The effect of repetition tempo on training volume, heart rate, blood lactate, and muscle oxygenation when time under tension is matched in recreationally-trained lifters

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The effect of repetition tempo on training volume, heart rate, blood lactate, and muscle oxygenation when time under tension is matched in recreationally-trained lifters

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DISSERTATION

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ABSTRACT

It is commonly reported that resistance training (RT) with slower-repetition tempos leads to greater metabolic stress because they increase the time under tension (TUT) during sets of exercise. However, little information is available on the effect of different repetition tempos on blood lactate concentration, muscle oxygenation, and heart rate (HR) when TUT and proximity to concentric muscular failure are matched during lower-body RT. In a repeated-measures, cross-over design, 11 recreationally-trained females (n = 5) and males (n = 6) performed five sets of belt squat under the following conditions: Slow-repetition tempo (SLOW; 10 reps with 4:2 second tempo) and traditional-repetition tempo (TRAD; 20 reps with 2:1 second tempo). Time under tension (60 seconds) was matched between conditions and external load was adjusted so
that lifters were close to concentric muscular failure at the end of each set. External load, total volume load (TVL), impulse (IMP), blood lactate, ratings of perceived exertion (RPE), HR, and muscle oxygenation were measured during both RT protocols. Data indicated that total volume load (p < .001), blood lactate (p = 0.017), RPE (p = 0.015), and HR (p < .001) were significantly greater during TRAD while external load (p = 0.030) and IMP (p = 0.002) were significantly greater during SLOW. Whether it was expressed as minimal values or change scores, muscle oxygenation was not different between protocols. When TUT is matched, cardiovascular stress, metabolic stress, and perceived exertion are greater during TRAD. These differences may be explained by higher TVL as TRAD required 2X greater repetition volume and mechanical work. Future research should determine if these styles of RT lead to divergent physiological adaptations and performance outcomes.
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Chapter 1: Introduction

Resistance training (RT) is a commonly used exercise modality in which skeletal muscle contracts against an external load such as body weight (1), free weights (2), machines (3), kettlebells (4), and battle ropes (5). There are many neuromuscular adaptations associated with RT, making it useful for a variety of populations that range from pre-adolescent children (6) to elderly adults (7). Specifically, RT stimulates increases in local muscular endurance (8), hypertrophy (9), strength (10), power (11), sprint performance (12), and change of direction (13). In addition, the cardiometabolic health benefits of RT have recently been summarized (14) which include increased resting energy expenditure (15), fat loss (16), improved glucose metabolism (17), decreased concentration of low-density lipoproteins (18), and reduced blood pressure (19). These positive health benefits may explain why a recent meta-analysis of eleven studies (n = 370,256) concluded that those who performed RT and aerobic training (AT) had a 40% reduction in all-cause mortality compared to the 21% reduction among those who performed AT alone (20). Moreover, another recent meta-analysis concluded that when compared to AT, small doses of RT have independent cardioprotective benefits (21), and others have proposed that RT should be used as a primary countermeasure for obesity (22), cardiovascular disease (23), type 2 diabetes (24), and cancer (25).

In addition to muscle mass and muscular strength (26), there is a well-defined relationship between aerobic fitness and longevity, as higher levels of maximal oxygen consumption (VO2max) are associated with reduced risk for cardiovascular disease and all-cause mortality (27, 28, 29). In a similar manner, aging, obesity, cardiovascular disease, peripheral artery disease, and type 2 diabetes are associated with mitochondrial dysfunction and reduced oxidative capacity (24, 30, 31, 32), which implies that hallmark adaptations to AT are important...
for health. In congruence with the principle of specificity, it is generally accepted that AT will elicit greater increases in cardiovascular fitness by increasing stroke volume (SV), cardiac output (Q), capillary density, percentage of oxidative muscle fibers, and mitochondrial enzyme activity (33, 34, 35). Indeed, when compared to RT, local energy turnover and metabolic stress are greater during AT (32, 36) which explains why these two modes of exercise generally elicit divergent adaptations, especially at the skeletal muscle (37, 38, 39, 40, 41). To be specific, the mechanical tension associated with RT stimulates muscle protein translation initiation and hypertrophy through the mammalian target of rapamycin (mTORC1) pathway (42), while the metabolic stress associated with AT stimulates mitochondrial biogenesis through the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) signaling cascade (43).

Several metabolic stressors serve as upstream stimulators of the PGC-1α signaling cascade, such as reactive oxygen species, calcium cycling, glycogen depletion, hydrogen ion accumulation, lactate, and ATP turnover (i.e., increased AMP:ATP ratio) (35, 38, 43). This is the proposed mechanism by which AT modalities, such as high-intensity interval training, stimulate increased mitochondrial density, mitochondrial enzyme activity, oxidative enzyme activity, and capillary density (34, 44, 45). Some have hypothesized that RT is capable of stimulating similar adaptations through this mechanism (46, 47). More specifically, recent evidence suggests that low-intensity (30% 1-RM), high-volume (~30 repetitions per set) RT increased markers of mitochondrial biogenesis and mitophagy more than high-intensity, low-volume RT (48). These results supported recent postulations that higher-volume RT with longer time under tension (TUT) would increase mitochondrial biogenesis and density compared to lower volume RT with shorter TUT (32, 49). This concept is further solidified by the positive relationship between TUT and metabolic stress as measured by blood lactate (50, 51, 52). Indeed, to increase TUT during a
set of RT, it is most conventional to use lower intensity (i.e., 50% of 1-RM) loads that can be lifted for many repetitions (i.e., 20 repetitions per set). Although less commonly employed, using slower repetitions (i.e., repetition tempo) is another way to increase TUT during sets of RT (53). For example, if TUT is matched at 60 seconds, a set of RT can be comprised of 20 repetitions performed with a 3-second tempo or 10 repetitions with a 6-second tempo (54).

The limited research that has been done to evaluate the role of repetition tempo and TUT on metabolic stress has led to the conclusion that performing 8 repetitions per set with a 7 second tempo (i.e., TUT of 56 seconds) elicits more ischemia and metabolic stress compared to 8 repetitions per set with a 3 second tempo (i.e., TUT of 24 seconds) (55, 56, 57, 58). It is worth noting that these research designs are limited because proximity to muscular failure (i.e., effort given per set) and TUT were not matched between conditions, meaning that the 7-second-repetition, 56-second-TUT sets were significantly more difficult than the 3-second-repetition, 24-second-TUT sets. Other studies that matched TUT and effort between conditions have concluded that performing more repetitions per set (e.g., 20 vs. 10) with faster repetition tempos (e.g., 3 vs. 6 seconds) leads to significantly higher levels of blood lactate concentration (54, 59). However, the physiological implications of these outcomes and the mechanisms by which they occur are not well-understood (i.e., when TUT is matched, do different repetition tempos elicit divergent adaptations?). It is now established that hypertrophy and strength occur along a spectrum of repetition-ranges from 3-30 RM which corresponds with intensities of 30-90% of 1-RM (60, 61, 62, 63). Because range of effective intensities is so wide, it is practical to consider the unique benefits that occur at opposite ends of the spectrum. For example, it is consistently reported that higher-intensity loads that lend themselves to shorter TUT and faster repetition tempos are more efficient for stimulating muscular strength (64, 65, 66). Although speculative, it is possible that
lower-intensity loads that are associated with longer TUT are more effective for stimulating local muscular endurance and mitochondrial biogenesis (32, 48, 49). To date, limited research has compared the effect of different variations of low-intensity, long-TUT RT (i.e., slow vs. fast repetition tempos) on metabolic stress, ischemia, and mitochondrial biogenesis.

Indeed, research is needed to establish the relationship between TUT, repetition tempo, and metabolic stress during RT, because metabolic stress may play a key role in stimulating mitochondrial biogenesis (46, 67-69). There is much debate about the effect of RT on mitochondrial biogenesis and oxidative capacity as some have demonstrated positive effects (46, 67) while others have reported negligible effects (68, 69). However, the current literature is limited because most research designs have only used hypertrophy style RT (e.g., 8-10 repetitions, 70-80% of 1-RM) and few have examined the effect of different repetition ranges (48, 68, 69). In fact, the current literature is bereft of research that has measured the effect of different low-intensity, high-volume RT programs on metabolic stress, ischemia, and mitochondrial biogenesis. We believe that research of this kind will improve the technical capability and clinical practice of several fields including physical therapy (e.g., patients using low-intensity RT while recovering from an injury), personal training (e.g., elderly clients who want to increase their strength and oxidative capacity concomitantly), and strength & conditioning (e.g., power athletes seeking an alternative form of conditioning). As previously mentioned, there are positive health ramifications from increasing lean mass (14), muscular strength (29), and oxidative capacity (28), and low-intensity RT with long TUT can potentially allow exercisers to train for all three in one session.
Problem Statement

When repetition tempo is considered without proximity to failure or TUT being matched between conditions, metabolic stress, as measured as blood lactate and/or local muscle hypoxia, is typically greater during slower repetition tempo RT (55, 56). However, when proximity to failure and time under tension are matched, metabolic stress, perception of effort, and muscle activation are greater during faster muscular contractions (54, 59). To date, researchers have not matched TUT and proximity to muscular failure during a ground-based, lower-body exercise (e.g., belt squat) and have not provided an in-depth discussion pertaining to the effect of repetition tempo on heart rate, local muscle hypoxia, or various training variables (e.g., external load and volume).

Purpose

The primary aim of the proposed study is to compare the effect of slow- (5 sets, 10 repetitions, 4:2 second repetitions) and traditional-tempo RT (5 sets, 20 repetitions, 2:1 second repetitions) on blood lactate concentration, perceived exertion, heart rate, and muscle oxygenation during a ground-based, lower-body exercise (e.g., belt squat). To allow for a direct comparison between the repetition tempos, external load (e.g., 50-60% of 1-RM), time under tension (e.g., 60 seconds), and proximity to failure (e.g., ratings of perceived exertion (RPE) of 8-9 out of 10) will be matched between conditions. The secondary aim of the proposed study is to compare the effect of slow-tempo RT and traditional tempo RT on total volume load (TVL; sets x reps x external load) and impulse (IMP; sets x reps x external load x repetition duration), which are both important quantifications of mechanical work performed during sessions of RT with different repetition tempos.
Hypotheses

Hypothesis 1: Total volume load, the product of sets x reps x external load, will be greater during the traditional-tempo condition compared to the slow-tempo condition.

