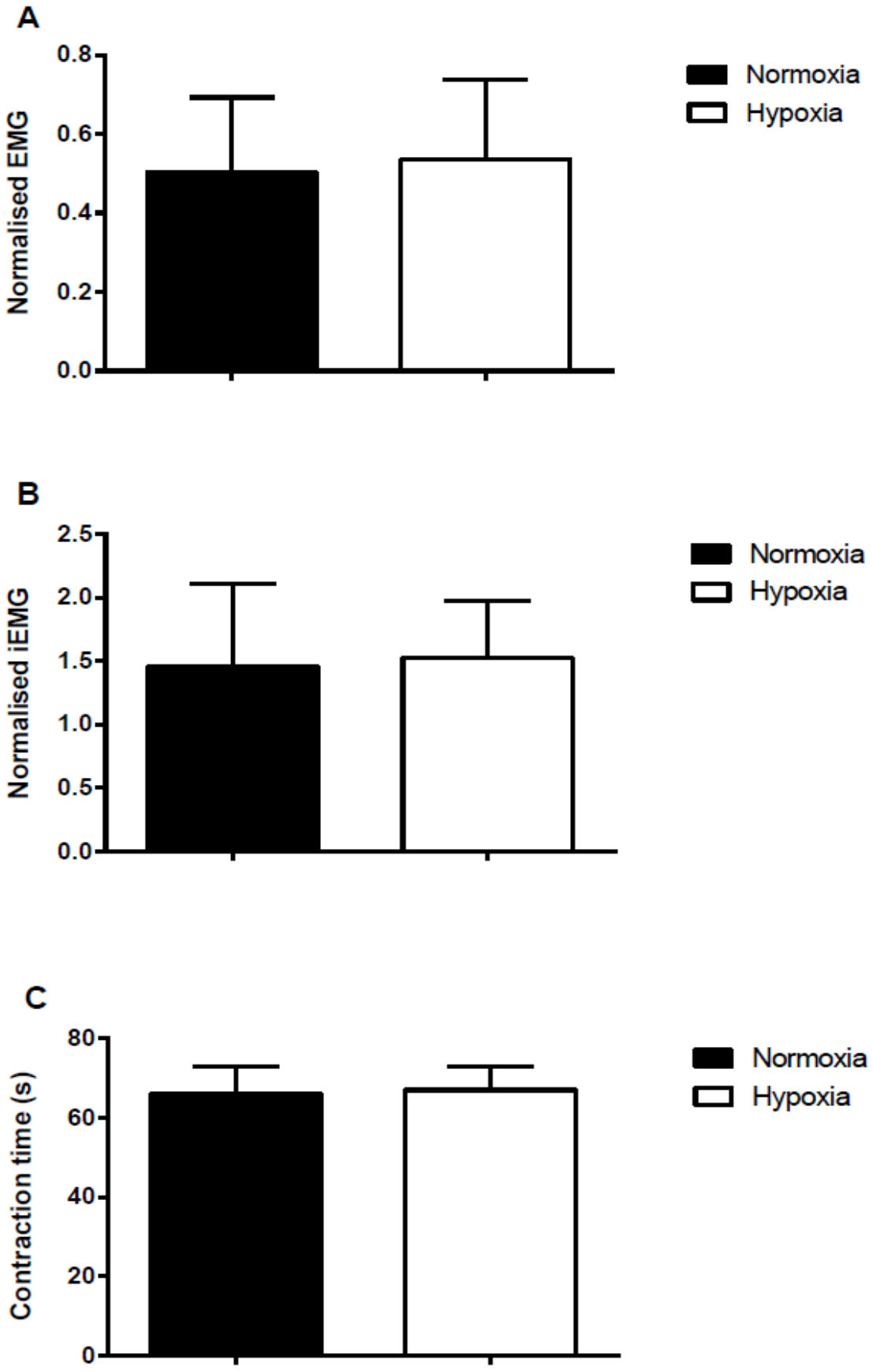


Figure 12. (A) Normalised mean electromyography (EMG), and (B) normalised integrated electromyography (iEMG) of the vastus lateralis (right leg only) during the leg press exercise. (C) Leg press contraction time (seconds). Values are means ± SD (n = 15).

4.7 Eccentric Mean and Integrated EMG

Mean and integrated EMG activity of the vastus lateralis during eccentric contractions were *unclear* between HYP and NOR trials (mean ES 0.20 ± 0.62, integrated ES 0.17 ± 0.54) (Figure 13. A and B). Similarly, contraction time during the eccentric phase of the leg press between HYP and NOR trials were also *unclear* (ES -0.06 ± 0.69) (Figure 13. C).

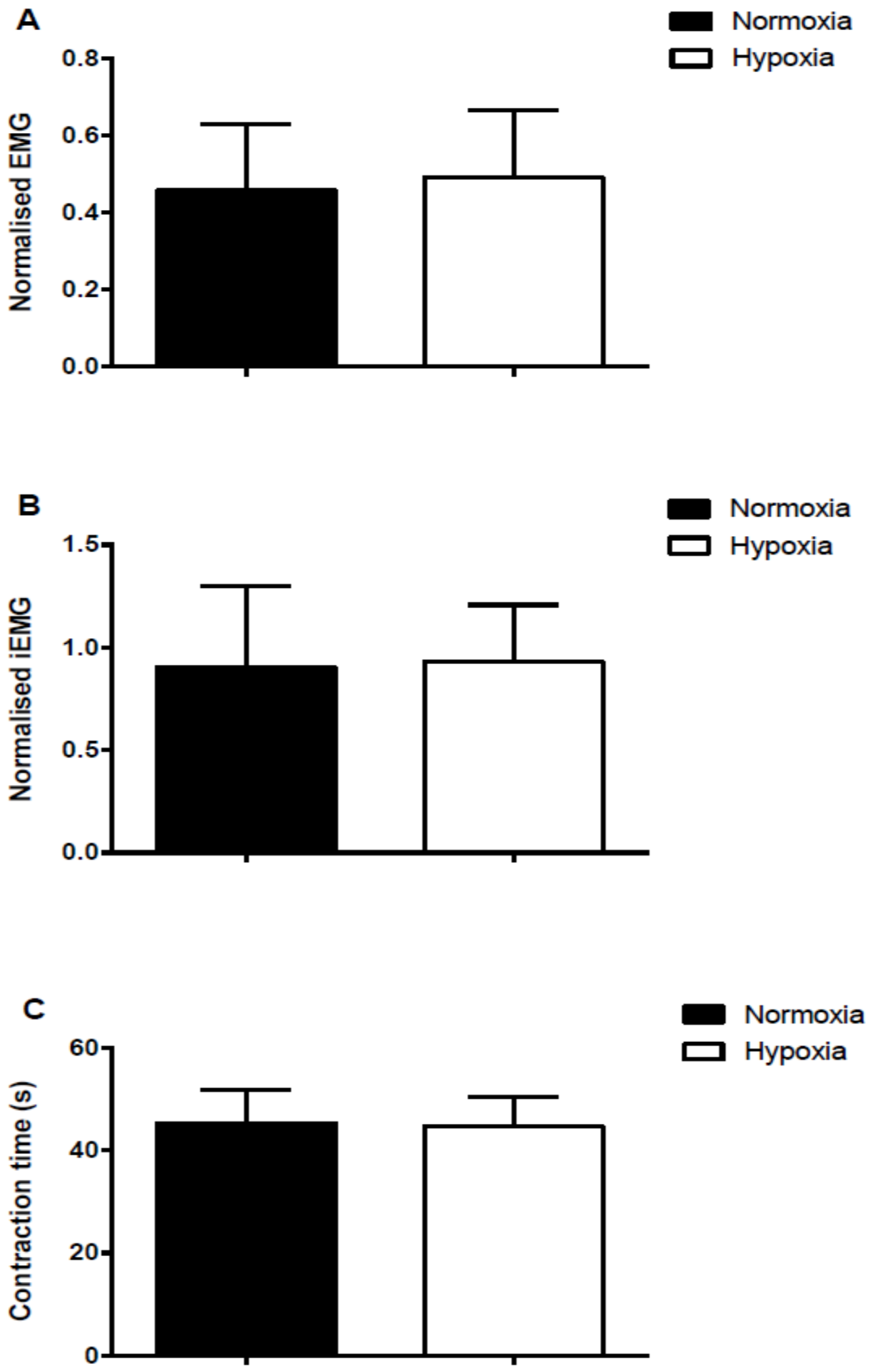


Figure 13. (A) Normalised mean eccentric electromyography (EMG) and (B) normalised integrated eccentric electromyography (iEMG) of the vastus lateralis (right leg only) during the leg press. (C) Eccentric leg press contraction time (seconds). Values are means ± SD (n=15).

4.7 Concentric Mean and Integrated EMG

The difference in concentric mean and integrated EMG activity between HYP and NOR trials was *unclear* (mean ES 0.15 ± 0.55, integrated ES 0.24 ± 0.47) (Figure 14. A and B). However, an *important* increase in leg press contraction time during the concentric phase of the lift was observed in HYP compared with NOR (ES 0.31 ± 0.26) (Figure 14. C).

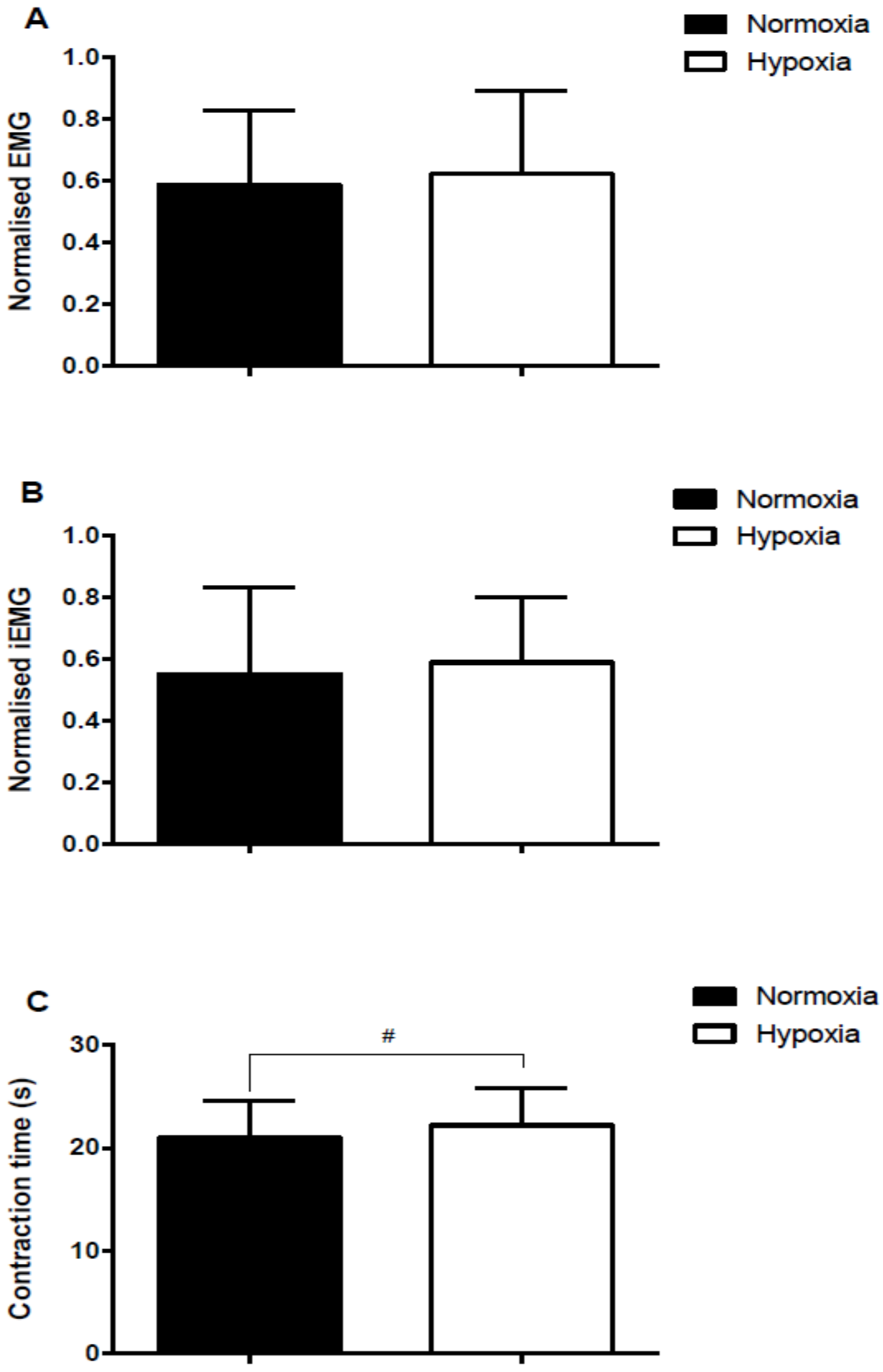


Figure 14. (A) Normalised mean concentric electromyography (EMG) and (B) normalised integrated concentric electromyography (iEMG) of the vastus lateralis (right leg only) during the leg press. (C) Concentric leg press contraction time (seconds). # *Important* difference between trials. Values are means ± SD (n = 15).

4.9 Bench Press Contraction Time

There was an *important* difference in bench press contraction time, with the HYP trial increasing the length of time taken to complete the bench press exercise (ES 0.55 ± 0.41) (Figure 15. A). This was potentially due to a change in the concentric portion of the lift where an *important* difference was observed in the HYP trial compared with NOR (ES 0.48 ± 0.28) (Figure 15. C). In contrast, the difference between HYP and NOR trials during the eccentric contraction phase was *unclear* (ES 0.01 ± 0.37) (Figure 15. B).