*Rationale:* Previous research has demonstrated that TVL is higher when faster-repetition tempos are used and more repetitions are performed per set (59, 70, 71).

Hypothesis 2: Impulse, the product of sets x reps x external load x repetition duration, will be greater during the slower-tempo condition compared to the traditional-tempo condition.

*Rationale:* Previous research has demonstrated that TVL is greater during faster-tempo RT, but IMP is higher during slower-repetition tempo RT (70, 72).

Hypothesis 3: Traditional-tempo RT will increase blood lactate concentration significantly more than slow-tempo RT.

*Rationale:* Previous research has demonstrated that faster-repetition tempos result in greater blood lactate concentration, which implies that repetition volume and mechanical work are key drivers for metabolic stress (54, 59).

Hypothesis 4: Traditional-tempo RT will result in higher HR than slow-tempo RT.

*Rationale:* Previous research has shown that cardiorespiratory drive, measured as HR (73) and ventilation/oxygen uptake (74), is greater during faster-repetition tempo RT.

Hypothesis 5: Traditional-tempo RT will decrease oxygenation of the vastus lateralis muscle more than slow-tempo RT.
**Rationale:** Previous research has demonstrated that metabolic stress is greater (50, 51) and muscle oxygenation is lower (54, 59) during RT with faster-repetition tempos.

Hypothesis 6: There will be no difference between slow-tempo and traditional-tempo conditions for RPE, meaning that proximity to failure will be similar between them.

**Rationale:** We will use the RPE + repetitions in reserve (RIR) scale and teach our subjects to accurately approximate their proximity to failure (75). Therefore, effort measured by RPE should not differ between conditions.

**Scope of Study**

- **Subjects for research:** The proposed study was conducted on young (18-35) resistance-trained female and male subjects. More specifically, we recruited subjects who consistently performed lower-body RT (≥ 2-days/week for ≥ 12 months) which included a variation of leg press, squat, or belt squat in their lower-body RT routine. Furthermore, their sets of lower-body RT typically consisted of 3-10 repetitions per set with moderate-high intensities (75-90% of 1-RM), traditional tempos (e.g., 2-4 seconds per repetition), and some of their sets were performed close to momentary muscular failure. Importantly, they were not currently performing high-repetition sets (15-20 reps) with traditional tempos or any variation of slow-tempo RT (e.g., 7-14 seconds per repetition). In other words, although they were resistance trained, the subjects were naïve to the specific RT methods used in the current experiment.

- **Practical applications:** The results from the proposed study can be applied by physical therapists, personal trainers, and strength & conditioning specialists. For example, a physical therapist can apply low-intensity, high-volume RT with slow or traditional repetition tempos for a patient who is recovering muscle mass, local muscular endurance, and strength following an
injury and/or surgery. This is especially useful because high-intensity, low-volume RT might be contraindicated in this scenario. Moreover, low-intensity, high-volume RT is effective for stimulating positive neuromuscular adaptations for young (60) and elderly (7) lifters who want to increase/maintain their functional capacity and lean mass. Thus, personal trainers can apply the information from the proposed study to use two variations of low-intensity, high-volume RT to stimulate aerobic adaptations in addition to traditional RT adaptations (e.g., hypertrophy and strength) for a variety of exercise enthusiasts. Last, a strength and conditioning specialist may seek alternative metabolic conditioning strategies for their power athletes (e.g., baseball players, football players, Olympic lifters) in lieu of traditional styles such as long-distance running. The results obtained from the proposed research will provide insight for how a strength and conditioning specialist can manipulate repetition tempo and TUT to use RT as a tool to deliver oxidative adaptations for such athletes.

Assumptions

This study was conducted based on the following assumptions

1. Participants answered the health history and physical activity questionnaires honestly and followed pre-test guidelines before each of their visits.

2. Participants maintained the same lifestyle routine throughout the duration of their involvement in the study, especially as it pertained to their RT habits.

3. Participants executed their 1-RM, 10-RM, and 20-RM trials with maximal effort.

4. Participants performed all sets of RT close to concentric muscular failure and accurately reported their RPE after each set.
5. Each repetition was performed with perfect uniformity and the lifter maintained the desired tempo during each condition.

6. All equipment used in the study was in good working order, including the HR monitor, lactate analyzer, and muscle oxygenation device.

Limitations

1. **External validity**- Our data will be collected in young, resistance-trained females and males who are unfamiliar with low-intensity, high-volume, long-TUT sets of RT. The results should be applied to populations with different ages and training statuses with caution. Also, we operationalized slow and traditional repetition tempos as 6 and 3 seconds, respectively, meaning that the results should not be extrapolated to slower (> 6 seconds) or faster (< 3 seconds) repetition tempos or to any repetition tempo within that range (4-5 seconds).

2. **Internal validity**- It is important to acknowledge the limitations of the measurement tools that will be used to acquire data for the dependent variables in this study. First, blood lactate concentration provides a systemic measurement for this anaerobic metabolic byproduct and does not perfectly reflect the metabolic stress occurring at the skeletal muscle. Second, the near-infrared spectroscopy (NIRS) device provides information about oxygen concentration at one part (medial) of one muscle (vastus lateralis) and does not perfectly reflect deoxygenation of the entire lower body musculature. Third, although the RPE/RIR scale is a useful, practical tool for personal trainers (75), it is unlikely that lifters will approximate their fatigue and proximity to failure with 100% accuracy (78). However, the repeated measures design allows each lifter to serve as their own control,
meaning that if they do not use the RPE/RIR scale accurately, it will likely be inaccurate during both conditions.

3. **Ecological validity** - Although we will attempt to control effort and proximity to failure during both sessions of RT, we will need to cap the number of repetitions at 10 and 20 for slow and traditional repetition tempos, respectively, to keep the TUT similar between conditions (60 seconds). When applied to practice, it is possible that a lifter will complete more repetitions per set, train at a closer proximity to failure, or use different external loads for either RT condition. Also, it is likely that lifters in the real world will use a variety of exercises (e.g., belt squat, hip thrust, lunge) when performing a session of lower-body RT. We chose to use one exercise (e.g., belt squat) for the convenience of data collection and to minimize the number of required repetition-max testing and familiarization sessions.

**Significance of Study**

Adaptations to exercise are often perceived through a dichotomous lens where AT stimulates increased mitochondrial volume and oxidative capacity while RT stimulates increased hypertrophy and force production (38, 39, 40, 41). However, it is now known that AT can stimulate RT adaptations (72, 73), and vice versa (67, 68, 69), meaning that there is considerable overlap between these supposedly divergent stimuli. As it pertains to RT, it has been proposed that low-intensity, high-volume, high-TUT training can lead to “aerobic” peripheral adaptations via a similar mechanism as high-intensity interval training (32, 47, 48, 49). Specifically, this style of RT is associated with greater deoxygenation (55), metabolic stress (50), and phosphorylation of proteins involved in mitochondrial biogenesis (48) compared to high-
intensity, low-volume, low-TUT training. To date, studies have measured the effect of various styles (e.g., low vs. high volume) on each of these dependent variables separately, but the literature does not include a research design that has measured all three. Moreover, the current RT literature is bereft of studies that have measured the acute effect of different low-intensity RT protocols with TUT matched on metabolic stress, oxygenation, or heart rate (i.e., most studies compare low vs. high intensity and do not match TUT). Thus, the significance of the proposed research is that it will be the first to elucidate the effect of repetition tempo on blood lactate concentration, muscle deoxygenation, and heart rate, which may inspire future research that measures the effect of such training on aerobic fitness.

**Abbreviations**

AMP = adenosine monophosphate

ANOVA = analysis of variance

AT = aerobic training

ATP = adenosine triphosphate

BF% = body fat percentage

BFR = blood flow restriction

Ca\(^{2+}\) = calcium

CaMKII = calcium calmodulin kinase

cm = centimeter

COX = cytochrome c oxidase
DNA = deoxyribonucleic acid

GH = growth hormone

GRP81 = G-protein-coupled receptor 8

HHb = deoxyhemo(+myo)globin

HIIT = high-intensity interval training

ICC = intraclass correlation coefficient

IGF-1 = insulin growth factor 1

IMP = impulse

kg = kilogram

max = maximum

min = minimum

mTORC1 = mammalian target of rapamycin complex 1

mRNA = messenger ribonucleic acid

NAD+ = nicotinamide adenine dinucleotide

NIRS = near-infrared spectroscopy

NRF-1 = nuclear respiratory factor one

NRF-2 = nuclear respiratory factor two

NSCA = National Strength and Conditioning Association
O₂Hb = oxy(+myo)hemoglobin

P38 MAPK = protein 38 mitogen-activated protein kinase

P53 = tumor suppressor protein 53

PGC-1α = peroxisome proliferator-activated receptor gamma coactivator 1-alpha

Q = cardiac output

RIR = repetitions in reserve

RM = repetition maximum

RT = resistance training

ROS = reactive oxygen species

RPE = ratings of perceived exertion

SD = standard deviation

SIRT = NAD⁺-dependent deacetylase family of sirtuins

SV = stroke volume

SLOW = slow tempo

TFAM = mitochondrial transcription factor A

tHb = total hemo(+myo)hemoglobin

TRAD = traditional tempo

TSC-2 = tuberous sclerosis complex 2
TSI = tissue saturation index

TUT = time under tension

TVL = total volume load

VEGF = vascular endothelial growth factor

$\text{VO}_2\text{max} = \text{maximal oxygen uptake}$

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Chapter 2: Literature Review

This chapter presents a review manuscript entitled “Aerobic adaptations to resistance training: The role of time under tension” that has been submitted for publication in the International Journal of Sports Medicine. It is authored by Zachary Mang, Jeremy Ducharme, Flavio de Castro Magalhaes, Christine Mermier, Len Kravitz, and Fabiano Amorim. The manuscript follows the formatting and style guidelines of the journal and the references cited are provided at the end of the manuscript.

Aerobic Adaptations to Resistance Training: The Role of Time Under Tension

Running header: Adaptations to high time under tension resistance training

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**Abstract**

Generally, skeletal muscle adaptations to exercise are perceived through a dichotomous lens where the metabolic stress imposed by aerobic training leads to increased mitochondrial adaptations while the mechanical tension from resistance training leads to myofibrillar adaptations. However, there is emerging evidence for cross over between modalities where aerobic training stimulates traditional adaptations to resistance training (e.g., skeletal muscle hypertrophy) and resistance training stimulates traditional adaptations to aerobic training (e.g., mitochondrial biogenesis). The latter is the focus of the current review in which we propose high-volume resistance training (i.e., high time under tension) leads to aerobic adaptations such as angiogenesis, mitochondrial biogenesis, and increased oxidative capacity. As time under tension increases, skeletal muscle energy turnover, metabolic stress, and ischemia also increase, which act as signals to activate the peroxisome proliferator-activated receptor gamma coactivator 1-alpha, which is known as a master regulator of mitochondrial biogenesis. For practical application, the acute stress and chronic adaptations to three specific forms of high-time under tension are also discussed: Slow-tempo, low-intensity resistance training, and drop-set resistance training. These modalities of high-time under tension lead to hallmark adaptations to resistance training such as muscle endurance, skeletal muscle hypertrophy, and strength, but little is known about their effect on traditional aerobic training adaptations.
1. Introduction: Specific Adaptations to Divergent Stressors from Exercise

According to the principle of specificity, physiological adaptations reflect the specific stress imposed on the body during various bouts of exercise [1]. Resistance training (RT) is associated with several positive adaptations [2] such as increased muscular endurance [3], muscular strength [4], power [5], sprint speed [6], and agility [7]. These tangible measures of performance stem from adaptations that occur at the nervous system and skeletal muscle. For example, common neurological adaptations to RT include increased motor unit recruitment, faster transmission of action potentials, increased rate coding, motor unit synchronization, and increased surface area of the neural muscular junction [8, 9]. At the skeletal muscle, RT increases fascicle length, pennation angle, and hypertrophy (i.e., cross-sectional area of fibers and/or muscle thickness) [10, 11, 12], which potentially contribute to increased maximal force production [9, 13]. These adaptations are caused by the manipulation of several program variables including intensity, volume, the order and exercises selected, rest intervals between sets, velocity of contraction, and frequency [2]. Studies investigating the role of the intensity and volume of RT have indicated that low-intensity, high-volume RT and high-intensity, low-volume RT are effective to increase muscle size and strength [14, 15].

In contrast, aerobic training (AT) is associated with greater endurance capacity and improvements in maximal oxygen uptake (VO$_2$max), lactate threshold, ventilatory threshold, and improved exercise economy [16, 17, 18]. Improved cardiovascular performance, stimulated by AT, stems from central and peripheral adaptations. Central adaptations to AT generally include increased stroke volume, cardiac output, and myocardial efficiency, meaning that the cardiovascular system becomes more efficient at delivering oxygen to the exercising muscle [1, 19, 20]. Peripheral adaptations to AT include increased capillary density, slow-twitch muscle
fiber distribution, mitochondrial density, and mitochondrial enzyme activity, meaning that the skeletal muscle becomes more efficient at extracting oxygen from the blood stream and using it in the process to synthesize adenosine triphosphate (ATP) via oxidative phosphorylation [1, 19, 20]. Research has demonstrated that high-volume, low-intensity (i.e. long slow-distance) and low-volume, high-intensity AT (i.e. high-intensity interval training or sprint interval training) are both capable of stimulating central and peripheral aerobic adaptations [20, 21, 22].

As it pertains to skeletal muscle physiology at the molecular level, adaptations to AT and RT are often viewed through a dichotomous lens in which they are not compatible [23, 24, 25]. In particular, the mechanical tension imposed by RT activates an unidentified protein kinase that upregulates the mammalian target of rapamycin (mTOR) by inhibiting the inhibitor of mTOR, tuberous sclerosis complex 2 (TSC-2) [25, 26]. This process (i.e., mechanotransduction) initiates acute protein translation which eventually leads to long-term skeletal muscle hypertrophy [25, 26]. In contrast, the metabolic stress associated with AT upregulates various protein kinases that stimulate mitochondrial biogenesis through activation of the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) [27], that is recognized as the master regulator of mitochondrial biogenesis [28]. Although chronic adaptations depend on training status and the type of exercise performed, there is some evidence that AT can stimulate RT adaptations and vice versa [29, 30], which means there is cross-over between these signaling pathways. Specifically, some research has demonstrated that AT elicits significant skeletal muscle hypertrophy [31, 32], and others have determined that RT can stimulate increased skeletal muscle oxidative capacity [33] and markers of mitochondrial biogenesis [34]. The latter phenomenon is of particular interest in the current review because the potential RT variables (i.e., volume, intensity, and tempo) that lead to aerobic adaptations are not well understood.
Previously, Steele et al. [35] concluded that RT can stimulate several AT adaptations such as increased cardiac output and VO$_2$max when sets are performed to momentary muscular failure. As it pertains to skeletal muscle adaptations, the effects of RT on mitochondrial biogenesis [36] and mitochondrial volume [37] have also recently been reviewed and a similar conclusion was reached: Low-intensity, high-volume RT (e.g., high time under tension – TUT) is likely a stronger stimulus for traditionally aerobic adaptations compared to high-intensity, low-volume RT (e.g., low-TUT) [36, 37]. However, these review papers did not discuss the mechanisms by which high-TUT RT elicits such adaptations or provide a general overview of acute and chronic adaptations to high-TUT training modalities. Hence, the purpose of the current review is to detail the mechanisms of exercise-induced mitochondrial biogenesis, provide a case for why high-TUT can stimulate this pathway, and highlight what is known about three specific types of high-TUT RT: Slow repetition tempo RT, traditional low-intensity RT, and drop-set RT. Specifically, the acute physiological responses and long-term muscular adaptations will be reviewed for each style of training.

2. Mitochondrial Biogenesis: The Central Role of PGC-1α Activation

Mitochondrial biogenesis is the synthesis of new reticular components that increase mitochondrial volume (i.e., increased quantity) and the activity of enzymes within the mitochondria (i.e., increased quality). Although other signaling cascades contribute to mitochondrial biogenesis [38], PGC-1α is considered to be the master regulator and key influencer for aerobic adaptations and oxidative phenotypes [1, 19, 28]. In fact, PGC-1α has been implicated in the regulation of skeletal muscle mitochondrial biogenesis as muscle specific deletion of PGC-1α results in attenuated mitochondrial biogenesis in response to physical training[39]. During exercise, repeated muscular contractions lead to an increase in several
contractile-induced stressors such as AMP/ATP ratio, reactive oxygen species (ROS), intracellular Ca\(^{2+}\), lactate, ischemia, and decreased energy availability [1, 19, 22, 25, 27]. These signals activate several protein kinases such as calcium/calmodulin protein kinase II (CaMKII), p38 mitogen-activated protein kinase (p38MAPK), and AMP-activated protein kinase (AMPK), which activate downstream transcription factors and co-activators to increase the expression of mitochondrial proteins [1, 19, 22, 25, 27]. Specifically, CaMKII, p38MAPK, and AMPK directly stimulate mitochondrial biogenesis by phosphorylating PGC-1\(\alpha\), causing it to translocate to the nucleus [25, 27, 30]. Moreover, AMPK, lactate, and nicotinamide adenine dinucleotide (NAD\(^+\)) activate NAD\(^+\)-dependent deacetylase family of sirtuins (SIRT), which controls metabolic flux through the citric acid cycle and has been implicated in mitochondrial biogenesis by regulating PGC1-\(\alpha\) activity through its deacetylase activity [39]. Tumor suppressor protein 53 (p53) is also activated by AMPK and p38MAPK, and it exerts regulatory effects on transcription factors and mitochondrial content [1, 19, 27]. In short, exercise-induced metabolic stress and increased skeletal muscle energy turnover activate upstream regulators of PGC-1\(\alpha\), which converge on and phosphorylate PGC-1\(\alpha\), allowing for its translocation.

When PGC-1\(\alpha\) translocates to the nucleus, it activates several transcription factors such as nuclear respiratory factors one and two (NRF-1 and -2), which increase the transcription of PGC-1\(\alpha\), cytochrome c oxidase (COX) subunits, and mitochondrial transcription factor A (TFAM) [1, 19, 24, 27]. TFAM modulates mitochondrial biogenesis by affecting mitochondrial deoxyribonucleic acid (DNA) transcription and replication [41]. There is also evidence that PGC-1\(\alpha\) influences angiogenesis by upregulating the activity of vascular endothelial growth factor (VEGF) [18, 42, 43]. Thus, the repeated upregulation of PGC-1\(\alpha\) leads to post-exercise transcription of genes involved in mitochondrial biogenesis and angiogenesis, which eventually
leads to peripheral physiological adaptations. For example, data from acute studies suggest that high-intensity interval training (HIIT) elicits significant metabolic stress and the activation of PGC-1α, which leads to increased levels of gene transcripts regulated by PGC-1α [27, 44, 45]. When training bouts are repeated, HIIT leads to increased oxygen uptake, mitochondrial volume, mitochondrial enzyme activity, and capillary density [18, 21, 22].