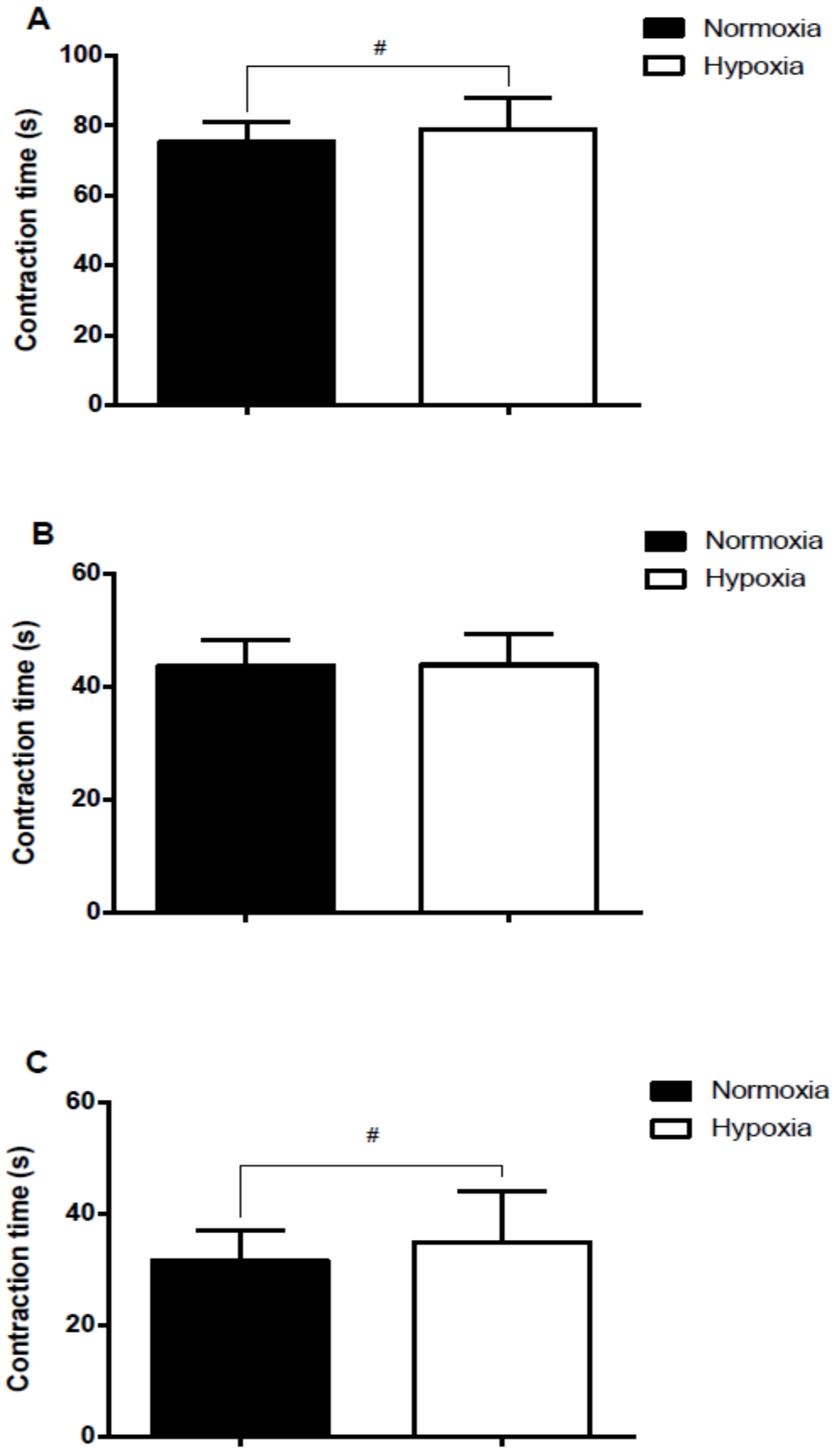


Figure 15. (A) Bench press contraction time (seconds), (B) eccentric bench press contraction time (seconds), (C) concentric bench press contraction time (seconds). # *Important* difference between trials. Values are means ± SD (n=15).

4.10 Individual Set Mean and Integrated EMG

There were only *trivial* differences between HYP and NOR trials when comparing mean and integrated EMG activity across individual work sets (sets 1-5) (mean ES 0.06 ± 0.16, integrated ES 0.15 ± 0.55) (Figure 16. A and B). Differences in individual set contraction time across the whole resistance exercise protocol between HYP and NOR trials were *unclear* (ES 0.00 ± 0.24) (Figure 16. C).

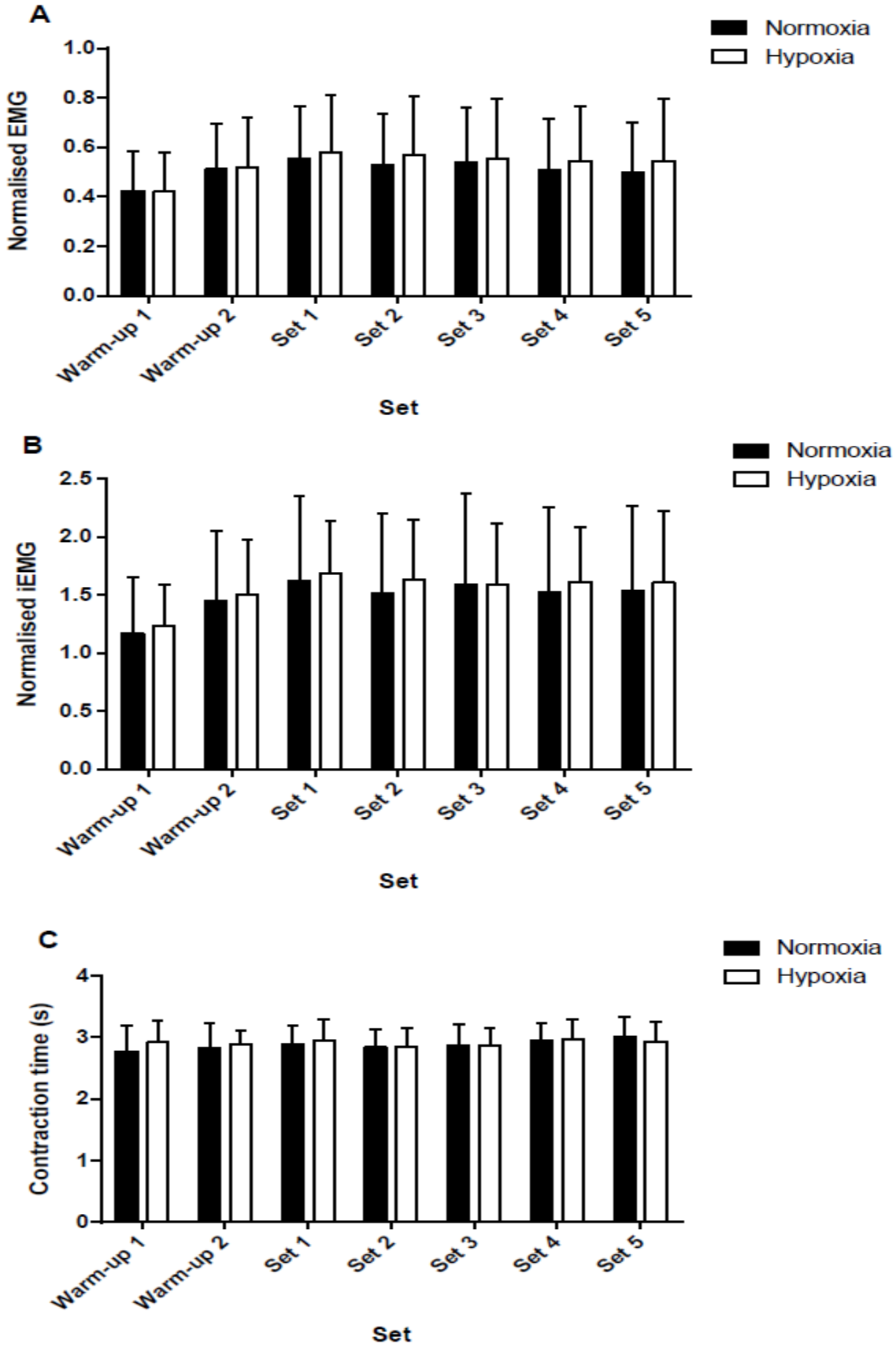


Figure 16. (A) Normalised mean electromyography (EMG) and (B) integrated electromyography (iEMG) of the vastus lateralis (right leg only) during individual sets of leg press. (C) Individual set leg press contraction time (seconds). Warm-up 1 = 50% 1RM, Warm-up 2 = 75% 1RM, Set 1-5 = 85% 1RM. Values are means ± SD (n=15).

4.11 Individual Set Eccentric Mean and Integrated EMG

Trivial differences were found between HYP and NORM trials when comparing each individual work sets (sets 1-5) for both mean and integrated EMG (mean ES 0.10 ± 0.17, integrated ES 0.02 ± 0.22) (Figure 17. A and B). Alternatively, individual set leg press contraction time between HYP and NOR trials during the eccentric phase were *unclear* (ES 0.03 ± 0.73) (Figure 17. C).

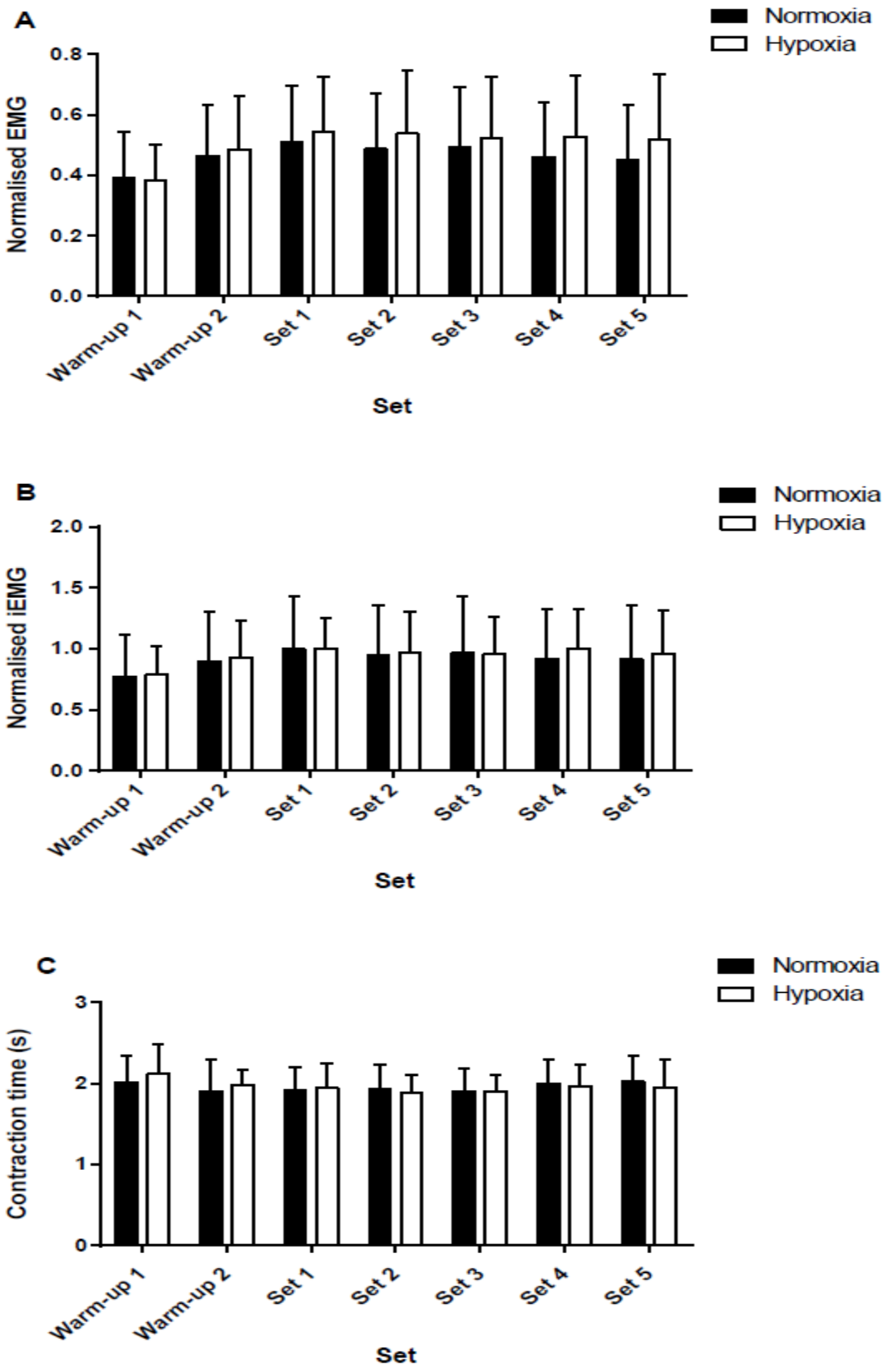


Figure 17. (A) Individual set eccentric normalised mean electromyography (EMG), (B) individual set eccentric normalised integrated electromyography (iEMG) of the vastus lateralis (right leg only) during the leg press. (C) Individual set eccentric leg press contraction time (seconds). Warm-up 1 = 50% 1RM, Warm-up 2 = 75% 1RM, Set 1-5 = 85% 1RM. Values are means ± SD (n=15).

4.12 Individual Set Concentric Mean and Integrated EMG

There were only *trivial* differences between HYP and NOR trials when comparing mean and integrated EMG activity across the individual work sets (sets 1-5) during concentric contractions (mean ES 0.01 ± 0.21, integrated ES 0.03 ± 0.35) (Figure 18. A and B). However, when comparing leg press contraction time during the concentric phase, Set 2 demonstrated an *important* increase in HYP compared with NOR (ES 0.59 ± 0.41). In contrast, differences between all other sets remained *trivial* (ES 0.25 ± 0.45) (Figure 18. C).