Some have compared HIIT to RT because they are both characterized by brief periods of high-energy turnover interspersed by periods of rest [34, 46, 47]. Considering that energy depletion (e.g., reduced ATP and creatine phosphate) and metabolic stress increase with the number of repetitions completed per set [48, 49], we speculate that sets of RT with high-TUT may stimulate the activation of upstream modulators of PGC-1α similar to HIIT, leading to greater PGC-1α messenger ribonucleic acid (mRNA) response, and ultimately to enhanced mitochondrial biogenesis. For example, a set of RT performed for 5 repetitions with a 3-second tempo (e.g., 2:1 seconds) and high intensity (e.g., 90% of 1-RM) would have a TUT of 15 seconds while a set of RT performed for 20 repetitions with the same tempo but low intensity (e.g., 50% of 1-RM) would have a TUT of 60 seconds. Gronneback and Vissing [36] suggested in a recent review that the latter style of RT (i.e., high-TUT) would have a positive effect on mitochondrial biogenesis because it stimulates greater turnover rate of ATP, metabolic stress, and tissue deoxygenation compared to low-TUT RT. More recently, Parry et al. [37] stated that future research should be done to assess the effect of high-intensity (i.e., low-TUT) and low-intensity (i.e., high-TUT) RT on mitochondrial biogenesis, and hypothesized that the latter would have a greater effect due to greater metabolic perturbations (i.e., higher blood lactate). We submit that this hypothesis is interesting and the relationship between blood lactate and mitochondrial biogenesis is worth further discussion.
3. Upregulating PGC-1α: The Potential Role of Lactate

Mechanistic studies in cell cultures and rodents have provided strong evidence that lactate is involved in mitochondrial adaptations. Specifically, it has been demonstrated that incubation of L6 cells with lactate increased mRNA expression of PGC-1α [50], and similar results were achieved in vivo by lactate intraperitoneal administration in mice [51]. Interestingly, attenuation of the increase in lactate during exercise by administration of dichloroacetate, an activator of pyruvate dehydrogenase, reduced HIIT-induced increases in mitochondrial enzyme content in mouse skeletal muscles [52], implicating exercise-induced lactate production in mitochondrial adaptations. Moreover, Takahashi et al. [53] demonstrated that 3-week lactate intraperitoneal administration increased mitochondrial enzyme activity (e.g., citrate synthase, 3-hydroxyacyl CoA dehydrogenase, and cytochrome c oxidase), and showed that lactate administration prior to endurance exercise training enhanced training-induced mitochondrial enzyme activity in the skeletal muscle [53]. Later, the same group showed that four weeks of oral lactate administration + exercise increased cytochrome c oxidase activity in skeletal muscle more than exercise alone in mice [54]. Finally, it was reported that chronic intramuscular lactate treatment increased PGC-1α and citrate synthase protein content in the gastrocnemius of rats [55]. Altogether, these findings suggest that lactate increases mitochondrial enzymes through PGC-1α activation, and that exercise-induced mitochondrial adaptations are related to lactate production.

Although the precise pathways activated by lactate to induce PGC-1α-mediated mitochondrial adaptations are still under investigation, it has been reported that lactate injection can increase AMPK activity in the soleus muscle in mice [56]. Because AMPK is an upstream activator of PGC-1α [27], it could be involved in lactate-induced PGC-1α activation and
mitochondrial adaptations. Conversely, in vitro [57] and in vivo [58] evidence shows that when ROS production is blunted, contraction-induced PGC-1α response is impaired, suggesting that ROS is an important mediator of exercise-induced PGC-1α activation. Although it has been suggested that the lactate upregulation of PGC-1α is mediated by ROS [59], there is currently no direct evidence to confirm this hypothesis. However, it was recently reported that lactate increased ROS generation in a dose-dependent manner in skeletal muscle [60]. Therefore, we speculate that lactate accumulation during exercise increases ROS production, which would lead to a ROS-mediated PGC-1α activation culminating in mitochondrial biogenesis. Finally, lactate might also affect mitochondrial biogenesis in an autocrine and/or paracrine fashion. It has been reported that a selective receptor for lactate, called G-protein-coupled receptor 81 (GPR81) exists in various tissues, including skeletal muscle [61, 62]. Interestingly, silencing of GRP81 in lactate-treated cancer cells did not increase PGC-1α mRNA expression, in contrast to the increase observed in control cells [63], suggesting that lactate induces PGC-1α gene transcription by GRP81 activation. Whether the lactate-GRP81 mechanism plays a role in exercise-induced mitochondrial biogenesis requires further investigation.

The aforementioned mechanistic studies suggest that lactate may be implicated as a signaling molecule that mediates mitochondrial adaptations through PGC-1α activation, but research in human subjects is equivocal. For instance, greater lactate accumulation during cycle ergometry (i.e., repeated supramaximal sprints) has been associated with higher exercise-induced phosphorylation of CaMKII and p38 MAPK, along with higher PGC-1α mRNA response [64]. Although a direct cause-and-effect relationship between lactate accumulation and PGC-1α activation cannot be established with their study design, the authors speculated that greater metabolic stress (i.e., higher blood lactate) is related to greater activation of the PGC-1α mRNA
response [64]. In contrast, Moberg et al. [65] recently reported that higher levels of muscle lactate did not facilitate increased mRNA encoding of PGC-1α following RT with and without preceding lower-body cycle ergometry. However, these results should be interpreted with caution because both conditions elicited a robust muscle lactate response (10.8 vs. 13.5 mmol/L) which did not allow for a dose-response assessment between lactate and PGC-1α mRNA. In other words, 10.8 and 13.5 mmol/L elicited similar responses, but it is unknown if values of 4, 6, or 8 mmol/L would have led to an inferior mRNA response (i.e., there may exist a saturation point above which lactate does not affect PGC-1α). Ultimately, it is difficult to isolate the effect of lactate on mitochondrial biogenesis in human skeletal muscle during exercise because several stressors/signals (e.g., lactate, energy turnover, hypoxia) converge on PGC-1α where they elicit their effects concurrently.

Regardless of the exact mechanisms (Figure 1), there is evidence that lactate accumulation is associated with the activation of mitochondrial biogenesis [50-55; 61-63] and that blood lactate has a positive, linear relationship with TUT during sets of RT [66-71]. Moreover, Burd et al. [72] reported that higher-TUT RT (i.e., 30% 1-RM) resulted in greater sarcoplasmic protein synthesis (e.g., which includes mitochondrial proteins) compared to lower-TUT RT (i.e., 90% 1-RM). Later, the same researchers measured greater mitochondrial protein synthesis following a bout of RT with high-TUT [73]. Thus, it is clear that high-TUT RT leads to greater metabolic stress (i.e. greater lactate accumulation) than low-TUT RT, but whether these styles of RT lead to divergent peripheral aerobic adaptations deserves further discussion.

**Insert Figure 1 Here**
4. Low vs. High-intensity RT: Effect on Peripheral Aerobic Adaptations

Many studies that have compared low vs. high-intensity RT are comprised of blood flow restriction (BFR) interventions. The effect of such training on angiogenesis and mitochondrial biogenesis has recently been reviewed [18]. Because BFR training evokes high levels of ischemia, metabolic stress, and hypoxia, its effect on muscle capillary density and oxidative metabolism are particularly interesting. In fact, research on acute bouts of RT have demonstrated that the addition of BFR to low-intensity RT decreased muscle oxygenation [42], increased gene expression for proteins involved in angiogenesis [42], and increased markers of mitochondrial biogenesis [43]. Thus, it is logical that low-intensity BFR training has stimulated increased capillarization [74] and muscular endurance [75] when repeated for 3-8 weeks. As it pertains to mitochondrial adaptations, one study has compared the effects of high-intensity RT vs. low-intensity RT with BFR [76]. After six weeks of training, data revealed that both BFR (4 sets, 30% of 1-RM) and high-load RT (4 sets, 70% of 1-RM) had positive effects on mitochondrial protein fractional synthetic rate and mitochondrial respiration with no differences between groups. Citrate synthase increased only in the BFR group, but the difference did not achieve statistical significance [76]. As it pertains to aerobic adaptations, more research is needed to determine if low-intensity RT with BFR is superior to traditional forms of high-intensity RT.

Regarding traditional RT (i.e., no BFR), only two studies have assessed the effect of low vs. high-intensity RT (i.e., without BFR) on capillarization, cellular respiration, and markers of mitochondrial biogenesis and mitophagy. Holloway et al. [77] compared the effect of low-repetition (8-12 reps; 75-90% of 1-RM) vs. high-repetition (20-25 reps; 30-50% of 1-RM) RT in resistance-trained men. Data revealed that both programs had a positive effect on capillarization and protein markers of vasodilation, implying that positive adaptations to the microvasculature
occurred irrespective of intensity and TUT [77]. Other findings were reported by Lim et al. [34] who compared the effect of three RT programs in untrained males: 30% of 1-RM to failure, 80% of 1-RM to failure, or 30% of 1-RM with work matched to the 80% of 1-RM group. Results indicated that protein markers for mitochondrial biogenesis, mitochondrial capacity, and mitophagy increased only in the group that trained with 30% of 1-RM to failure [34]. In their discussion, the authors speculated that when sets of RT are performed with high-volume (i.e., high-TUT), the metabolic stress incurred during the session leads to aerobic/oxidative adaptations [34]. In short, the hypothesis that low-intensity, high-TUT training would have a positive effect on peripheral aerobic adaptations is logical, but the limited research done in this area remains inconclusive. Future research should be done to assess this hypothesis and determine if training status influences the effect of different intensities on such adaptations.

As displayed in Figure 2 it is now known that hypertrophy occurs along a wide spectrum of intensities (30-90% of 1-RM) and corresponding rep-ranges (3-35 reps per set) [3, 14, 15, 78, 79]. Assuming a traditional 2:1 second repetition tempo, this effective repetition range corresponds with 9-105 seconds of TUT per set. Because the effective range of TUT for hypertrophy is wide, it behooves us to explore unique adaptations that occur at extreme ends of the spectrum. For example, it is generally accepted that RT with low-TUT (i.e., 80-95% of 1-RM) is superior for increasing maximal strength [80, 81] while RT with high-TUT (i.e., 30-50% of 1-RM) is superior for muscular endurance [3, 78]. The latter is the focus of the current review, and the following section will summarize research on acute and chronic RT for three specific techniques that use high-TUT: Slow-tempo, high-volume low-intensity, and drop-set training.

**Insert Figure 2 Here**
5. Applications of RT with High-TUT

5.1 Slow Tempo Resistance Training

Repetition tempo, which is sometimes referred to as repetition duration, equals the length of time that comprises the eccentric, isometric, and concentric phases during one repetition of exercise [82]. For example, a repetition with a three-second concentric phase, one-second isometric pause, and three-second eccentric phase would be a seven-second tempo and would be denoted as 3:1:3 sec [66, 83]. As it pertains to muscular strength, in a recent meta-analysis of 15 studies, Davies et al. [84] concluded that fast (e.g., eccentric phase = 1-3 seconds; concentric phase = < 1 second) and moderate-slow (e.g., eccentric phase = 1.7-3 seconds; concentric phase = 1.7-3 seconds) repetition tempos significantly improve muscular strength. When considering skeletal muscle hypertrophy, in another recent meta-analysis of 8 studies, Schoenfeld et al. [85] concluded that similar muscle growth occurred along a wide repetition tempo spectrum (0.5-8 seconds) when sets were performed to momentary muscle failure. Clearly, there is a wide range of effective repetition tempos.

To the best of our knowledge, not much evidence is available regarding the effect of repetition duration on muscular endurance and aerobic fitness. However, the prospect of lengthening repetition duration to stimulate cardiovascular adaptations is a noteworthy topic, because this will have a direct effect on the TUT during sets of RT [86]. For example, a set of 12 repetitions with a 12-second duration (6:6 sec) would have a TUT of 144 seconds, while a set of 12 repetitions with a 2-second duration (1:1 sec) would have a TUT of 24 seconds [73]. Although speculative, it is possible that sets of RT with slower repetition tempos, and thereby longer TUT, have a positive effect on peripheral aerobic adaptations because some research suggests that metabolic stress (e.g., blood lactate) increases linearly with TUT [66-71]. Others
have shown that as TUT increases, muscle oxygenation decreases [66, 83] while mitochondrial protein synthesis increases [73]. Thus, the notion that slow-repetition, high-TUT RT can potentially stimulate aerobic peripheral adaptations is a logical speculation.

5.1.1 Acute effect of repetition tempo on metabolic stress

There are several variations of repetition tempos that may influence metabolic stress incurred during a bout of RT. Gentil et al. [89] compared the effect of four types of RT: 10-RM (2:2 second tempo), functional isometrics (2:5:2 second tempo), vascular occlusion (20-second isometric followed by repetitions with a 2:2 second tempo), and one super-slow repetition (30:30 second tempo). The greatest blood lactate response occurred in the functional isometric (4.5 mmol/L) and vascular occlusion (4.2 mmol/L) conditions, and the authors suggested that performing isometric pauses (5 or 20 seconds) had a more profound effect on metabolic stress than overall TUT [89]. If their assertion is true, a 2:5:2 second tempo (i.e., 5 second isometric phase) would increase blood lactate by more than a 6:3 second tempo (i.e., no isometric phase) even though the repetition duration is the same (e.g., 9 seconds). To date, this hypothesis has not been tested. In other research, Mazzetti et al. [90] had ten resistance-trained men perform lower-body RT under three conditions: Slow (2:2 sec, 4 x 8 reps, 60% 1-RM), fast (2:1 sec, 4 x 8 reps, 60% 1-RM), and heavy-fast (2:1 sec, 6 x 4 reps, 80% 1-RM). Data indicated that blood lactate increased linearly with TUT as slow (TUT = 32 sec) was greater than fast (TUT = 24 sec), which was greater than heavy-fast (TUT = 12 sec). However, it is difficult to provide definitive conclusions from this study because subjective effort and proximity to failure were not reported and the difference between tempos was narrow (3 vs. 4 sec).

With TUT matched at 36 seconds per set, Lacerda et al. [91] demonstrated that faster tempo repetitions (3 seconds) increased blood lactate more than slower tempo repetitions (6
seconds). Similar results were achieved by Vargas-Molina et al. [92] when TUT was matched at 60 seconds per set. This study improved upon the methods of Lacerda et al. [91] because effort was matched between conditions as every set was performed to momentary muscular failure. Thus, there is agreement in the current literature that metabolic stress increases with TUT [66-71]. Moreover, when TUT is matched, metabolic stress is greater under conditions where more repetitions are performed per set (e.g., 20 vs. 10 reps) and faster/traditional tempos (e.g., 3 vs. 6 sec) are used (91, 92). In the future, researchers should emulate the design of Vargas-Molina et al. [92] by matching TUT and assessing the effect of several tempo schemes on a variety of exercises (i.e., single vs. multiple joint, upper vs. lower body). Furthermore, it would be beneficial to measure muscle oxygenation during these exercises [66, 83], and to include advanced biochemical analysis (e.g., western blotting and immunohistochemistry) to measure markers of mitochondrial biogenesis and angiogenesis.

5.1.2 Effect of tempo and TUT on long-term adaptations.

Several recent systematic reviews and meta-analyses have conclusions positing that significant hypertrophy and strength occur along a spectrum of fast, traditional, slow, and super slow repetition tempos (e.g., 0.5-10 seconds) [82, 84, 85]. Moreover, Tanimoto et al. [66] reported that low-intensity RT with slow contractions (50% of 1-RM, 3:1:3 second tempo) and high-intensity RT with normal contractions (80% of 1-RM, 1:1:1 second tempo) similarly increased hypertrophy and muscular strength after training with the knee-extension exercise. Years later, the same researchers reached similar conclusions when applying these training styles to total body lifting with five exercises [83]. Similar results were found when these training styles were applied to elderly lifters [93], even when lower RT intensity was used (30% of 1-RM) [94]. Together, these studies demonstrate that the low-intensity, slow-tempo style of RT
(i.e., 7 seconds per repetition) can stimulate positive neuromuscular adaptations when used in concert with low external loads corresponding to 30-60% of 1-RM.

Unfortunately, the researchers did not measure or report longitudinal outcomes for muscular endurance or aerobic fitness in these studies [66, 83, 93, 94]. However, in their discussions, the authors made a case that the slow-tempo style of lifting causes strong metabolic perturbation because the muscles slowly/constantly occlude blood vessels, which causes deoxygenation in a manner similar to BFR. This speculation warrants further investigation, and the assessment of whether low-intensity slow-tempo training stimulates increases in muscular endurance and aerobic fitness should be done. Moreover, it will be important for future researchers to match the TUT between conditions as the majority of the papers summarized in this section compared very different TUT (i.e. 56 vs 24 seconds) conditions, making it difficult to determine the effect of repetition tempos.

5.2 Traditional high-volume, low-intensity RT

Resistance training adaptations (e.g., endurance, strength, and power) tend to be specific to the combination of training variables used during a program. The specificity of RT was best exemplified by Campos et al. [95] who reported that improvements in muscular endurance were greatest in the high-repetition group (2 sets; 20-28 reps), increases in muscular strength were greatest in the low-repetition group (4 sets; 3-5 reps), and hypertrophy only occurred in the low and intermediate-repetition groups (3 sets; 9-11 reps) [95]. Although their conclusions suggested that RT adaptations were largely specific to intensity, more recent evidence suggests that improvements for hypertrophy, strength, and power occur along a spectrum of 20-80% of 1-RM [78, 79]. Moreover, Schoenfeld (14), in a recent meta-analysis concluded that low (<60% 1-RM) and high (>65% 1-RM) intensity RT have similar and positive effects on muscular strength (9
studies, n = 251) and hypertrophy (8 studies, n = 191). Thus, because high-volume, low-intensity RT stimulates hypertrophy and strength, it is intriguing to see if this style elicits unique benefits such as increased muscular endurance and aerobic fitness.

5.2.1 Acute metabolic effects of high-volume, low-intensity RT

Lactate, an anaerobic by-product that is formed when pyruvate binds to two hydrogen ions after glycolysis [92, 96], is often used as a proxy measure of metabolic stress during various styles of RT [89, 90]. Rogatzki et al. [67] demonstrated that endurance-style RT (2 sets, 20 reps, 50% of 1-RM) elicited greater blood lactate response than hypertrophy (3 sets, 10 reps, 70% of 1-RM) and strength (5 sets, 5 reps, 85% of 1-RM) RT during back squat exercise. Similarly, da Silva et al. [68] showed a dose-response relationship between TUT and blood lactate concentration during 8, 10, and 12 RM training on the bench press. In addition to lactate, transient increases in the “anabolic hormones”, such as growth hormone (GH), insulin growth factor 1 (IGF-1), and testosterone [97], have been indicated as proxy markers of metabolic stress during RT [98]. Fink et al. [87] demonstrated that training with 40% of 1-RM significantly increased IGF-1 and GH after training with bench press and back squat. Compared to training with 8 RM, the same researchers reported that GH concentration was only elevated after training with 20 RM [88].

The preponderance of research summarized above suggests that metabolic stress increases as TUT and repetition number increase, especially when it is measured via blood lactate. However, there is a paucity of research that has compared the acute effect of different repetition ranges (e.g., 10-RM vs. 20-RM) and TUT (e.g., 30 vs. 60 seconds) on markers of metabolic stress, muscle oxygenation, and mitochondrial biogenesis during RT. Future researchers could design studies to match proximity to failure and repetition tempo (e.g., 2:1
sec), and have participants perform a lower-body exercise (e.g., belt squat) with external loads of 10-RM, 20-RM, and 30-RM with corresponding TUT of 30, 60, and 90 seconds. As suggested before, the researchers could measure muscle oxygenation, blood lactate, and markers of mitochondrial biogenesis for all conditions.