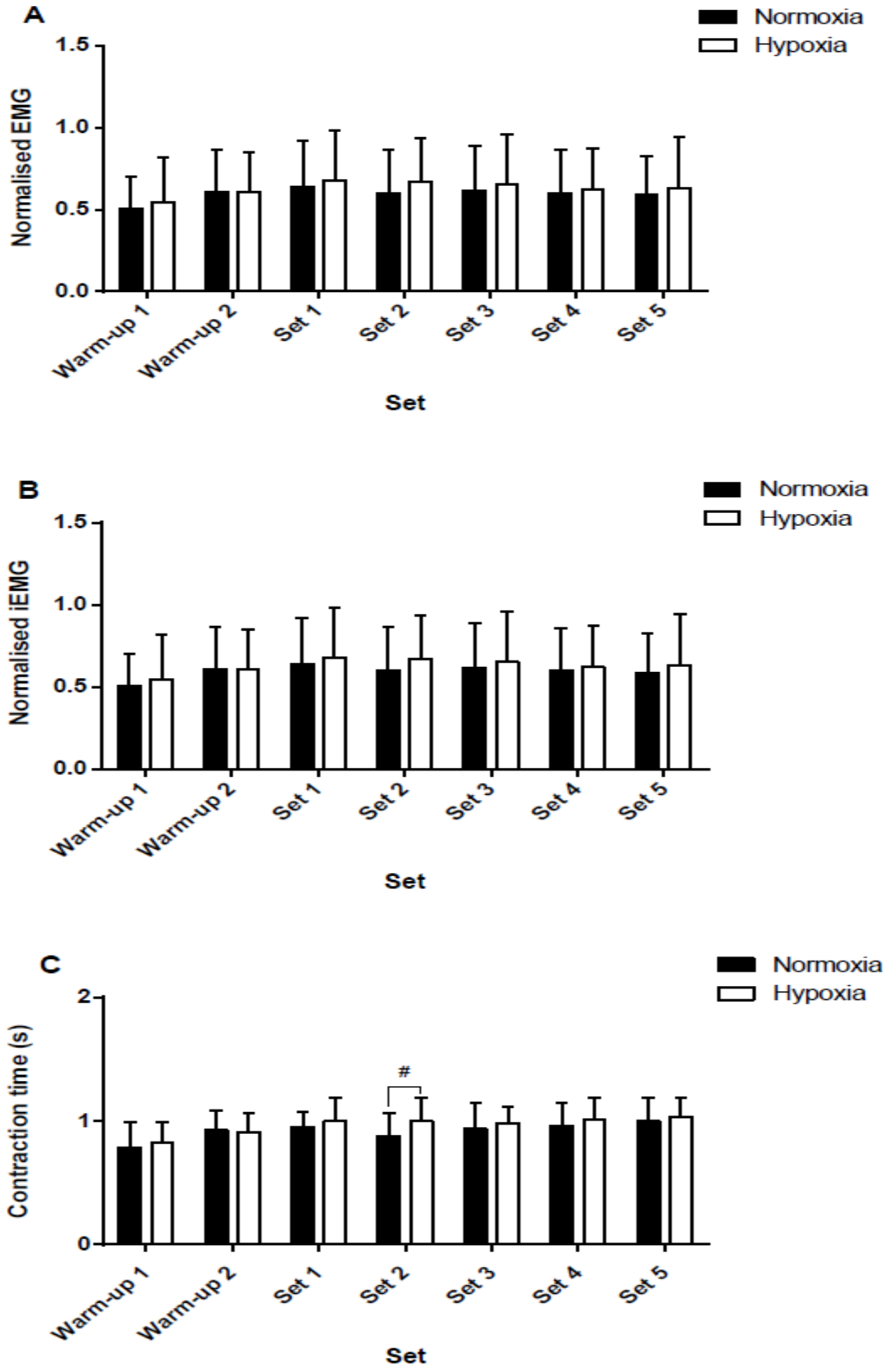


Figure 18. (A) Individual set concentric normalised mean electromyography (EMG), (B) individual set concentric normalised integrated electromyography (iEMG) of the vastus lateralis (right leg only) during the leg press. (C) Individual set concentric leg press contraction time (seconds). # *Important* difference between trials. Warm-up 1 = 50% 1RM, Warm-up 2 = 75% 1RM, Set 1-5 = 85% 1RM. Values are means ± SD (n=15).

4.13 Individual Set Bench Press Contraction Time

An *important* increase in bench press contraction time occurred during HYP compared with NOR at three specific time points; warm-up set 2 (ES 0.71 ± 0.44), Set 4 (ES 0.39 ± 0.29), and Set 5 (ES 0.60 ± 0.34), while the difference between all other sets were *trivial* or *unclear* (ES 0.20 ± 0.48) (Figure 19. A). This was potentially due to an increase in contraction time during the concentric phase of the lift, as an *important* increase was observed at the identical time points during the HYP trial; warm-up set 2 (ES 0.42 ± 0.49), Set 4 (ES 0.44 ± 0.22), and Set 5 (ES 0.62 ± 0.34) (Figure 19. C). In contrast, during the eccentric phase, contraction time between HYP and NOR trials were *unclear* (ES 0.09 ± 0.38) (Figure 19. B).

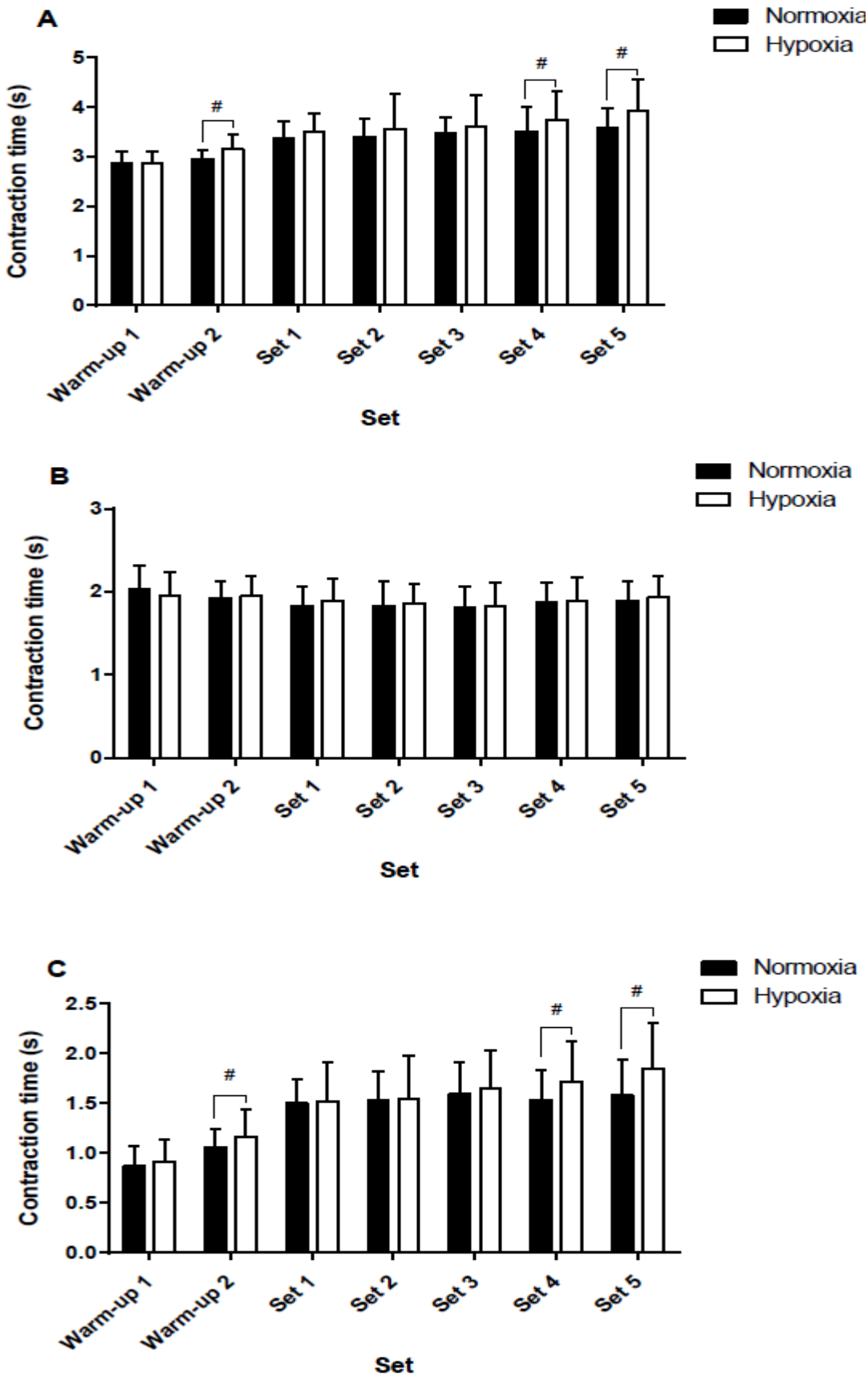


Figure 19. (A) Individual set bench press contraction time (seconds), (B) individual set eccentric bench press contraction time (seconds), (C) individual set concentric bench press contraction time (seconds). Warm-up 1 = 50% 1RM, Warm-up 2 = 75% 1RM, Set 1-5 = 85% 1RM. # Important difference between trials. Values are means ± SD (n=15).

4.14 Rating of Perceived Exertion

Participants perceived the hypoxic resistance exercise to be harder. This was reflected with an *important* increase in RPE scores after leg press (ES 0.64 ± 0.44), bench press (ES 0.65 ± 0.36) and the overall session (ES 0.44 ± 0.34) (Figure 20).

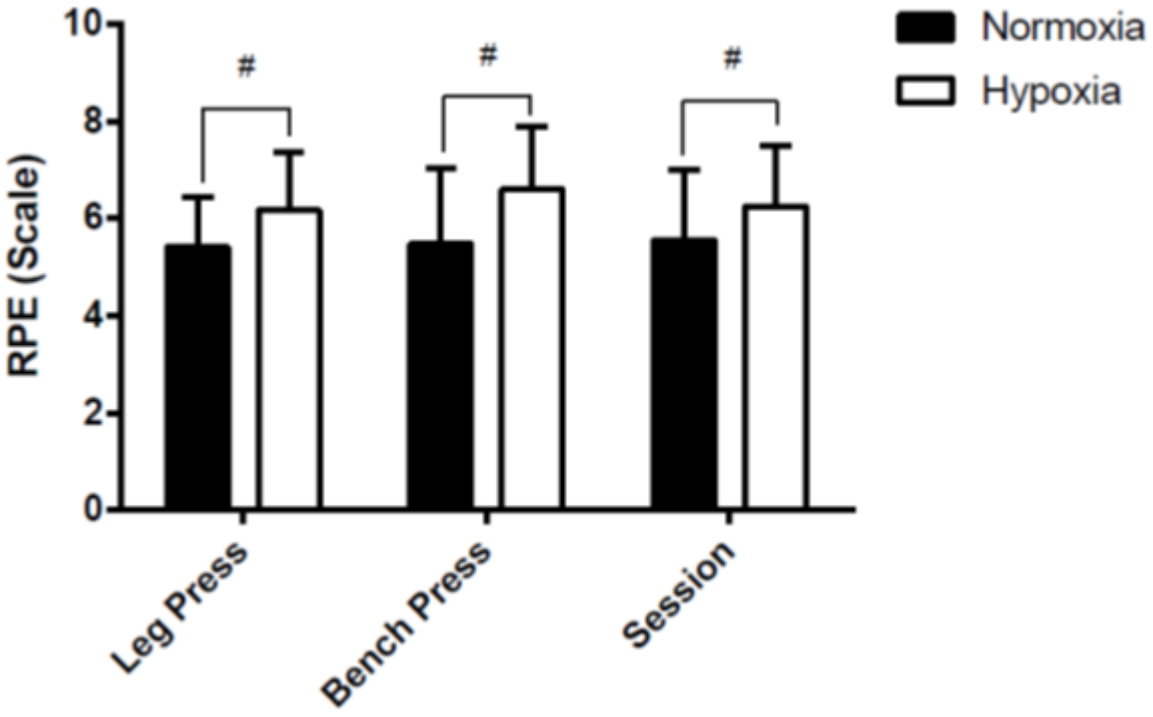


Figure 20. Rating of perceived exertion (RPE) post-leg and bench press exercises, and overall session RPE in normoxia and hypoxia. # *Important* difference between trials. Values are means ± SD (n=15).

Chapter Five: Discussion

5.1 Main Findings

The aim of this investigation was to determine if hypoxia augmented the GH response to a single session of high-intensity, low-volume resistance exercise. The main finding of this investigation was that high-intensity, low-volume resistance exercise in systemic hypoxia was able to induce greater elevations in GH concentrations and metabolic stress compared to the identical exercise performed in normoxia, despite inconclusive differences in muscle activity.

5.2 Effects of High-Intensity Resistance Exercise in Hypoxia or Normoxia on Growth Hormone

The major finding of this investigation was that high-intensity resistance exercise induced an increase in GH levels following both HYP and NOR trials. Several previous studies have examined the GH response to various resistance exercise protocols. Typically, the greatest GH response to resistance training has been observed following hypertrophy-type protocols (moderate-intensity, high-volume, short rest intervals) compared to conventional strength-type protocols (high-intensity, low-volume, long rest intervals) [75, 77-81]. The current investigation employed a typical strength-type protocol comprising of 5 sets of 3 repetitions at 85% 1RM (leg and bench press exercise) with 3 minutes rest (total of 30 repetitions) [23]. Compared with previous studies (Table 1), a similar acute GH response was observed following both HYP and NOR trials to that of Kraemer et al. [75], Smilios et al. [79] and Zafeiridis et al. [81]. Kraemer et al. [75] employed a strength-type protocol (5 x 5RM with 3 min rest) that consisted of eight exercises and reported an increase GH of ~5 ng/mL. In contrast, when the participants performed a similar protocol to control for load (5 x 5 repetitions at 10RM with 1 min rest), the increase in GH was ~2 ng/mL, which is similar to the response observed following the NOR trial in current investigation. Despite the same amount of total volume being

performed, it is possible that the intensity of exercise may have contributed to the differences seen in GH concentrations (i.e. 10RM vs 5RM).

Smilios et al. [79] demonstrated similar increases in GH concentrations (~2 ng/mL from baseline) using a strength-type protocol that was comparable to the values following the NOR trial in the current investigation. However, when Similios et al. [79] asked participants to perform a protocol with twice the amount of volume (i.e. four exercises, 4 x 5 repetitions at 88% 1RM), a two-fold increase in GH was observed (~4 ng/mL). Interestingly, in the current investigation, when the identical exercise was performed in systemic hypoxia, a 2-fold increase in GH was also demonstrated (~4 ng/mL) (Figure 10. B). Therefore, a greater GH response was generated with the use of systemic hypoxia at a lower exercise volume compared with the protocol employed by Similios et al [79].

While the intensity of exercise was similar between the current investigation and strength-type protocols reported in Table 1 [75, 79, 81] (i.e. between 80-90% of 1RM), the point of difference lies within the volume of the protocols. For example, total volume during Kraemer et al. [75] resistance exercise protocol consisted of 200 repetitions (eight exercises, 5 x 5RM), and Smilios et al. [79] four exercises, 4 x 5 repetitions (total volume 80 repetitions), and 6 x 5 repetitions (total volume 120 repetitions). As a result, it has been shown that resistance exercise protocols which produce a greater amount of total volume, observed greater increases in GH concentrations [75, 79, 81]. The results from the current investigation indicated that performing high-intensity, low-volume resistance exercise (total volume 30 repetitions) in systemic hypoxia, leads to similar GH responses compared with protocols that have completed over twice the amount of volume [75, 79, 81].