5.2.2 Chronic effects of high-volume, low-intensity RT

Several studies have compared the effect of low vs. high intensity RT to delineate if adaptations to RT are determined by the external load used. For instance, Leger et al. [99] recruited 25 healthy, untrained males and randomly assigned them to low (4 sets, 3-5 repetitions) or high (2 sets, 20-28 repetitions per set) volume RT. Their results showed that both training programs stimulated increased muscular hypertrophy, endurance, and strength with no differences between groups [85]. In a unilateral, within-subject research design, Mitchell et al. [78] recruited 18 healthy, untrained males, and randomly assigned their legs to one of three RT conditions: 3 sets with 30% 1-RM, 1 set with 80% 1-RM, and 3 sets with 80% 1-RM. Data indicated that all groups significantly increased hypertrophy and strength. Interestingly, for muscular endurance tasks, the 30% 1-RM condition, participants increased the number of repetitions that they could perform with 30% and 80% of their 1-RM. By contrast, neither 80% 1-RM condition increased participants’ repetition performance with 30% of 1-RM [78].

Extending these research designs to trained subjects, Schoenfeld et al. [3] reported that low-load (25-35 reps, 30-50% of 1-RM) and high-load (8-12 reps, 70-80% of 1-RM) significantly increased hypertrophy and strength. Of note, muscular endurance (i.e., repetitions to failure with 50% of 1-RM on bench press) only increased in the low-load group [3]. Moreover, when compared to a group of lifters who performed the same intensity for every training session (8-10 RM), those who performed a daily undulating periodization plan (2-4 RM, 8-10 RM, 25-35
RM) significantly increased repetition performance with 50% of 1-RM on bench press [100].

This means that one weekly session of low-intensity RT was enough to improve muscular endurance. Collectively, the literature demonstrates that low-intensity, high-volume RT delivers several adaptations to RT (e.g., endurance, hypertrophy, and strength), and future research should be done to determine if such RT leads to increased oxidative capacity (i.e., at the skeletal muscle) and improved aerobic performance. In particular, it would be interesting to determine if there are sex differences for such adaptations, as some research has demonstrated that females tolerate metabolic stress better [101] and can perform more repetitions at relative intensities compared to males [102].

5.3 Drop-set Resistance Training

A brief research review by Schoenfeld and Grgic [103] identified drop-set RT as an effective way to accrue high levels of training volume and to stimulate significant muscular adaptations in a short amount of time. To perform a drop-set, the initial set of RT with a fixed external load (e.g., 80% 1-RM) is performed to muscular failure. From there, the load is immediately reduced by 20-25% (i.e., no rest) and the lifter performs a subsequent set to muscular failure [103]. Although it is not strictly defined, the authors suggest that two to three drops are performed during one drop-set, and that the rest interval between drops should be kept to a minimum (i.e., just long enough to adjust the load and ensure that the lifter is in a proper starting position) [103]. When following these guidelines, it is likely that a lifter will perform 20-30 consecutive repetitions at intensities that correspond to 40-80% 1-RM in just one set of exercise. Assuming a traditional 2:1 second eccentric to concentric repetition tempo (i.e., three second contractions), this translates to an approximate TUT of 60-90 seconds, which leads to significant metabolic stress, ischemia, and hypoxia [103]. Although the authors presented drop-
set training as a means to evoke skeletal muscle hypertrophy [103], we submit that this style of RT could be used to stimulate peripheral adaptations that are typically associated with AT.

5.3.1 Acute metabolic effects of drop-set RT

Few studies have quantified the metabolic stress incurred during sessions of drop-set RT. For example, Goto et al. [104] demonstrated that the addition of one drop with 20, 30, or 50% of 1-RM after finishing a standard session of RT (5 sets, 90% of 1-RM) significantly increased GH and blood lactate. Years later, the same research team concluded that drop-set training stimulated significant decreases in muscle oxygenation, especially in trained lifters who have greater muscle thickness than their untrained counterparts [105]. Compared to straight-set training (i.e., no drop sets), Fink et al. [106] reported that drop-set RT elicited greater muscular swelling while increases in blood lactate were similar. Considering that volume (reps x % of 1-RM) was similar between groups (38.3 vs. 38.9 arbitrary units) the results from this study suggest that both training styles elicited significant metabolic stress but drop-set training did so in a more time-efficient manner (145 vs. 315 sec).

By examining the acute RT data summarized above, it is clear that drop-set training delivers a strong metabolic load to the skeletal muscle as indicated by increased blood lactate and decreased oxygenation during exercise. As previously theorized, metabolic stress and ischemia may be key factors that lead to peripheral adaptations that are intrinsic in AT such as increased vascularization, blood flow, and mitochondrial biogenesis. Future research should be done to evaluate the effect of drop-set RT on protein markers of these adaptations while measuring lactate and muscle oxygenation to help determine a cause-effect relationship between such training and peripheral aerobic adaptations.
5.3.2 *Chronic effects of drop-set RT*

In a longitudinal design, Goto et al. [104] concluded that strength training (5 sets, 90% of 1-RM) and strength training with the addition of one drop set (25-35 repetitions with 40-50% of 1-RM) both led to significant increases in endurance, strength, and rate of force development. However, the drop-set group had significantly greater increases in 1-RM for leg press, maximal isokinetic strength at a fast velocity (e.g., 300 degrees/second), and muscular endurance, which was quantified as total work performed (load x repetitions) during one set of knee-extension to failure with 30% of maximal voluntary contraction [104]. Because total training volume was not matched, it is difficult to conclude if the differences between groups occurred strictly because of the metabolic stress imposed by the drop-set condition. Others reported that drop-set and traditional RT had similar effects on neuromuscular performance, especially muscular endurance [108]. Ozaki et al. [109] revealed that high-intensity RT (80% of 1-RM) and drop-set RT (1 set with 80% of 1-RM, 4 drop sets at 65, 50, 40, and 30% of 1-RM) elicited similar increases in hypertrophy and strength while the drop-set condition led to better endurance. It is important to note that the drop-set training delivered significant adaptations despite the performance of ~1/3 of the training volume (5,308 vs. 15,365 kg) with sessions that required ~1/5 of the training time (2.1 vs. 11.6 minutes) compared to the low-load group [109].

Taken together, these studies support that drop-set RT is a time-efficient strategy to promote meaningful neuromuscular adaptations, especially muscular endurance. Indeed, when training volume is similar, it seems that drop-sets do not confer additional adaptations when compared to traditional forms of RT, but the concept of delivering such adaptations with shorter gym sessions is important considering that time is reported to be a barrier to exercise [103, 110].
Future research should be done to determine if drop-set RT leads to AT-like peripheral adaptations and if these adaptations lead to improved aerobic exercise performance.

6. Conclusions and Directions for Future Research

Traditionally, the physiological adaptations to AT and RT have been viewed through a dichotomous lens where AT stimulates the synthesis of mitochondrial proteins and RT stimulates the synthesis of myofibrillar proteins. Recent research suggests cross-over between these seemingly divergent training modalities as AT can cause RT adaptations and vice versa. As it pertains to RT, we submit that low-intensity, high-volume RT with high-TUT is an effective stimulus for peripheral aerobic adaptations such as increased capillary density, mitochondrial volume, and oxidative metabolism. This logical conjecture stems from the fact that RT with high-TUT leads to significant metabolic perturbation, ischemia, and skeletal muscle hypoxia, which upregulate signaling cascades for angiogenesis and mitochondrial biogenesis. More research is needed to identify the exact mechanism, but the results from several cell and rodent studies suggest that lactate may facilitate mitochondrial adaptations through the PGC-1α signaling cascade. In other words, the stress imposed by high-TUT RT reflects traditional forms of AT (i.e., HIIT), and the specific adaptations to this stress may be similar between modalities. Research shows that slow-tempo, traditional, and drop-set training are all effective variations of high-TUT RT that increase skeletal muscle endurance, hypertrophy, and strength. Based on acute data, these training modalities also evoke significant metabolic stress and skeletal muscle hypoxia during exercise, and future research can determine if this stress leads to aerobic adaptations.

Thus, there are several opportunities for future studies. Specifically, researchers should better quantify the acute metabolic stress of high-TUT RT by measuring muscle oxygenation,
blood lactate, and upregulation of protein markers involved in angiogenesis and mitochondrial biogenesis. Moreover, it would be interesting to measure the chronic effect of high-TUT RT on aerobic capacity (e.g., VO2max) and aerobic performance (e.g., 5-km time trial). The influence of training status is another possible area for research [30]. For example, it is likely that compared to trained lifters, untrained counterparts would incur more metabolic stress during high-TUT RT, which could potentially lead to superior long-term aerobic adaptations. It would be interesting to apply this logic to resistance trained participants who typically perform high-intensity, low-TUT RT. In other words, researchers can determine if performing sets of RT with 60-90 seconds of TUT provides a novel, aerobic stimulus for well-trained lifters who typically perform their RT sets with 10-30 seconds of TUT, and are, therefore, relatively untrained in high-TUT RT [111]. Finally, in a recent review by Schoenfeld et al. [112] it was concluded that the repetition range for hypertrophy and strength is very wide and that unique adaptations occur at either end of this spectrum (Figure 2). At the low intensity end of the spectrum, it would be interesting to follow the design of Lacerda et al. [91] and Vargas-Molina et al. [92] by matching TUT (e.g., 60 seconds) and proximity to failure (e.g., RPE of 8-9 out of 10) while varying repetition tempo within the matched TUT (e.g., 20 reps at 2:1 vs. 10 reps at 4:2 vs. 6 reps at 6:4) to evaluate the true effect of repetition tempo on aerobic (e.g., mitochondrial biogenesis) and resistance (e.g., strength) adaptations. Similar study designs can be applied to higher-intensity RT with shorter TUT (e.g., 30 seconds).
Figure 1: An overview of the proposed mechanism for how resistance training (RT) with high time under tension (TUT) stimulates peripheral aerobic adaptations by upregulating the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) signaling cascade. Slow-tempo, traditional, and drop-set are three applications of RT with high-TUT that lead to high muscle and blood lactate concentrations. Mechanistic studies in cells and rodents have demonstrated that lactate increases activation of adenosine monophosphate activated protein kinase (AMPK) and concentration of reactive oxygen species (ROS) which directly upregulate the PGC-1α signaling cascade. Additionally, lactate may stimulate PGC-1α by directly binding to its G-protein-coupled receptor 81 (GPR81). Because high-TUT leads to greater lactate concentration than low-TUT, and lactate has been implicated as a potential signaling molecule in the PGC-1α signaling cascade, it is logical to suggest that RT with high-TUT may facilitate aerobic adaptations through PGC-1α.
**Figure 2:** A summary of the effective repetition range for hypertrophy (3-35 reps) that emphasizes potential unique adaptations to resistance training (RT) with low and high time under tension (TUT). Assuming that a traditional repetition tempo is used (e.g., 2:1 seconds), this repetition range also corresponds with a TUT of 9-105 seconds per set. Here, we submit that high-intensity RT is associated with greater mechanical tension and increased strength while low-intensity RT is associated with greater metabolic stress and aerobic adaptations such as increased capillary density, mitochondrial volume, and skeletal muscle oxidative capacity.
References


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Chapter 3: Experimental Study

This chapter presents a complete manuscript that describes the study in traditional journal article form including an abstract, introduction, methods, results, discussion, and references. The manuscript, entitled “The effect of repetition tempo on cardiovascular and metabolic stress when time under tension is matched during lower-body exercise” will be submitted to the Journal of Sports Science. It is authored by Zachary Mang, Rogelio Realzola, Jeremy Ducharme, Gabriella Bellissimo, Jason Beam, Christine Mermier, Flavio de Castro Magalhaes, Len Kravitz, and Fabiano Amorim. The manuscript follows the formatting and style guidelines of the journal and the references cited are provided at the end of the manuscript.