The current investigation demonstrated performing maximal strength training in a hypoxic environment can approximately double the level of GH released. However, the acute GH response observed in the HYP trial was less than previous reports following hypertrophy-type

protocols, in which most studies have demonstrated an increase in GH concentrations of between ~12 to 27 ng/mL from baseline [75, 77-81] (Table 1).

To date, only three studies have examined the GH response to RTH in an acute exercise setting [129-131]. Kon et al. [130] and [129] reported significantly greater increases in GH levels (peak ~6 and 17 ng/mL, respectively) when resistance exercise was performed in hypoxia compared to normoxia. In contrast, Ho et al. [131] observed no significant difference in GH concentrations between hypoxic and normoxic trials. A recent review, postulated that several major factors can influence the response to RTH, these include; the load or intensity of exercise, inter-set rest interval periods and the level of hypoxia [149]. As a result, the differences in methodological design in the aforementioned studies may have influenced the GH response. For example, Kon et al. [130] employed two exercises (5 x 14 repetitions at 50% 1RM) with a total volume of 140 repetitions, and Kon et al. [129] utilised the same exercises (5 x 10 repetitions at 70% 1RM) with a total volume of 100 repetitions. Both studies comprised of the same rest intervals between sets (60 s) and a hypoxic exposure of F_iO_2 = 0.13. However, Ho et al. [131] employed a single exercise for 5 sets of 15 repetitions (total volume 75 repetitions) at 30% 1RM, 90 s rest intervals, with a lower hypoxic stress (F_iO_2 = 0.15). Despite similar rest interval periods, the largest difference lies with the intensity of exercise and total volume. As a result, differences in the GH responses observed between the aformentioned studies may be explained by Ho et al. [131] performing approximately half the total volume and a reduction in intensity.

Unlike the studies employed by Kon et al. [129, 130] and Ho et al. [131], who both used hypertrophy-type protocols where an increase in GH secretion is expected [55], the methodological design of the current investigation was aimed at a strength-type protocol, which has not been examined previously. However, a clear augmentation in the GH response was observed. Although, peak elevations in GH concentrations post-exercise observed in the current investigation (~4 ng/mL from baseline) did not increase to the same extent as Kon et al. [129]

(~15 ng/mL from baseline) or Kon et al. [130] (~6 ng/mL from baseline). These are more likely due to the protocol design (i.e. lower intensity, more volume, and shorter rest periods), resulting in a greater amount of total volume and metabolic stress.

5.3 Growth Hormone Hypothesis and Muscle Hypertrophy

Growth hormone is secreted in a pulsatile fashion with diurnal variations [150]. Studies analysing the GH response to both acute aerobic and resistance exercise have shown that the magnitude of the post-exercise response following acute resistance exercise is within the limits of normal daily diurnal variations [150, 151]. In the current investigation, it is difficult to draw conclusions as to whether or not the GH response observed following HYP and NOR trials was greater than the normal daily fluctuations, as there was no control group for GH secretion (i.e. non-exercise group). However, in an effort to reduce the impact of diurnal variations, and to analyse the difference in individual GH responses between HYP and NOR trials, participants were required to perform both trials at the same time of the day.

Recently, the role of systemic elevations in GH has come into question [152]. It has been proposed that acute-post resistance exercise elevations in GH may not play a pivotal role in skeletal muscle anabolism and hypertrophy [102-105]. Several studies have demonstrated increased myofibrillar protein synthesis post resistance-exercise without elevations in anabolic hormones such as GH [102-105]. However, others have demonstrated that increases in GH post resistance-exercise are necessary to increase muscle strength and hypertrophic adaptations [76, 106]. Considering the inconsistent evidence, it is difficult to draw definitive conclusions as to whether or not acute post-exercise elevations in anabolic hormones contribute to muscle protein synthesis over an acute or prolonged training period.

Growth hormone is a stress related hormone that might be contributing to skeletal muscle hypertrophy. However, one of its primary functions is to induce fat metabolism and the

mobilisation of triglycerides. This increase in lipolysis can favourably affect body composition by increasing lean body mass [153]. Furthermore, GH has been associated with an increase in the synthesis of collagen for tissue remodelling [154]. While GH effects on skeletal muscle hypertrophy are debateable, it may promote hypertrophic adaptations by increasing whole-body protein and collagen synthesis, as well as altering body composition [152].

5.4 Effects of High-Intensity Resistance Exercise in Hypoxia or Normoxia on Metabolic Stress

Similar to anabolic hormone production, higher-volume hypertrophy type protocols have been demonstrated to produce greater elevations in metabolic stress compared to low-volume but higher loads (strength-type) protocols [78, 101]. The results from the current investigation demonstrate that high-intensity resistance exercise can increase metabolic stress following both HYP and NOR trials. Further to this, when the identical exercise was performed in hypoxic conditions, an *important* elevation in blood lactate concentration was observed during the post-exercise period. Similos et al. [79] performed a strength-type protocol (four exercises, 4 x 5 and 6 x 5 repetitions at 88% 1RM, 3 min rest) similar to the protocol used in the current investigation. Both protocols employed by Similos et al. [79] reported an increase in blood lactate (~4 mmol/L) immediately post-exercise. The elevation in blood lactate concentrations was similar to the levels observed following the NOR trial. However, when the identical exercise was performed in hypoxia, an increase in blood lactate (~6 mmol/L) post-exercise was observed (Figure 10. A). Even though the protocols of Similos et al. [79] consisted of greater total volume (80-120 repetitions), the resistance-exercise protocol employed in the current investigation demonstrated a greater increase in metabolic stress, with less than half the total volume (30 repetitions) when resistance exercise was performed in systemic hypoxia.

Similar to GH, conflicting data surrounds observations of metabolic stress following RTH. Although data exists with this training modality, larger increases in metabolic stress occur with

protocols that employ hypertrophy-type protocols in combination with systemic hypoxia. Ho et al. [131] and Kurobe et al. [138] reported no significant difference in blood lactate concentrations between hypoxic and normoxic trials following 5 sets of 15 repetitions of squats (30% 1RM) with 90 s rest intervals (F_iO_2 = 0.15), and 3 sets of 10 repetitions of elbow extensions (10RM) with 60 s rest intervals (F_iO_2 = 0.13), respectively. However, the studies employed by Kon et al. [129] and Kon et al. [130] reported that RTH resulted in a greater increase in metabolic stress than the identical exercise in normoxia. This result is similar to the results reported in the current investigation. Differences again lie within the methodological design of the studies, which may cause the variances in the observed metabolic stress. All studies employed a hypertrophy-type protocol, however, both studies by Kon et al. [129] and [130] performed resistance exercise with twice the volume (two exercises; 5 x 10 at 70% 1RM and 5 x 14 at 50% 1RM with 60 s rest [F_iO_2 = 0.13]), compared with the protocol implemented by Ho et al. [131] and Kurobe et al. [138]. This suggests that a greater metabolic stress response results from protocols comprised of moderate-intensity, high volume, short rest intervals and aim to stress a large muscle mass [12].

Strength-type training protocols have not previously been investigated in systemic hypoxia. The decrease in oxygen availability (i.e. decrease in SpO_2, Figure 9. A) to the muscle may cause an increased reliance on anaerobic energy pathways. It has been postulated that during maximal strength and power type training that rest intervals between sets should be between 3-8 minutes to allow sufficient neuromuscular recovery and replenishment of adenosine triphosphate (ATP) and phosphocreatine (PCr) stores [155]. Not only does the rest interval affect the resynthesis of ATP-PC stores between sets, it may also influence the ability to remove metabolic by-products (i.e. lactate and H^+) from the exercising muscle prior to the next set. When exercise is performed in hypoxic conditions, PCr recovery rates are slower compared with exercise in normoxic conditions [156], causing an alteration in energetic metabolism during each set. For this reason, if repeated sets of resistance exercise are reliant on the ATP-PC energy system, the PCr stores

may not be completely recovered. Therefore, each subsequent set would be performed under more demanding metabolic conditions. Hence, resistance exercise in hypoxic conditions leads to greater increases in metabolic stress.

Several BFR studies have reported strong correlations between metabolic stress and GH secretion [94, 111, 113, 157]. Local muscle hypoxia can alter the intramuscular acidity levels to stimulate sympathetic nerve activity through a chemoreceptive reflex that is mediated by intramuscular metaboreceptors [158]. As a result, the accumulation of metabolites may play a role in the secretion of GH following resistance exercise in acute hypoxia. Furthermore, post-resistance exercise elevations in metabolic stress have also been implicated in the mediation of hypertrophic adaptions [110]. Increased levels of metabolic stress can have an impact on several downstream mechanisms to facilitate muscular hypertrophy [110]. It is possible that metabolic stress can lead to an elevation in systemic anabolic hormones, greater production of local myokines and reactive oxygen species, cellular swelling, as well as an increase in motor unit recruitment [110]. Therefore, RTH may be a favourable training modality to potentiate the associated mechanisms to promote skeletal muscle hypertrophic adaptations.

5.5 Effects of High-Intensity Resistance Exercise in Hypoxia or Normoxia on Motor Unit Recruitment

The current investigation reported *unclear* differences in EMG activity between HYP and NOR trials (Figure 12. A and B). Therefore, it is difficult to draw definitive conclusions regarding the influence of muscle activity on the GH and metabolic stress response.

Studies that have combined resistance exercise with BFR (which creates a localised hypoxic environment), have reported increased levels of motor unit recruitment [113, 118, 119]. As most of the methodologies used during BFR training employ hypertrophy-type protocols and/or repetitions to fatigue, the greater increase in motor unit recruitment following this training

modality has been associated with shift from type I (more fatigable) to type II (more glycolytic) motor units due to the localised hypoxic environment [116]. It has been proposed that muscular fatigue leads to a decrease in force production, which results in a further increase in motor unit recruitment [159]. Thus, muscle fibre recruitment during BFR training has been proposed as a potential mechanism to facilitate a hypertrophic response [117]. As previously discussed, protocols that aim to recruit a large amount of muscle mass, tend to elicit a greater level of GH release and metabolic stress [12]. This may partly explain why superior increases in GH concentrations and metabolic stress have been observed following BFR training. The results from the current investigation demonstrated *unclear* differences in EMG activity between HYP and NOR trials, therefore, it is uncertain if muscle activity played a role in the elevations of GH concentration and metabolic stress following resistance exercise in systemic hypoxia. Interestingly, there were outlying individual variations in the EMG response, which may have led to the *unclear* differences observed between HYP and NOR trials. A limitation of this investigation was that EMG activity was only measured during the leg press exercise. If EMG activity of the pectoralis major or triceps brachii were measured during the bench press exercise, differences in muscle activity may have been observed.

5.6 Effects of High-Intensity Resistance Exercise in Hypoxia or Normoxia on Contraction Mode and Time

In an attempt to control the total work completed in each trial, contraction time was maintained through the use of a metronome. Despite this, overall, there was still an *important* difference in total contraction time, with the HYP trial increasing the length of time taken to complete the leg and bench press exercise (Figure 11). Upon further analysis it was revealed that the increase in contraction time during both leg and bench press exercise was only observed during the concentric phase of the lift (Figure 14. C and 15. C). These results could be attributed to the instructions given to participants prior to the performance of each repetition. The participants

were ordered to lower the weight (eccentric phase) with a 2 s contraction and to lift the load (contraction phase) as explosively as possible, and this explosive phase was where the slowing of the contraction occurred.

However, it is interesting to note that the differences in contraction time between trials were more prominent during the bench press exercise, which was always performed after the leg press. It is possible during this task that the relative intensity of exercise following repeated sets of hypoxic resistance exercise was greater than normoxia, as this was demonstrated by an *important* increase in HR (Figure 9. B) and RPE (Figure 20). Therefore, it may be possible that as the duration of exercise increased during the hypoxic trial, the more difficult it was for the participants to perform the bench press exercise, which may have led to a greater contraction time.

5.7 Effects of Contraction Mode and Time on the Hormonal Response

Based on the contraction type and time under tension, different hormonal and metabolic responses have been observed during resistance exercise. Several important training variables have been shown to have a significant influence on the GH response to resistance exercise (i.e. intensity, volume, rest intervals, and exercise selection) [12]. An alternative important training variable to consider in maximising the anabolic response, is the type of muscle contraction [160, 161] and the amount of time the muscle is placed under tension [54]. It has been reported that greater time under tension can result in superior anabolic alterations within the muscle [162, 163]. Furthermore, different hormonal and metabolic responses have been observed following eccentric and concentric exercise [160]. Resistance exercise is typically performed in a dynamic manner that combines both eccentric and concentric contractions. However, when exercise is performed at the same absolute load, concentric exercise has been shown to significantly increase GH concentrations and blood lactate levels to a greater extent than eccentric exercise [160]. The results from this investigation showed that an *important* increase in concentric

contraction time, during both leg and bench press exercise, led to an overall increase in total contraction time during the HYP trial (Figure 14. C and 15. C). Therefore, it is possible that the augmented GH and lactate responses observed during the HYP trial may have been influenced by a combination of both the contraction type and the time under tension. However, it is questionable as to whether the difference in contraction time observed in this investigation (total of 5 s) is of a great enough magnitude to drive changes in hormonal release. Burd et al. [162] demonstrated that muscle time under tension during resistance exercise (3 sets of multiple contractions) over a total of 407 s compared to 50 s (difference of 357 s) produced superior anabolic responses. The differences in contraction time observed in the current investigation (HYP 146 v NOR 141 s) were not to the same extent, and it is doubtful that this had an influence on the greater increase in GH concentrations observed following the HYP trial.

5.8 Effects of High-Intensity Resistance Exercise in Hypoxia or Normoxia on Perceptual Responses

The results from the current investigation indicate that high-intensity resistance exercise in HYP is more physically and psychologically demanding than NOR conditions. In particular, the greatest differences were observed immediately following bench press exercise (Figure 20). Currently, there is limited data investigating the difference in perceived effort and/or pain during RTH. Conflicting results exists within the literature with both Nishimura et al. [134] and Kon et al. [130] reporting no significant difference in RPE and subjective fatigue between HYP and NOR trials,. However, in contrast, Manimmanakorn et al [135] reported a significantly higher pain score following RTH compared to control. The results observed in the current investigation are in agreement with the study by Manimmanakorn et al. [135] even though differences in the methodological design exits. For example, the current investigation employed a strength-type protocol (two exercises, 5 x 3 repetitions at 85% 1RM, 3 min rest),

while Manimmanakorn et al. [135] consisted of a hypertrophy-type protocol (two exercises, 3 x ~30 repetitions, 30 s rest).