The effect of repetition tempo on cardiovascular and metabolic stress when time under tension is matched during lower-body exercise

Running header: The effect of repetition tempo on metabolic stress

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Abstract

It is commonly reported that resistance training (RT) with slower-repetition tempos lead to greater metabolic stress because they increase the time under tension (TUT) during sets of exercise. However, little information is available on the effect of different repetition tempos on blood lactate concentration, muscle oxygenation, and heart rate (HR) when TUT and proximity to concentric muscular failure are matched during lower-body RT. In a repeated-measures, crossover design, 11 recreationally-trained females (n = 5) and males (n = 6) performed five sets of belt squat under the following conditions: Slow-repetition tempo (SLOW; 10 reps with 4:2 second tempo) and traditional-repetition tempo (TRAD; 20 reps with 2:1 second tempo). Time under tension (60 seconds) was matched between conditions and external load was adjusted so that lifters were close to concentric muscular failure at the end of each set. External load, total volume load (TVL), impulse (IMP), blood lactate, ratings of perceived exertion (RPE), HR, and muscle oxygenation were measured during both RT protocols. Data indicated that total volume load (p < .001), blood lactate (p = 0.017), RPE (p = 0.015), and HR (p < .001) were significantly greater during TRAD while external load (p = 0.030) and IMP (p = 0.002) were significantly greater during SLOW. Whether it was expressed as minimal values or change scores, muscle oxygenation was not different between protocols. When TUT is matched, cardiovascular stress, metabolic stress, and perceived exertion are greater during TRAD. These differences may be explained by higher TVL as TRAD required 2X greater repetition volume and mechanical work. Future research should be done to determine if these styles of RT lead to divergent physiological adaptations and performance outcomes.
Introduction

Resistance training (RT) is a commonly used form of exercise that leads to several positive neuromuscular adaptations such as increased local muscular endurance, skeletal muscle hypertrophy, maximal strength, and power (1). From a skeletal muscle perspective, these adaptations are generally stimulated by a blend of mechanical tension (i.e., force applied to the sarcolemma) and metabolic stress (i.e., increased energy turnover and glycolytic metabolism) (2, 3). The latter is particularly interesting because metabolic stress has been shown to stimulate skeletal muscle hypertrophy (4), mitochondrial biogenesis (5), and angiogenesis (6), meaning that it can lead to a variety of adaptations. Lactate, a metabolic byproduct of glycolysis that forms when pyruvate is bound to two hydrogen ions (7), is commonly used as a proxy measure for metabolic stress during various styles of RT (8-10). Generally, blood lactate concentration increases with the duration of a set (i.e., time under tension; TUT) (11-14), which means that RT with high-repetition volume is associated with substantial metabolic stress (15-17).

In addition to the number of repetitions completed per set, repetition tempo (i.e., the duration of each individual repetition) has a direct effect on the TUT during sets of RT (18). Repetition tempo can be divided into eccentric, isometric, and concentric phases for each repetition (19), but researchers tend to focus on the eccentric and concentric phases of a lift. For example, if a lifter lowers a weight for two seconds and raises the weight for one second, this would be considered a 3-second repetition with a 2:1 second tempo (19). In general, researchers have demonstrated that slower tempos are associated with greater hormonal response (20, 21), higher blood lactate concentration (22, 23), and lower levels of muscle oxygenation (11). The latter is an important factor to consider because local tissue hypoxia has been implicated in skeletal muscle hypertrophy (24), angiogenesis (25), and improved oxidative capacity (26).
Regardless, a common confounding variable of the available research on repetition tempo is that TUT (20-23) and/or proximity to concentric muscular failure (i.e., effort) were not matched between protocols with different tempos (11) making it difficult to isolate the effect of tempo on metabolic stress.

Interestingly, when sets are performed close to concentric muscular failure (27) (i.e., the inability to complete the concentric phase of a repetition due to fatigue), and TUT is matched, two studies have demonstrated that performing faster tempos (i.e., 3 seconds) leads to greater blood lactate concentration than slower tempos (i.e., 6 seconds) (28, 29). This difference may be caused by different patterns of motor unit recruitment (28). It is also plausible that faster tempos resulted in greater total volume load (TVL; sets x reps x external load), which generally leads to higher levels of blood lactate. However, because slower tempos result in fewer repetitions per set (30), TVL may not be the best method to quantify training volume when comparing different repetition tempos (23). In addition to TUT (31), it may be beneficial to calculate impulse (IMP; sets x reps x external load x tempo) to quantify the mechanical work performed during sessions of RT with slower tempos (32). Research comparing TVL and IMP during different RT protocols is scarce, and these data are important for characterizing training volume with different tempos.

A recent study concluded that RT with faster tempos resulted in greater blood lactate and higher ratings of perceived exertion (RPE) than RT with slower-repetition tempos (29). However, the authors used a single-joint, upper-body exercise (e.g., biceps curl) and did not report training variables (e.g., TVL) or other physiological measurements of central (e.g., heart rate) or local (e.g., muscle oxygenation) stress. Hence, the purpose of the current study was to measure the effect of slow-repetition tempo (SLOW; 4:2 sec) and traditional-repetition tempo
(TRAD; 2:1 sec) on various training variables (external load, TVL, and IMP), blood lactate, muscle oxygenation, and heart rate (HR) during sets of a multiple-joint, lower-body exercise with TUT matched at 60 seconds. We hypothesized that external load would not differ between conditions, TVL would be greater during TRAD, and IMP would be greater during SLOW. Moreover, we hypothesized that blood lactate and HR would be greater during TRAD, and that muscle oxygenation would be lower during TRAD.

**Methods**

**Study Design**

This study was a randomized, repeated-measures, cross-over design that compared the effect of SLOW and TRAD on external load, TVL, IMP, blood lactate, muscle oxygenation, and HR during belt squat exercise with TUT (60 seconds) and RPE (8-10) matched. During their first visit, subjects had their 1-RM, 10-RM (4:2 sec), and 20-RM (2:1 sec) measured for the belt squat exercise, and these measurements were replicated during their second visit. For visits three and four, the subjects performed five sets of belt squat with SLOW and TRAD protocols in a randomized and counterbalanced order. To allow for adequate recovery from exercise, visits one and two were separated by three days, visits two and three were separated by seven days, and visits three and four were separated by fourteen days.

**Subjects**

Eleven healthy, resistance-trained females (n = 5) and males (n = 6) volunteered for this study. The number of subjects was based on a power of 0.95, an alpha level of 0.05, and an a priori analysis which included the effect size (partial $\eta^2 = 0.59$) for a group x time interaction from a similar study that used a cross-over design and repeated measures ANOVA to determine
the effect of repetition tempo on blood lactate accumulation during RT (28). In order to qualify, the subjects reported that they had consistently performed lower-body RT (≥2-days/week for ≥12 months) and were currently using a variation of leg press, squat, or belt squat in their lower-body RT routine. This information was obtained by a physical activity questionnaire that each participant completed during their first visit. By completing a health history questionnaire, all subjects reported that they were free of orthopedic injuries that may prevent them from exercise as well as cardiovascular, metabolic, viral, kidney, and liver diseases. During the first visit, height (cm) and body weight (kg) were measured using a stadiometer and floor scale, respectively, and sex specific three-site skinfolds were measured to estimate body density and body fat percentage (BF%) (33, 34). Previous research reported test-retest and inter-rater reliability were very high for this technique with ICCs of 0.98 and 0.99, respectively (35). The study was approved by the University Institutional Review Board and each participant signed an informed consent document before beginning the study.

Procedures

Repetition Maximum Testing: 1-RM, 10-RM, and 20-RM

Before the one-repetition maximum (1-RM) test began, subjects performed the following standardized warm-up: Five minutes of pedaling on a cycle ergometer, ten bodyweight squats, and ten kettlebell goblet squats. From there, they were given 2-3 minutes to complete any specific warm-up exercise that they would typically perform before a session of lower-body RT. Of note, they repeated this warm-up during visits two, three, and four. After the warm-up, proper lifting technique for the belt squat was demonstrated by the same researcher, who is certified by the National Strength and Conditioning Association (NSCA) (e.g., certified strength and
conditioning specialist). Next, subjects performed a warm-up set of 5-6 repetitions with ~50% of their estimated 1-RM, followed by two warm-up sets of 2-3 repetitions with 60-80% of their estimated 1-RM. Subjects then performed successive sets of one repetition with increasing load until a successful 1-RM was determined. Rest intervals were 3-5 minutes between every set and the 1-RM was determined within five attempts. This procedure was previously described by Schoenfeld et al. (36), which was adapted from the NSCA guidelines and recommendations (37).