An increase in the perception of effort may also exist when it is accompanied by a greater increase in blood lactate and HR during resistance exercise [164]. It is possible that the higher RPE observed during and following the HYP trial may be associated with a greater increase in blood lactate and HR response. While the results in this investigation reported an *important* increase in RPE following the HYP trial, it is important to consider that the numerical rating chosen relative to the descriptor lies within the same category (i.e. Hard) (Appendix C). Therefore, in a practical setting, differences in this measurement may not be as meaningful.

The aim of this investigation was to blind the participants to the exposure. Throughout the experimental trials, hypoxic and normoxic exposure was produced from a hypoxic generator and stored in a series of Douglas bags with the participants unable to view the oxygen percentage. Participants were also blinded to HR and SpO_2 values during data collection. After each experimental trial, the participants were asked to describe which condition (i.e. hypoxia or normoxia) they were exposed to. Out of the thirty-two trials, twenty-nine were correctly identified. Consequently, participants may have been aware of the side effects associated with hypoxia, which may have altered their perceived exertion.

5.9 Summary and Conclusion

The novel aspect of this investigation is that it provided experimental evidence regarding the effects of performing a strength-type protocol in systemic hypoxia on GH and metabolic stress responses, which to our knowledge has not been examined previously. This investigation indicates that low-volume, high-intensity resistance exercise in hypoxia leads to a greater augmentation in GH concentrations and metabolic stress compared to the identical exercise in normoxia. While the participants performed resistance exercise at the same absolute load during

both trials, the differences in EMG activity was not clear. Therefore, it is difficult to make definitive conclusions regarding the influence of motor unit recruitment on GH and metabolic stress responses.

While, GH may not directly facilitate an increase in skeletal muscle hypertrophy, an augmentation in GH levels may contribute to an increase in lean body mass and connective tissue synthesis. More recently, enhanced metabolic stress has also been discussed as an important regulator in maximising muscle hypertrophy. We hypothesised that performing low-volume, high-intensity resistance exercise in systemic hypoxia would be able to generate greater GH and metabolic responses compared to the identical exercise in normoxia. It would be speculative to assume that the magnitude of these alterations actually provided a supplementary benefit to skeletal muscle hypertrophy from training normally aimed at maximal strength. Therefore, further research is required to explore the association between high-intensity, low-volume resistance exercise in hypoxia and its role in promoting hypertrophic adaptions.

5.10 Practical Applications

The findings from this investigation provide evidence that systemic hypoxia can lead to greater alterations in GH concentrations and metabolic stress from a training protocol normally aimed at maximal strength. Typically, RTH has employed low-intensity, high-volume hypertrophy-type protocols to induce greater elevations in hormonal responses and metabolic stress, which may play a role in mediating hypertrophic adaptations. However, this type of protocol may not be optimal for athletic populations as it eliminates the neurological benefits of maximal strength adaptations, which have a significant impact on athletic performance. Therefore, performance coaches may consider high-intensity resistance exercise in systemic hypoxia as a potential training method to maximise the neurological and morphological adaptations associated with enhanced performance.

5.11 Recommendations for Future Research

Given the evidence provided in this investigation, future research should examine the response of other anabolic systemic hormones such as testosterone and IGF-1, following a typical maximal strength training session in hypoxia. Also, future investigations should examine if the greater exercise-induced hormone response would enhance intramuscular protein synthesis following an acute strength training bout in hypoxia. Lastly, future research should investigate whether high-intensity, low-volume resistance exercise in systemic hypoxia can lead to favourable strength and hypertrophic adaptations over a prolonged training period to enhance athletic performance.

References

1. McGuigan, M.R., G.A. Wright, and S.J. Fleck. Strength training for athletes: does it really help sports performance. International Journal of Sports Physiology and Performance, 2012. 7(1): 2-5.
2. Bloomer, R.J. and J.C. Ives. Varying neural and hypertrophic influences in a strength program. Strength and Conditioning Journal, 2000. 22(2): 30.
3. Aagaard, P. Training-induced changes in neural function. Exercise and Sport Sciences Reviews, 2003. 31(2): 61-67.
4. Komi, P.V. and I.M. Commission. Strength and power in sport. 1993: Blackwell scientific publications.
5. Aagaard, P., J.L. Andersen, P. Dyhre-Poulsen, A.M. Leffers, A. Wagner, S.P. Magnusson, J. Halkjær-Kristensen, and E.B. Simonsen. A mechanism for increased contractile strength of human pennate muscle in response to strength training: changes in muscle architecture. The Journal of Physiology, 2001. 534(2): 613-623.
6. Folland, J.P. and A.G. Williams. Morphological and neurological contributions to increased strength. Sports Medicine, 2007. 37(2): 145-168.
7. Baechle, T.R. and R.W. Earle. Essentials of strength training and conditioning. Vol. 7. 2008: Human Kinetics Champaign, IL.
8. Kraemer, W.J., K. Adams, E. Cafarelli, G.A. Dudley, C. Dooly, M.S. Feigenbaum, S.J. Fleck, B. Franklin, A.C. Fry, and J.R. Hoffman. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Medicine and Science in Sports and Exercise, 2002. 34(2): 364-380.
9. Deschenes, M.R. and W.J. Kraemer. Performance and physiologic adaptations to resistance training. American Journal of Physical Medicine and Rehabilitation, 2002. 81(11): S3-S16.

10. Velloso, C. Regulation of muscle mass by growth hormone and IGF-I. British Journal of Pharmacology, 2008. 154(3): 557-568.
11. Vingren, J.L., W.J. Kraemer, N.A. Ratamess, J.M. Anderson, J.S. Volek, and C.M. Maresh. Testosterone physiology in resistance exercise and training: the up-stream regulatory elements. Sports Medicine, 2010. 40(12): 1037-1053.
12. Kraemer, W.J. and N.A. Ratamess. Hormonal responses and adaptations to resistance exercise and training. Sports Medicine, 2005. 35(4): 339-361.
13. Loenneke, J.P. and T.J. Pujol. The use of occlusion training to produce muscle hypertrophy. Strength and Conditioning Journal, 2009. 31(3): 77-84.
14. Scott, B.R., K.M. Slattery, D.V. Sculley, and B.J. Dascombe. Hypoxia and resistance exercise: a comparison of localized and systemic methods. Sports Medicine, 2014. 44(8): 1037-1054.
15. Wisløff, U., C. Castagna, J. Helgerud, R. Jones, and J. Hoff. Strong correlation of maximal squat strength with sprint performance and vertical jump height in elite soccer players. British Journal of Sports Medicine, 2004. 38(3): 285-288.
16. Ronnestad, B.R., N.H. Kvamme, A. Sunde, and T. Raastad. Short-term effects of strength and plyometric training on sprint and jump performance in professional soccer players. The Journal of Strength and Conditioning Research, 2008. 22(3): 773-780.
17. Tsimahidis, K., C. Galazoulas, D. Skoufas, G. Papaiakovou, E. Bassa, D. Patikas, and C. Kotzamanidis. The effect of sprinting after each set of heavy resistance training on the running speed and jumping performance of young basketball players. The Journal of Strength and Conditioning Research, 2010. 24(8): 2102-2108.
18. Millet, G.P., B. Jaouen, F. Borrani, and R. Candau. Effects of concurrent endurance and strength training on running economy and VO2 kinetics. Medicine and Science in Sports and Exercise, 2002. 34(8): 1351-1359.

19. Storen, O., J. Helgerud, E.M. Stoa, and J. Hoff. Maximal strength training improves running economy in distance runners. Medicine and Science in Sports and Exercise, 2008. 40(6): 1087.

20. Newman, M.A., K.M. Tarpenning, and F.E. Marino. Relationships between isokinetic knee strength, single-sprint performance, and repeated-sprint ability in football players. The Journal of Strength and Conditioning Research, 2004. 18(4): 867-872.

21. Edge, J., S. Hill-Haas, C. Goodman, and D. Bishop. Effects of resistance training on H+ regulation, buffer capacity, and repeated sprints. Medicine and Science in Sports and Exercise, 2006. 38(11): 2004.

22. Lauersen, J.B., D.M. Bertelsen, and L.B. Andersen. The effectiveness of exercise interventions to prevent sports injuries: a systematic review and meta-analysis of randomised controlled trials. British Journal of Sports Medicine, 2014. 48(11): 871-877.

23. Bird, S.P., K.M. Tarpenning, and F.E. Marino. Designing resistance training programmes to enhance muscular fitness. Sports Medicine, 2005. 35(10): 841-851.

24. Kaneko, M., T. Fuchimoto, H. Toji, and K. Suei. Training effect of different loads on the force-velocity relationship and mechanical power output in human muscle. Scandinavian Journal of Medicine and Science in Sports, 1983. 5(2): 50-55.

25. Wilson, G.J., R.U. Newton, A.J. Murphy, and B.J. Humphries. The optimal training load for the development of dynamic athletic performance. Medicine and Science in Sports and Exercise, 1993. 25(11): 1279-1286.

26. Wilson, G., A. Murphy, and A. Walshe. Performance benefits from weight and plyometric training: Effects of initial strength level. International Journal of Sports Science and Coaching, 1997. 2(1): 3-8.

27. Kawamori, N. and G.G. Haff. The optimal training load for the development of muscular power. The Journal of Strength and Conditioning Research, 2004. 18(3): 675-684.

28. Henneman, E., G. Somjen, and D.O. Carpenter. Functional significance of cell size in spinal motorneurons. Journal of Neurophysiology, 1965. 28: 560-580.

29. Haff, G.G., A. Whitley, and J.A. Potteiger. A Brief Review: Explosive Exercises and Sports Performance. Strength and Conditioning Journal, 2001. 23(3): 13.

30. Aagaard, P., E.B. Simonsen, J.L. Andersen, P. Magnusson, and P. Dyhre-Poulsen. Increased rate of force development and neural drive of human skeletal muscle following resistance training. Journal of Applied Physiology, 2002. 93(4): 1318-1326.

31. Milner-Brown, H. and R. Lee. Synchronization of human motor units: possible roles of exercise and supraspinal reflexes. Electroencephalography and Clinical Neurophysiology, 1975. 38(3): 245-254.

32. Semmler, J. and M. Nordstrom. Motor unit discharge and force tremor in skill-and strength-trained individuals. Experimental Brain Research, 1998. 119(1): 27-38.

33. Semmler, J.G. Motor unit synchronization and neuromuscular performance. Exercise and Sport Sciences Reviews, 2002. 30(1): 8-14.

34. Gabriel, D.A., G. Kamen, and G. Frost. Neural adaptations to resistive exercise. Sports Medicine, 2006. 36(2): 133-149.

35. Aagaard, P., E. Simonsen, J. Andersen, S. Magnusson, J. Halkjaer-Kristensen, and P. Dyhre-Poulsen. Neural inhibition during maximal eccentric and concentric quadriceps contraction: effects of resistance training. Journal of Applied Physiology, 2000. 89(6): 2249-2257.

36. Fry, A.C., J.M. Webber, L.W. Weiss, M.P. Arber, M. Vaczi, and N.A. Pattison. Muscle fiber characteristics of competitive power lifters. The Journal of Strength and Conditioning Research, 2003. 17(2): 402-410.

37. Tesch, P. and J. Karlsson. Muscle fiber types and size in trained and untrained muscles of elite athletes. Journal of Applied Physiology, 1985. 59(6): 1716-1720.

38. Fry, A.C., B.K. Schilling, R.S. Staron, F.C. Hagerman, R.S. Hikida, and J.T. Thrush. Muscle fiber characteristics and performance correlates of male Olympic-style weightlifters. The Journal of Strength and Conditioning Research, 2003. 17(4): 746-754.

39. MacDougall, J., D. Sale, G. Elder, and J. Sutton. Muscle ultrastructural characteristics of elite powerlifters and bodybuilders. European Journal of Applied Physiology and Occupational Physiology, 1982. 48(1): 117-126.

40. Widrick, J.J., J.E. Stelzer, T.C. Shoepe, and D.P. Garner. Functional properties of human muscle fibers after short-term resistance exercise training. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 2002. 283(2): R408-R416.

41. Häkkinen, K., P. Komi, and P. Tesch. Effect of combined concentric and eccentric strength training and detraining on force-time, muscle fiber and metabolic characteristics of leg extensor muscles. Scandinavian Journal of Medicine and Science in Sports, 1981. 3: 50-58.

42. MacDougall, J., G. Elder, D. Sale, J. Moroz, and J. Sutton. Effects of strength training and immobilization on human muscle fibres. European Journal of Applied Physiology and Occupational Physiology, 1980. 43(1): 25-34.

43. Schoenfeld, B.J., N.A. Ratamess, M.D. Peterson, B. Contreras, G. Sonmez, and B.A. Alvar. Effects of different volume-equated resistance training loading strategies on muscular adaptations in well-trained men. The Journal of Strength and Conditioning Research, 2014. 28(10): 2909-2918.

44. Abe, T., T. Yasuda, T. Midorikawa, Y. Sato, C. Kearns, K. Inoue, K. Koizumi, and N. Ishii. Skeletal muscle size and circulating IGF-1 are increased after two weeks of twice daily" KAATSU" resistance training. International Journal of KAATSU Training Research, 2005. 1(1): 6-12.

45. Sumide, T., K. Sakuraba, K. Sawaki, H. Ohmura, and Y. Tamura. Effect of resistance exercise training combined with relatively low vascular occlusion. Journal of Science and Medicine in Sport, 2009. 12(1): 107-112.

46. Takarada, Y., Y. Sato, and N. Ishii. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. European Journal of Applied Physiology, 2002. 86(4): 308-314.

47. Takarada, Y., T. Tsuruta, and N. Ishii. Cooperative effects of exercise and occlusive stimuli on muscular function in low-intensity resistance exercise with moderate vascular occlusion. Japanese Journal of Physiology, 2004. 54(6): 585-592.

48. Schoenfeld, B.J. The mechanisms of muscle hypertrophy and their application to resistance training. The Journal of Strength and Conditioning Research, 2010. 24(10): 2857-2872.

49. Glass, D.J. Skeletal muscle hypertrophy and atrophy signaling pathways. The International Journal of Biochemistry and Cell Biology, 2005. 37(10): 1974-1984.

50. Clemmons, D.R. Role of IGF-I in skeletal muscle mass maintenance. Trends in Endocrinology and Metabolism, 2009. 20(7): 349-356.

51. Coffey, V.G. and J.A. Hawley. The molecular bases of training adaptation. Sports Medicine, 2007. 37(9): 737-763.

52. Nader, G.A. Molecular determinants of skeletal muscle mass: getting the "AKT" together. The International Journal of Biochemistry and Cell Biology, 2005. 37(10): 1985-1996.

53. Hornberger, T., W. Chu, Y. Mak, J. Hsiung, S. Huang, and S. Chien. The role of phospholipase D and phosphatidic acid in the mechanical activation of mTOR signaling in skeletal muscle. Proceedings of the National Academy of Sciences of the United States of America, 2006. 103(12): 4741-4746.

54. Toigo, M. and U. Boutellier. New fundamental resistance exercise determinants of molecular and cellular muscle adaptations. European Journal of Applied Physiology, 2006. 97(6): 643-663.

55. Crewther, B., J. Keogh, J. Cronin, and C. Cook. Possible stimuli for strength and power adaptation. Sports Medicine, 2006. 36(3): 215-238.

56. Bideci, A. and O. Çamurdan. Physiology of growth hormone secretion. Journal of Clinical Research in Pediatric Endocrinology, 2009: 1–7.

57. Sonksen, P. Insulin, growth hormone and sport. Journal of Endocrinology, 2001. 170(1): 13-25.

58. Goldenberg, N. and A. Barkan. Factors regulating growth hormone secretion in humans. Endocrinology and Metabolism Clinics of North America, 2007. 36(1): 37.

59. Kraemer, W.J., C. Dunn-Lewis, B.A. Comstock, G.A. Thomas, J.E. Clark, and B.C. Nindl. Growth hormone, exercise, and athletic performance: a continued evolution of complexity. Current Sports Medicine Reports, 2010. 9(4): 242-252.

60. Godfrey, R.J., Z. Madgwick, and G.P. Whyte. The exercise-induced growth hormone response in athletes. Sports Medicine, 2003. 33(8): 599-613.

61. Giustina, A. and J.D. Veldhuis. Pathophysiology of the Neuroregulation of Growth Hormone Secretion in Experimental Animals and the Human. Endocrine Reviews, 1998. 19(6): 717-797.

62. Hagberg, J.M., D.R. Seals, J.E. Yerg, J. Gavin, R. Gingerich, B. Premachandra, and J. Holloszy. Metabolic responses to exercise in young and older athletes and sedentary men. Journal of Applied Physiology, 1988. 65(2): 900-908.

63. Holt, R.I.G., E. Webb, C. Pentecost, and P.H. Sönksen. Aging and physical fitness are more important than obesity in determining exercise-induced generation of GH. Journal of Clinical Endocrinology and Metabolism, 2001. 86(12): 5715-5720.

64. Zaccaria, M., M. Varnier, P. Piazza, D. Noventa, and A. Ermolao. Blunted growth hormone response to maximal exercise in middle-aged versus young subjects and no effect of endurance training. Journal of Clinical Endocrinology and Metabolism, 1999. 84(7): 2303-2307.

65. Bunt, J., R. Boileau, J. Bahr, and R. Nelson. Sex and training differences in human growth hormone levels during prolonged exercise. Journal of Applied Physiology, 1986. 61(5): 1796-1801.

66. Giannoulis, M., M. Boroujerdi, J. Powrie, R. Dall, R. Napoli, C. Ehrnborg, C. Pentecost, A. Cittadini, J.O.L. Jørgensen, and P. Sonksen. Gender differences in growth hormone response to exercise before and after rhGH administration and the effect of rhGH on the hormone profile of fit normal adults. Clinical Endocrinology, 2005. 62(3): 315-322.

67. Wideman, L., J.Y. Weltman, N. Shah, S. Story, J.D. Veldhuis, and A. Weltman. Effects of gender on exercise-induced growth hormone release. Journal of Applied Physiology, 1999. 87(3): 1154-1162.

68. Kanaley, J., M. Weatherup-Dentes, E. Jaynes, and M. Hartman. Obesity attenuates the growth hormone response to exercise. Journal of Clinical Endocrinology and Metabolism, 1999. 84(9): 3156-3161.

69. Veldhuis, J., A. Liem, S. South, A. Weltman, J. Weltman, D. Clemmons, R. Abbott, T. Mulligan, M. Johnson, and S. Pincus. Differential impact of age, sex steroid hormones, and obesity on basal verus pulsatile growth hormone secretion in men as assessed in an ultrasensitive chemiluminescence assay. Journal of Clinical Endocrinology and Metabolism, 1995. 80(11): 3209-3222.

70. Veldhuis, J.D., A. Iranmanesh, K.K. Ho, M.J. Waters, M.L. Johnson, and G. Lizarralde. Dual defects in pulsatile growth hormone secretion and clearance subserve the hyposomatotropism of obesity in man. The Journal of Clinical Endocrinology and Metabolism, 1991. 72(1): 51-59.

71. Holt, R.I., E. Webb, C. Pentecost, and P.H. Sonksen. Aging and physical fitness are more important than obesity in determining exercise-induced generation of GH. The Journal of Clinical Endocrinology and Metabolism, 2001. 86(12): 5715-5720.

72. Felsing, N.E., J. Brasel, and D. Cooper. Effect of low and high intensity exercise on circulating growth hormone in men. The Journal of Clinical Endocrinology and Metabolism, 1992. 75(1): 157-162.

73. Pritzlaff, C.J., L. Wideman, J.Y. Weltman, R.D. Abbott, M.E. Gutgesell, M.L. Hartman, J.D. Veldhuis, and A. Weltman. Impact of acute exercise intensity on pulsatile growth hormone release in men. Journal of Applied Physiology, 1999. 87(2): 498-504.

74. Karagiorgos, A., J.F. Garcia, and G.A. Brooks. Growth hormone response to continuous and intermittent exercise. Medicine and Science in Sports, 1978. 11(3): 302-307.

75. Kraemer, W.J., L. Marchitelli, S.E. Gordon, E. Harman, J.E. Dziados, R. Mello, P. Frykman, D. McCurry, and S.J. Fleck. Hormonal and growth factor responses to heavy resistance exercise protocols. 1990. 69(4): 1442-1450.

76. McCall, G.E., W.C. Byrnes, S.J. Fleck, A. Dickinson, and W.J. Kraemer. Acute and chronic hormonal responses to resistance training designed to promote muscle hypertrophy. Canadian Journal of Applied Physiology, 1999. 24(1): 96-107.

77. Häkkinen, K. and A. Pakarinen. Acute hormonal responses to two different fatiguing heavy-resistance protocols in male athletes. Journal of Applied Physiology, 1993. 74: 882-882.

78. Hoffman, J.R., J. Im, K.W. Rundell, J. Kang, S. Nioka, B. Spiering, R. Kime, B. Chance, and B. Speiring. Effect of muscle oxygenation during resistance exercise on anabolic hormone response. Medicine and Science in Sports and Exercise, 2003. 35(11): 1929-1934.

79. Smilios, I., T. Pilianidis, M. Karamouzis, and S.P. Tokmakidis. Hormonal responses after various resistance exercise protocols. Medicine and Science in Sports and Exercise, 2003. 35(4): 644-654.

80. Walker, S., R.S. Taipale, K. Nyman, W.J. Kraemer, and K. Häkkinen. Neuromuscular and hormonal responses to constant and variable resistance loadings. Medicine and Science in Sports and Exercise, 2011. 43(1): 26-33.

81. Zafeiridis, A., I. Smilios, R.V. Considine, and S.P. Tokmakidis. Serum leptin responses after acute resistance exercise protocols. Journal of Applied Physiology, 2003. 94(2): 591-597.

82. Kraemer, W.J., S.J. Fleck, J.E. Dziados, E.A. Harman, L.J. Marchitelli, S.E. Gordon, R. Mello, P.N. Frykman, L.P. Koziris, and N.T. Triplett. Changes in hormonal concentrations after different heavy-resistance exercise protocols in women. Journal of Applied Physiology, 1993. 75(2): 594-604.

83. Loenneke, J., G. Wilson, and J. Wilson. A mechanistic approach to blood flow occlusion. International Journal of Sports Medicine, 2010. 31(1): 1-4.

84. Viru, M., E. Jansson, A. Viru, and C.J. Sundberg. Effect of restricted blood flow on exercise-induced hormone changes in healthy men. European Journal of Applied Physiology and Occupational Physiology, 1998. 77(6): 517-522.

85. Sutton, J., N. Jones, and C. Toews. Growth hormone secretion in acid-base alterations at rest and during exercise. Clinical Science and Molecular Medicine, 1976. 50(4): 241-247.

86. Goto, K., K. Sato, and K. Takamatsu. A single set of low intensity resistance exercise immediately following high intensity resistance exercise stimulates growth hormone secretion in men. The Journal of Sports Medicine and Physical Fitness, 2003. 43(2): 243-249.

87. Adams, G.R. Role of insulin-like growth factor-I in the regulation of skeletal muscle adaptation to increased loading. Exercise and Sport Sciences Reviews, 1997. 26: 31-60.

88. Philippou, A., E. Papageorgiou, G. Bogdanis, A. Halapas, A. Sourla, M. Maridaki, N. Pissimissis, and M. Koutsilieris. Expression of IGF-1 isoforms after exercise-induced muscle damage in humans: characterization of the MGF E peptide actions in vitro. In Vivo, 2009. 23(4): 567-575.

89. Philippou, A., M. Maridaki, A. Halapas, and M. Koutsilieris. The role of the insulin-like growth factor 1 (IGF-1) in skeletal muscle physiology. In Vivo, 2007. 21(1): 45-54.

90. Goldspink, G. Mechanical signals, IGF-I gene splicing, and muscle adaptation. Physiology, 2005. 20(4): 232-238.

91. Hameed, M., R. Orrell, M. Cobbold, G. Goldspink, and S. Harridge. Expression of IGF-I splice variants in young and old human skeletal muscle after high resistance exercise. The Journal of Physiology, 2003. 547(1): 247-254.

92. Goldspink, G. Changes in muscle mass and phenotype and the expression of autocrine and systemic growth factors by muscle in response to stretch and overload. Journal of Anatomy, 1999. 194(03): 323-334.

93. Yang, S.Y. and G. Goldspink. Different roles of the IGF-I Ec peptide (MGF) and mature IGF-I in myoblast proliferation and differentiation. Federation of European Biochemical Societies, 2002. 522(1-3): 156-60.

94. Takano, H., T. Morita, H. Iida, K.-i. Asada, M. Kato, K. Uno, K. Hirose, A. Matsumoto, K. Takenaka, and Y. Hirata. Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. European Journal of Applied Physiology, 2005. 95(1): 65-73.

95. Fujita, S., T. Abe, M.J. Drummond, J.G. Cadenas, H.C. Dreyer, Y. Sato, E. Volpi, and B.B. Rasmussen. Blood flow restriction during low-intensity resistance exercise

increases S6K1 phosphorylation and muscle protein synthesis. Journal of Applied Physiology, 2007. 103(3): 903-910.

96. Patterson, S.D., M. Leggate, M.A. Nimmo, and R.A. Ferguson. Circulating hormone and cytokine response to low-load resistance training with blood flow restriction in older men. European Journal of Applied Physiology, 2013. 113(3): 713-719.

97. Ahtiainen, J.P., A. Pakarinen, M. Alen, W.J. Kraemer, and K. Häkkinen. Muscle hypertrophy, hormonal adaptations and strength development during strength training in strength-trained and untrained men. European journal of applied physiology, 2003. 89(6): 555-563.

98. Vingren, J.L., W.J. Kraemer, N.A. Ratamess, J.M. Anderson, J.S. Volek, and C.M. Maresh. Testosterone physiology in resistance exercise and training. Sports Medicine, 2010. 40(12): 1037-1053.

99. Sinha-Hikim, I., M. Cornford, H. Gaytan, M.L. Lee, and S. Bhasin. Effects of testosterone supplementation on skeletal muscle fiber hypertrophy and satellite cells in community-dwelling older men. The Journal of Clinical Endocrinology and Metabolism, 2006. 91(8): 3024-3033.

100. Kvorning, T., M. Andersen, K. Brixen, P. Schjerling, C. Suetta, and K. Madsen. Suppression of testosterone does not blunt mRNA expression of myoD, myogenin, IGF, myostatin or androgen receptor post strength training in humans. The Journal of Physiology, 2007. 578(2): 579-593.

101. Kraemer, W.J., S. Gordon, S. Fleck, L. Marchitelli, R. Mello, J. Dziados, K. Friedl, E. Harman, C. Maresh, and A. Fry. Endogenous anabolic hormonal and growth factor responses to heavy resistance exercise in males and females. International Journal of Sports Medicine, 1991. 12(02): 228-235.

102. West, D.W., N.A. Burd, T.A. Churchward-Venne, D.M. Camera, C.J. Mitchell, S.K. Baker, J.A. Hawley, V.G. Coffey, and S.M. Phillips. Sex-based comparisons of

myofibrillar protein synthesis after resistance exercise in the fed state. Journal of Applied Physiology, 2012. 112(11): 1805-1813.

103. West, D.W., N.A. Burd, J.E. Tang, D.R. Moore, A.W. Staples, A.M. Holwerda, S.K. Baker, and S.M. Phillips. Elevations in ostensibly anabolic hormones with resistance exercise enhance neither training-induced muscle hypertrophy nor strength of the elbow flexors. Journal of Applied Physiology, 2010. 108(1): 60-67.

104. West, D.W., G.W. Kujbida, D.R. Moore, P. Atherton, N.A. Burd, J.P. Padzik, M. De Lisio, J.E. Tang, G. Parise, and M.J. Rennie. Resistance exercise-induced increases in putative anabolic hormones do not enhance muscle protein synthesis or intracellular signalling in young men. The Journal of Physiology, 2009. 587(21): 5239-5247.

105. Wilkinson, S.B., M.A. Tarnopolsky, E.J. Grant, C.E. Correia, and S.M. Phillips. Hypertrophy with unilateral resistance exercise occurs without increases in endogenous anabolic hormone concentration. European Journal of Applied Physiology, 2006. 98(6): 546-555.

106. Rønnestad, B.R., H. Nygaard, and T. Raastad. Physiological elevation of endogenous hormones results in superior strength training adaptation. European Journal of Applied Physiology, 2011. 111(9): 2249-2259.

107. Schroeder, E.T., M. Villanueva, D.D. West, and S.M. Phillips. Are acute post-resistance exercise increases in testosterone, growth hormone, and IGF-1 necessary to stimulate skeletal muscle anabolism and hypertrophy? Medicine and Science in Sports and Exercise, 2013. 45(11): 2044-2051.

108. Medicine, A.C.o.S. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Medicine and Science in Sports and Exercise, 2009. 41(3): 687.

109. Takarada, Y., H. Takazawa, and N. Ishii. Applications of vascular occlusions diminish disuse atrophy of knee extensor muscles. Medicine and Science in Sports and Exercise, 2000. 32(12): 2035-2039.

110. Schoenfeld, B.J. Potential mechanisms for a role of metabolic stress in hypertrophic adaptations to resistance training. Sports Medicine, 2013. 43(3): 179-194.

111. Pierce, J.R., B.C. Clark, L.L. Ploutz-Snyder, and J.A. Kanaley. Growth hormone and muscle function responses to skeletal muscle ischemia. Journal of Applied Physiology, 2006. 101(6): 1588-1595.

112. Reeves, G.V., R.R. Kraemer, D.B. Hollander, J. Clavier, C. Thomas, M. Francois, and V.D. Castracane. Comparison of hormone responses following light resistance exercise with partial vascular occlusion and moderately difficult resistance exercise without occlusion. Journal of Applied Physiology, 2006. 101(6): 1616-1622.

113. Takarada, Y., Y. Nakamura, S. Aruga, T. Onda, S. Miyazaki, and N. Ishii. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. Journal of Applied Physiology, 2000. 88(1): 61-65.

114. Kawada, S. What phenomena do occur in blood flow-restricted muscle. International Journal of KAATSU Training Research, 2005. 1(2): 37-44.

115. Gordon, S.E., W.J. Kraemer, N.H. Vos, J.M. Lynch, and H.G. Knuttgen. Effect of acid-base balance on the growth hormone response to acute high-intensity cycle exercise. Journal of Applied Physiology, 1994. 76(2): 821-829.

116. Moritani, T., W.M. Sherman, M. Shibata, T. Matsumoto, and M. Shinohara. Oxygen availability and motor unit activity in humans. European Journal of Applied Physiology and Occupational Physiology, 1992. 64(6): 552-556.

117. Loenneke, J., C. Fahs, J. Wilson, and M. Bemben. Blood flow restriction: the metabolite/volume threshold theory. Medical Hypotheses, 2011. 77(5): 748-752.

118. Moore, D.R., K.A. Burgomaster, L.M. Schofield, M.J. Gibala, D.G. Sale, and S.M. Phillips. Neuromuscular adaptations in human muscle following low intensity resistance training with vascular occlusion. European Journal of Applied Physiology, 2004. 92(4-5): 399-406.

119. Takarada, Y., H. Takazawa, Y. Sato, S. Takebayashi, Y. Tanaka, and N. Ishii. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. Journal of Applied Physiology, 2000. 88(6): 2097-2106.

120. Wernbom, M., R. Järrebring, M.A. Andreasson, and J. Augustsson. Acute effects of blood flow restriction on muscle activity and endurance during fatiguing dynamic knee extensions at low load. The Journal of Strength and Conditioning Research, 2009. 23(8): 2389-2395.

121. Manini, T.M. and B.C. Clark. Blood flow restricted exercise and skeletal muscle health. Exercise and Sport Sciences Reviews, 2009. 37(2): 78-85.

122. Cook, S.B., B.G. Murphy, and K.E. Labarbera. Neuromuscular function after a bout of low-load blood flow-restricted exercise. Medicine and Science in Sports and Exercise, 2013. 45(1): 67-74.

123. Fry, C.S., E.L. Glynn, M.J. Drummond, K.L. Timmerman, S. Fujita, T. Abe, S. Dhanani, E. Volpi, and B.B. Rasmussen. Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. Journal of Applied Physiology, 2010. 108(5): 1199-1209.

124. Wernbom, M., W. Apro, G. Paulsen, T.S. Nilsen, E. Blomstrand, and T. Raastad. Acute low-load resistance exercise with and without blood flow restriction increased protein signalling and number of satellite cells in human skeletal muscle. European Journal of Applied Physiology, 2013. 113(12): 2953-2965.

125. Camera, D.M., J. Edge, M.J. Short, J.A. Hawley, and V.G. Coffey. Early time course of Akt phosphorylation after endurance and resistance exercise. Medicine and Science in Sports and Exercise, 2010. 42(10): 1843-1852.

126. Shinohara, M., M. Kouzaki, T. Yoshihisa, and T. Fukunaga. Efficacy of tourniquet ischemia for strength training with low resistance. European Journal of Applied Physiology and Occupational Physiology, 1998. 77(1-2): 189-191.

127. Nakajima, T., T. Morita, and Y. Sato. Key considerations when conducting KAATSU training. International Journal of KAATSU Training Research, 2011. 7(1): 1-6.

128. Etheridge, T., P.J. Atherton, D. Wilkinson, A. Selby, D. Rankin, N. Webborn, K. Smith, and P.W. Watt. Effects of hypoxia on muscle protein synthesis and anabolic signaling at rest and in response to acute resistance exercise. American Journal of Physiology-Endocrinology and Metabolism, 2011. 301(4): E697-E702.

129. Kon, M., T. Ikeda, T. Homma, T. Akimoto, Y. Suzuki, and T. Kawahara. Effects of acute hypoxia on metabolic and hormonal responses to resistance exercise. Medicine and Science in Sports and Exercise, 2010. 42(7): 1279-1285.

130. Kon, M., T. Ikeda, T. Homma, and Y. Suzuki. Effects of low-intensity resistance exercise under acute systemic hypoxia on hormonal responses. The Journal of Strength and Conditioning Research, 2012. 26(3): 611-617.

131. Ho, J.-Y., T.-Y. Huang, Y.-C. Chien, Y.-C. Chen, and S.-Y. Liu. Effects of acute exposure to mild simulated hypoxia on hormonal responses to low-intensity resistance exercise in untrained men. Research in Sports Medicine, 2014. 22(3): 240-252.

132. Scott, B.R., K.M. Slattery, D.V. Sculley, J.A. Hodson, and B.J. Dascombe. Physical performance during high-intensity resistance exercise in normoxic and hypoxic conditions. The Journal of Strength and Conditioning Research, 2015. 29(3): 807-815.

133. Friedmann, B., R. Kinscherf, S. Borisch, G. Richter, P. Bärtsch, and R. Billeter. Effects of low-resistance/high-repetition strength training in hypoxia on muscle structure and gene expression. European Journal of Physiology, 2003. 446(6): 742-751.

134. Nishimura, A., M. Sugita, K. Kato, A. Fukuda, A. Sudo, and A. Uchida. Hypoxia increases muscle hypertrophy induced by resistance training. International Journal of Sports Physiology and Performance, 2010. 5(4): 497-508.

135. Manimmanakorn, A., M.J. Hamlin, J.J. Ross, R. Taylor, and N. Manimmanakorn. Effects of low-load resistance training combined with blood flow restriction or hypoxia on muscle function and performance in netball athletes. Journal of Science and Medicine in Sport, 2013. 16(4): 337-342.

136. Manimmanakorn, A., N. Manimmanakorn, R. Taylor, N. Draper, F. Billaut, J.P. Shearman, and M.J. Hamlin. Effects of resistance training combined with vascular occlusion or hypoxia on neuromuscular function in athletes. European journal of applied physiology, 2013. 113(7): 1767-1774.

137. Kon, M., N. Ohiwa, A. Honda, T. Matsubayashi, T. Ikeda, T. Akimoto, Y. Suzuki, Y. Hirano, and A.P. Russell. Effects of systemic hypoxia on human muscular adaptations to resistance exercise training. Physiological Reports, 2014. 2(6).

138. Kurobe, K., Z. Huang, M. Nishiwaki, M. Yamamoto, H. Kanehisa, and F. Ogita. Effects of resistance training under hypoxic conditions on muscle hypertrophy and strength. Clinical Physiology and Functional Imaging, 2014.

139. Ho, J.-Y., T.-Y. Kuo, K.-L. Liu, X.-Y. Dong, and K. Tung. Combining normobaric hypoxia with short-term resistance training has no additive beneficial effect on muscular performance and body composition. The Journal of Strength and Conditioning Research, 2014. 28(4): 935-941.

140. Yan, B., X. Lai, L. Yi, Y. Wang, and Y. Hu. The effects of 5-week resistance training in hypoxia on hormones and muscle strength. The Journal of Strength and Conditioning Research, 2015.

141. Greenhaff, P.L., L. Karagounis, N. Peirce, E.J. Simpson, M. Hazell, R. Layfield, H. Wackerhage, K. Smith, P. Atherton, and A. Selby. Disassociation between the effects of amino acids and insulin on signaling, ubiquitin ligases, and protein turnover in human muscle. American Journal of Physiology-Endocrinology and Metabolism, 2008. 295(3): E595-E604.

142. Reilly, T. Human circadian rhythms and exercise. Critical Reviews in Biomedical Engineering, 1989. 18(3): 165-180.

143. Hermens, H.J., B. Freriks, C. Disselhorst-Klug, and G. Rau. Development of recommendations for SEMG sensors and sensor placement procedures. Journal of Electromyography and Kinesiology, 2000. 10(5): 361-374.

144. Knapik, J.J., J.E. Wright, R.H. Mawdsley, and J. Braun. Isometric, isotonic, and isokinetic torque variations in four muscle groups through a range of joint motion. Physical Therapy, 1983. 63(6): 938-947.

145. Borg, G. Psychophysical scaling with applications in physical work and the perception of exertion. Scandinavian Journal of Work, Environment and Health, 1990: 55-58.

146. Batterham, A.M. and W.G. Hopkins. Making meaningful inferences about magnitudes. International Journal of Sports Physiology and Performance, 2006. 1: 50-57.

147. Hopkins, W. A spreadsheet for analysis of straightforward controlled trials. Sportscience, 2003. 7(2-7): 15.

148. Hopkins, W.G. A scale of magnitudes for effect statistics. A new view of statistics, 2002. Available from: http://www.sportsci.org/resource/stats/.

149. Scott, B.R., K.M. Slattery, and B.J. Dascombe. Intermittent hypoxic resistance training: Is metabolic stress the key moderator. Medical Hypotheses, 2015. 84(2): 145-149.

150. Wideman, L., J.Y. Weltman, M.L. Hartman, J.D. Veldhuis, and A. Weltman. Growth hormone release during acute and chronic aerobic and resistance exercise. Sports Medicine, 2002. 32(15): 987-1004.

151. Nindl, B.C., J.R. Pierce, K.R. Rarick, A.P. Tuckow, J.A. Alemany, M.A. Sharp, M.D. Kellogg, and J.F. Patton. Twenty-hour growth hormone secretory profiles after aerobic and resistance exercise. Medicine and Science in Sports and Exercise, 2014. 46(10): 1917-1927.

152. West, D.W. and S.M. Phillips. Anabolic processes in human skeletal muscle: restoring the identities of growth hormone and testosterone. Physician and Sportsmedicine, 2010. 38(3): 97-104.

153. Gravholt, C.H., O. Schmitz, L. Simonsen, J. Bülow, J.S. Christiansen, and N. Møller. Effects of a physiological GH pulse on interstitial glycerol in abdominal and femoral adipose tissue. American Journal of Physiology-Endocrinology And Metabolism, 1999. 277(5): E848-E854.

154. Doessing, S. and M. Kjaer. Growth hormone and connective tissue in exercise. Scandinavian Journal of Medicine and Science in Sports, 2005. 15(4): 202-210.

155. Kraemer, W.J. and N.A. Ratamess. Fundamentals of resistance training: progression and exercise prescription. Medicine and Science in Sports and Exercise, 2004. 36(4): 674-688.

156. Haseler, L.J., M.C. Hogan, and R.S. Richardson. Skeletal muscle phosphocreatine recovery in exercise-trained humans is dependent on O2availability. Journal of Applied Physiology, 1999. 86(6): 2013-2018.

157. Goto, K., M. Nagasawa, O. Yanagisawa, T. Kizuki, N. Ishii, and K. Takamatsu. Muscular adaptations to combinations of high-and low-intensity resistance exercises. The Journal of Strength and Conditioning Research, 2004. 18(4): 730-737.

158. Victor, R.G. and D.R. Seals. Reflex stimulation of sympathetic outflow during rhythmic exercise in humans. American Journal of Physiology-Heart and Circulatory Physiology, 1989. 257(6): H2017-H2024.

159. Sale, D.G. Neural adaptation to strength training. Strength and Power in Sport, Second Edition, 2003: 281-314.

160. Durand, R.J., V.D. Castracane, D.B. Hollander, J.L. Tryniecki, M.M. Bamman, S. O'Neal, E.P. Hebert, and R.R. Kraemer. Hormonal responses from concentric and eccentric muscle contractions. Medicine and Science in Sports and Exercise, 2003. 35(6): 937-943.

161. Kraemer, R.R., D.B. Hollander, G.V. Reeves, M. Francois, Z.G. Ramadan, B. Meeker, J.L. Tryniecki, E. Hebert, and V.D. Castracane. Similar hormonal responses to concentric and eccentric muscle actions using relative loading. European Journal of Applied Physiology, 2006. 96(5): 551-557.

162. Burd, N.A., R.J. Andrews, D.W. West, J.P. Little, A.J. Cochran, A.J. Hector, J.G. Cashaback, M.J. Gibala, J.R. Potvin, and S.K. Baker. Muscle time under tension during resistance exercise stimulates differential muscle protein sub-fractional synthetic responses in men. The Journal of Physiology, 2012. 590(2): 351-362.

163. Burd, N.A., D.W. West, A.W. Staples, P.J. Atherton, J.M. Baker, D.R. Moore, A.M. Holwerda, G. Parise, M.J. Rennie, and S.K. Baker. Low-load high volume resistance exercise stimulates muscle protein synthesis more than high-load low volume resistance exercise in young men. Public Library of Science One, 2010. 5(8): e12033.

164. Suminski, R.R., R.J. Robertson, S. Arslanian, J. Kang, A.C. Utter, S.G. DaSilva, F.L. Goss, and K.F. Metz. Perception of effort during resistance exercise. The Journal of Strength and Conditioning Research, 1997. 11(4): 261-265.

Appendices

Appendix A

Letter to Participants

PARTICIPANT INFORMATION LETTER

PROJECT TITLE: What is the impact of hypoxia (low-oxygen) on GH levels in response to a maximal strength training session?

PRINCIPAL INVESTIGATOR: Dr. Doug Whyte

STUDENT RESEARCHER: Dean Filopoulos

STUDENT'S DEGREE: Masters of Exercise Science (Research)

Dear Participant,

You are invited to participate in the research project described below.

What is the project about?
You are invited to participate in a research project investigating the effects of hypoxia (low-oxygen) on resistance exercise. The purpose of this project is to determine if anabolic hormones change in response to strength training in hypoxic (low-oxygen) compared to normoxic (normal oxygen) conditions. The findings from this study may provide evidence to fitness coaches in elite sports of an alternative method in maximising gains in strength and hypertrophy (muscle mass).

Who is undertaking the project?
This project is being conducted by Dean Filopoulos and will form the basis for the degree of Master of Exercise Science (Research) at Australian Catholic University under the supervision of Dr. Doug Whyte.

Are there any risks associated with participating in this project?
Potential risks involved with this study include discomfort during or following maximal strength testing, and the possibility of injury, although these are very unlikely. To help prevent any adverse effects, you will be closely monitored and will be assisted during each lift. The leg press machine will have support levers for you to drop the weight and the bench press apparatus will have overhead support levers for you to rack the weight, at any time you feel uncomfortable or cannot perform the exercise tasks properly. Additionally, you will be assisted and supported at all times during the performance of these exercises. During hypoxia (low-oxygen environment), you may experience some headaches, fatigue, shortness of breath and nausea. If any of these symptoms arise you are able to stop immediately and take off the mask. There is also a risk that you may experience discomfort and bruising around the needle site as a result of having blood taken. To limit this risk, only a trained phlebotomist will take blood samples.

What will I be asked to do?
To be eligible to participate in this study you must be physically active and currently engaged in resistance training (i.e. >2 x per week for 6 months), male, aged between 18-35 years with no history of cardiovascular or respiratory disease, altitude related illness or any musculoskeletal injuries. In addition, should you have any bleeding or clotting disorders or allergies you should discuss these with the investigators to ensure they will not impact your health and safety during the experiment.

If you choose to participate you will be required to complete three laboratory testing sessions over a week period. You will be asked to complete a strength testing session that will involve determining your 1 repetition maximum (1RM) (the maximum amount of weight you can lift) for the leg press (lower body) and bench press exercise (upper body). The two experimental sessions will require you to perform a resistance exercise protocol consisting of 5 sets of 3 repetitions at 85% of 1RM with 3 min rest between all sets and exercises. Prior to the beginning of the session you will be prepared for electromyography (EMG) (which is a technique for evaluating and recording the electrical activity produced by skeletal muscle) of your quadriceps muscle and provide a forearm vein blood sample. After this you will then perform the resistance exercise protocol in either room air (20.9%) or low-oxygen (12%) conditions. Immediately prior to the experimental session, two warm up sets at 50 and 75% of 1RM will be performed, in addition to 2 sets of isometric maximal voluntary contractions (maximal force produced by the muscle pushing against an immovable object) to determine the maximal amount of EMG activity the quadriceps muscle can produce. Following the completion of the resistance exercise protocol a cannula will be inserted into your forearm vein while seated, and four blood samples will be drawn over a one hour period. . You will then return to the laboratory 3 days later to repeat the same experimental session under the opposite condition.

How much time will the project take?
You will be required to attend the ACU laboratory on three days occasions over a 2 week period. Each day will vary in time commitments ranging from 45 minutes for strength testing to 3hr for the experimental testing sessions.

What are the benefits of the research project?
While there are no direct benefits to you for participating in this study, you will be provided with specialised feedback of your current lower-body and upper body strength levels. Exercise Science students will also be eligible to receive up to 20 hours of industry experience for participating in this study.

Can I withdraw from the study?
Participation in this study is completely voluntary. You are not under any obligation to participate. If you agree to participate, you can withdraw from the study at any time without adverse consequences. Any withdrawal from the study will not impede on you future academic progress or employment, and at no point will you feel any pressure to change your decision.

Will anyone else know the results of the project?
Your results will be analysed statistically to identify which experimental group is more effective for altering hormonal responses. No persons other than the investigators will be given access to your information. You will have access to your own data. Only aggregated data from this study will be submitted to a journal for publication and any other written reports and presentations will exclude your name. No personal details will be revealed without your written consent

Will I be able to find out the results of the project?
At the conclusion of the study, there will be an opportunity for you to be provided with the overall and individual results of the project if that is your wish.

Who do I contact if I have questions about the project?

If you would like to participate in this study, please contact the research team (contact details are given below) for details of the next step. You will be provided with further information to ensure that your decision and consent to participate is fully informed.

Principal Investigator: Dr. Doug Whyte
Ph: 9953 3557
Faculty of Health Sciences
115 Victoria Parade Fitzroy Victoria 3065

Student Researcher: Mr. Dean Filopoulos
Ph: 0401 677 729
School of Exercise Science
115 Victoria Parade Fitzroy Victoria 3065

What if I have a complaint or any concerns?
The study has been reviewed by the Human Research Ethics Committee at Australian Catholic University (review number 2014 197V). If you have any complaints or concerns about the conduct of the project, you may write to the Manager of the Human Research Ethics Committee care of the Office of the Deputy Vice Chancellor (Research).

Manager, Ethics
c/o Office of the Deputy Vice Chancellor (Research)
Australian Catholic University
North Sydney Campus
PO Box 968
NORTH SYDNEY, NSW 2059
Ph.: 02 9739 2519
Fax: 02 9739 2870
Email: res.ethics@acu.edu.au

Any complaint or concern will be treated in confidence and fully investigated. You will be informed of the outcome.

I want to participate! How do I sign up?
If you agree to participate in this project, you should sign both copies of the Consent Form,

retain one copy for your records and return the other copy to the Principal Investigator (or

Supervisor) or Student Researcher.

Yours sincerely,

RESEARCHER NAME/S AND SIGNATURE/

.....	.....
Dr. Doug Whyte	Dean Filopoulos
Principal Investigator (or Supervisor)	Student Researcher

Appendix B

Consent Form

CONSENT FORM
(Copy for Participant)

TITLE OF PROJECT: What is the impact of hypoxia (low-oxygen) on GH levels in response to a maximal strength training session?

PRINCIPAL INVESTIGATOR (or SUPERVISOR): Dr. Doug Whyte

STUDENT RESEARCHER: Dean Filopoulos

I ..... *(the participant)* have read (*or, where appropriate, have had read to me)* and understood the information provided in the Letter to Participants. Any questions I have asked have been answered to my satisfaction.

- I agree to participate in this study involving strength testing, resistance exercise in a hypoxic environment, electromyography assessment, and blood collection.
- I understand I will be required to attend the laboratory on 3 occasions over a two week period and that each session will last between 45 min – 3hr.
- I agree to have blood taken on two of those occasions. I understand this will occur through both venous puncture and cannulation,
- I have informed the investigators of any relevant medical disorders including bleeding disorders, allergies or previous negative experiences associated with altitude.
- I understand that hypoxia may cause me to have headaches, dizziness, shortness of breath, mental confusion and nausea.

I understand I can withdraw my consent at any time. I agree that research data collected for the study may be published or may be provided to other researchers in a form that does not identify me in any way.

NAME OF PARTICIPANT:.....

SIGNATURE: ..... DATE:.....

SIGNATURE OF PRINCIPAL INVESTIGATOR: ..... DATE:…….

SIGNATURE OF STUDENT RESEARCHER: ..... DATE:.....

Appendix C

Rating of Perceived Exertion Scale

Rating	Descriptor
0	Rest
1	Very, very easy
2	Easy
3	Moderate
4	Somewhat Hard
5	Hard
6	-
7	Very Hard
8	-
9	-
10	Maximal

Appendix D

1RM Strength Testing Data Collection Sheet

Subject Number: _____ Height: _____

Date: _____ Weight: _____

Exercise: _____ Age: _____

Training history: _____

Step 1:	Light warm up: (5-10 reps)	_____	Rest 1 min
Step 1:	Warm-up: (3-5 reps)	_____	Rest 2 min
Step 3:	Near max weight (2-3 reps) UB + 5-10kg LB + 15-20kg	_____	Rest 3 min
Step 4:	1st Test UB + 5-10kg LB + 15-20kg	_____	Rest 3 min
Step 5:	2nd Test UB + 5-10kg LB + 15-20kg	_____	
Step 6:	3rd Test UB + 5-10kg LB + 15-20kg	_____	
Step 6:	4th Test UB + 5-10kg LB + 15-20kg	_____	
Step 6:	5th Test UB + 5-10kg LB + 15-20kg	_____	

Notes: If failed attempt occurs, rest 3 min, decrease load by 2-5kg UB or 5-10 LB; then attempt again

Familiarisation Isometric MVC (3 min rest)

Trial 1: _____

Trial 2: _____

Trial 3: _____

Foot Placement

Left: _____

Right: _____

Knee Angle: _____

Appendix E

Experimental Session Data Collection Sheet (Leg Press)

Subject number:		Date:		EMG:	ASIS-L.Patella	Foot Placement:	
Exercise:	Leg Press	Trial:		Distance:		Left:	
Condition:				Knee angle:		Right:	
1RM Weight:							

50% Isometric MVC	Rest 1 min		SpO2:		PO HR:	Polar HR:	
75% Isometric MVC	Rest 1 min						
Isometric MVC	Rest 3 min						
Isometric MVC	Rest 5 min						

Start time (exposure)		Pre Lactate:					
			SpO2:		PO HR:	Polar HR:	
Warm up (5 reps)	Rest 3 min						
50% 1RM	Load						

_____ SpO2: ____ PO HR: _____ Polar HR: _____

Warm-up
(3 reps)

75% 1RM Load

_____ SpO2: ____ PO HR: _____ Polar HR: _____

Work Set 1
(3 reps)

85% 1RM Load

_____ SpO2: ____ PO HR: _____ Polar HR: _____

Work Set 2
(3 reps)

85% 1RM Load

_____ SpO2: ____ PO HR: _____ Polar HR: _____

Work Set 3
(3reps)

85% 1RM Load

_____ SpO2: ____ PO HR: _____ Polar HR: _____

Work Set 4
(3 reps)

85% 1RM Load

_____ SpO2: ____ PO HR: _____ Polar HR: _____

Work Set 5
(3 reps)

85% 1RM Load

_____ SpO2: ____ PO HR: _____ Polar HR: _____

RPE: _____

Appendix E

Experimental Session Data Collection Sheet (Bench Press)

Subject number: _____

Exercise: Bench Press

Condition: _____

1RM Weight: _____

Warm-up (5 reps) 50% 1RM	Rest 3 min Load _____	SpO2:	_____	PO HR:	_____	Polar HR: _____
Warm-up (3 reps) 75% 1RM	Load _____	SpO2:	_____	PO HR:	_____	Polar HR: _____
Work Set 1 (3 reps) 85% 1RM	Load _____	SpO2:	_____	PO HR:	_____	Polar HR: _____
Work Set 2 (3 reps) 85% 1RM	Load _____	SpO2:	_____	PO HR:	_____	Polar HR: _____
Work Set 3 (3reps) 85% 1RM	Load _____	SpO2:	_____	PO HR:	_____	Polar HR: _____
Work Set 4 (3 reps) 85% 1RM	Load _____	SpO2:	_____	PO HR:	_____	Polar HR: _____

Work Set 5
(3 reps)
85% 1RM Load _____ SpO2: _____ PO HR: _____ Polar HR: _____

End time
(exposure) _____

Lactate:
Immediately
Post _____ 15min: _____ 30min: ____ 60min: _____

Post-blood
Sample
Time S1: _____ S2: _____ S3: ____ S4: _____

RPE: _____

Overall
Session RPE _____

What
condition
were you in: _____

Time of last
meal: _____

Appendix F

Ethics Application Approval

Dear Applicant,

Principal Investigator: Dr Douglas Whyte

Student Researcher: Mr Dean Filopoulos (HDR student)

Ethics Register Number: 2014 179V

Project Title: What is the impact of hypoxia on hormonal responses during a maximal strength training session?

Risk Level: Low Risk

Date Approved: 24/06/2014

Ethics Clearance End Date: 01/07/2015

This email is to advise that your application has been reviewed by the Australian Catholic University's Human Research Ethics Committee and confirmed as meeting the requirements of the National Statement on Ethical Conduct in Human Research.

This project has been awarded ethical clearance until 01/07/2015. In order to comply with the National Statement on Ethical Conduct in Human Research, progress reports are to be submitted on an annual basis. If an extension of time is required researchers must submit a progress report.

Whilst the data collection of your project has received ethical clearance, the decision and authority to commence may be dependent on factors beyond the remit of the ethics review process. The Chief Investigator is responsible for ensuring that appropriate permission letters are obtained, if relevant, and a copy forwarded to ACU HREC before any data collection can occur at the specified organisation. Failure to provide permission letters to ACU HREC before data collection commences is in breach of the National Statement on Ethical Conduct

in Human Research and the Australian Code for the Responsible Conduct of Research. Further, this approval is only valid as long as approved procedures are followed.

If you require a formal approval certificate, please respond via reply email and one will be issued.

Decisions related to low risk ethical review are subject to ratification at the next available Committee meeting. You will be contacted should the Committee raises any additional questions or concerns.

Researchers who fail to submit a progress report may have their ethical clearance revoked and/or the ethical clearances of other projects suspended. When your project has been completed please complete and submit a progress/final report form and advise us by email at your earliest convenience. The information researchers provide on the security of records, compliance with approval consent procedures and documentation and responses to special conditions is reported to the NHMRC on an annual basis. In accordance with NHMRC the ACU HREC may undertake annual audits of any projects considered to be of more than low risk.

It is the Principal Investigators / Supervisors responsibility to ensure that:

1. All serious and unexpected adverse events should be reported to the HREC with 72 hours.
2. Any changes to the protocol must be approved by the HREC by submitting a Modification Form prior to the research commencing or continuing.
3. All research participants are to be provided with a Participant Information Letter and consent form, unless otherwise agreed by the Committee.

For progress and/or final reports, please complete and submit a Progress /

Final Report form:

http://www.acu.edu.au/research/support_for_researchers/human_ethics/forms

For modifications to your project, please complete and submit a Modification form:

http://www.acu.edu.au/research/support_for_researchers/human_ethics/forms

Researchers must immediately report to HREC any matter that might affect the ethical acceptability of the protocol eg: changes to protocols or unforeseen circumstances or adverse effects on participants.

Please do not hesitate to contact the office if you have any queries.

Kind regards,

Kylie Pashley

on behalf of ACU HREC Chair, Dr Nadia Crittenden

Ethics Officer | Research Services

Office of the Deputy Vice Chancellor (Research)

Australian Catholic University