After the 1-RM was determined, subjects rested for 5-10 minutes before beginning their 10-RM testing with the 4:2 second tempo. The first set was performed with 40% of their 1-RM because previous research reported that the 10-RM with a similar tempo occurred between 50-60% of 1-RM (11, 38). Similar to the 1-RM test, load was increased until a successful 10-RM was determined, and subjects rested for 5-10 minutes before beginning their 20-RM with the 2:1 second tempo. As before, the first set was performed with 40% of their 1-RM as previous research reported that the 20-RM with this tempo occurred at ~50% of 1-RM (39). Subjects rested for 3-5 minutes between each attempt, and a successful 10-RM (4:2 sec) and 20-RM (2:1 sec) were determined within three attempts each. Of note, we considered a successful 10-RM and 20-RM to correspond with an RPE of 8 (40) because our pilot data revealed that subjects could successfully complete five consecutive sets with an external load that corresponded with this RPE after set #1. For all sets, subjects were instructed to perform the movement from standing to ~100 degrees of knee flexion (i.e., hips slightly below knees), which was controlled by a member of the research team. These procedures were conducted during the first and second lab visits and the ICC’s for the 1-RM, 10-RM, and 20-RM were 0.99, 0.97, and 0.98, respectively. To minimize the influence of fatigue on repetition performance, the 10-RM and 20-RM were performed in a randomized and counterbalanced order between subjects and visits.
**Resistance Training Sessions**

On the SLOW day, each set consisted of 10 repetitions with a four-second eccentric phase and two-second concentric phase (4:2 sec), which has been used in previous research (28, 29). In contrast, TRAD consisted of 20 repetitions with a two-second eccentric phase and one-second concentric phase (2:1 sec), which is commonly used for hypertrophy training (36, 39). For both protocols, five sets of belt squat were completed, three-minute rest intervals were provided between each set (41), and each set was completed close to concentric muscular failure (27). To match TUT at 60 seconds, it was important that SLOW and TRAD sets were terminated after 10 and 20 repetitions, respectively. However, to match effort between conditions, we adjusted the external load to maintain an RPE of 8-10 for each of the sets. This means if the subjects were unable to complete all 10 or 20 repetitions because they experienced concentric muscular failure, or if they were unable to maintain the desired tempo, the load was reduced by 5-10% on the subsequent set. By contrast, if the subject reported an RPE of lower than 8, or reported an RPE of 8 on consecutive sets, the load was increased by 5-10%.

**Resistance Training Variables**

Total volume load was calculated as the product of sets, repetitions, and external load, which has previously been described by Hernandez et al. (42). To allow for a more direct comparison between the protocols, IMP was also calculated as the product of sets, repetitions, external load, and repetition tempo (32). Although a metronome was used to control the tempo of each repetition, and the number of repetitions per set were fixed, it was unlikely that subjects would perform each repetition with perfect uniformity. To circumvent this issue, a stopwatch was used to measure the duration of each set, which was denoted as the length of time between
the initiation of the first repetition to the completion of the final repetition. This value was recorded as the TUT for that set. External load (i.e., the amount of weight lifted during each set) was also recorded for each set because this value sometimes differed from the 10-RM and 20-RM if the load was adjusted during the session.

**Ratings of Perceived Exertion**

To verify that subjects were performing their sets close to concentric muscular failure, they were asked to rank their RPE using the 1-10 OMNI-RPE scale (43) immediately after every set of exercise. Values of 1-2 corresponded with easy, 3-4 corresponded with somewhat easy, 5-6 was somewhat hard, 7-8 was hard, and 9-10 was extremely hard (29). Moreover, we used visits one and two to teach the subjects to relate the RPE chart with how many repetitions in reserve (RIR) they had. For example, an RPE of 8-9 corresponded with 1-2 repetitions remaining before failure, while an RPE of 10 would indicate that they could not perform another repetition (40). It has been previously determined that the 1-10 OMNI-RPE scale has strong concurrent validity, as the correlations between RPE scores and increases in external load were strong and positive (r = 0.8-0.9) (45).

**Lactate Measurement**

Lactate was measured using a handheld lactate meter (Lactate Plus, NOVA Biomedical, MA) and lactate strips. Researchers sterilized the earlobe with alcohol wipes before puncturing the earlobe to draw blood. Gauze was used to wipe the initial drop of blood away, the ear was gently squeezed, and the second drop of blood was sampled. Measurements were taken in duplicate before exercise, immediately post exercise, and 10-minutes-post exercise, and the average of the duplicate readings was recorded. It was previously reported that the Lactate Plus
device had a strong, positive correlation ($r = 0.91$) with a reference device, and the ICC for duplicate measurements was very strong ($r = 0.99$) (46).

**Heart Rate**

After completing the warm-up during visits three and four, subjects donned a HR monitor which was worn around their chest during exercise (Polar H10, Polar Electro Inc., Lake Success, NY, USA). Heart rate was monitored continuously during the entire session and the monitor was integrated with a corresponding watch (Polar M600, Polar Electro Inc., Lake Success, NY, USA). Beat-by-beat data was extracted after the session and analyzed on Microsoft Excel (Microsoft Office, 365, Microsoft, Washington, USA). Minimum (min) HR (i.e., lowest recorded HR immediately before the set began) and maximal (max) HR (i.e., highest recorded HR during the set of exercise) were recorded for each set of exercise. The average of all recorded heart rates for the entire session (i.e., first repetition of set #1 through the final repetition of set #5) was also recorded.

**Muscle Oxygenation**

Muscle oxygen saturation was measured using a portable near-infrared spectroscopy device (MOXY, Hutchinson, MN, USA) secured to the vastus lateralis of their dominant leg. The NIRS device measures oxy(+myo)hemoglobin, ($O_2$Hb), deoxyhemo(+myo)globin (HHb), and total hemo(+myo)globin (tHb) and records second-by-second % tissue saturation index (TSI; calculated by $[O_2$Hb/tHb x 100]) using the modified Beer-Lambert law (46). Tissue saturation index was measured for 120 seconds at rest prior to exercise and the average of these values was recorded as resting TSI. For each set of exercise, the lowest TSI value was expressed relative to resting TSI and recorded as minimum TSI. In addition, the highest TSI value was identified
during each rest interval and subtracted by the lowest TSI value identified during the subsequent set of exercise. This value was recorded as deltaTSI.

Statistical Analyses

Independent samples t-tests were used to detect differences between sexes for the following demographic, descriptive, and performance dependent variables: Height, weight, BF%, age, training experience, 1-RM, 10-RM, and 20-RM. A paired samples t-test was used to detect differences between SLOW and TRAD for average HR for the entire session of lifting (e.g., first repetition to final repetition). Several 2 (protocol) x 5 (time) repeated measures ANOVAs were used to compare external load, TVL, IMP, TUT, RPE, minimum TSI, delta TSI, min HR, and max HR between SLOW and TRAD across sets 1-5. Moreover, a 2 (protocol) x 3 (time) mixed repeated measures ANOVAs was used to compare blood lactate responses between SLOW and TRAD. Pairwise comparisons for statistically significant interactions were analyzed using Tukey’s HSD procedure and reported as means ± standard deviation (SD). Statistically significant main effects for protocol and time were analyzed using post hoc tests with Bonferonni correction for multiple comparisons and reported as means ± SDs. An alpha level of .05 was used to determine statistical significance for all analyses. The assumption of sphericity was checked using the Mauchly's test of sphericity during the repeated measures ANOVA analyses. If this assumption was violated (p ≤ .05), the Greenhouse-Geisser correction was applied. The assumption of normality was checked using the Shapiro-Wilk test for all t-tests. If this assumption was violated (p ≤ .05), the Mann-Whitney U test or Wilcoxon Sign test were used for independent and paired samples t-tests, respectively. Data were analyzed using the statistical package JASP (Version 0.12, Amsterdam, The Netherlands).
Results

Anthropometric and Descriptive Data

All anthropometric and descriptive data are displayed in Table 1. There were no significant differences detected between sexes for age and RT experience. In contrast, males were significantly taller (p = .004), heavier (p = .002), and had lower BF% (p = .003) compared to females.

Maximal Strength: 1-RM, 10-RM, and 20-RM

All data for 1-RM, 10-RM, and 20-RM are displayed in Table 1. With sexes combined, there were significant differences between 10-RM and 20-RM when expressed as absolute values (p = .049) but not when expressed relative to 1-RM. Males had higher 1-RM (p < .0001) and higher absolute values for 10-RM (p = .004), and 20-RM (p = .005). In contrast, when expressed relative to 1-RM, no differences were detected between sexes for 10-RM or 20-RM.

Resistance training variables: External Load, Volume, Impulse, and Time-under-tension

For external load, the 2 x 5 repeated measures ANOVA revealed a significant main effect for protocol (Table 2), F (1, 10) = 15.7, p = .003, $\omega^2 = .017$, a significant main effect for time, $F(1.19, 17.9) = 7.38$, p = .006, $\omega^2 = .003$, and a protocol x time interaction, $F(1.76, 17.6) = 9.28$, p = .002, $\omega^2 = .003$. Pairwise comparisons for the protocol x time interaction are displayed in Figure 1. For TVL, the 2 x 5 repeated measures ANOVA revealed a statistically significant main effect for protocol (Table 2), F (1, 10) = 90.9, p < .001, $\omega^2 = .450$, but a main effect for time or protocol x time interaction were not observed. For IMP, the 2 x 5 repeated measures ANOVA revealed a significant main effect for protocol (Table 2), F (1, 10) = 16.8, p = .002, $\omega^2 = .020$, a
significant main effect for time, F (1.74, 17.4) = 4.06, p = .040, $\omega^2 = .003$, and a protocol x time interaction, F (2.34, 23.4) = 5.73, p = .007, $\omega^2 = .003$. Pairwise comparisons for the protocol x time interaction are displayed in Figure 2. A paired samples t-test revealed that mean IMP was significantly higher during SLOW training (Table 2). For TUT, the 2 x 5 repeated measures ANOVA revealed no significant effects for protocol, time, or protocol x time interaction.

**Lactate and Ratings of Perceived Exertion**

For lactate, the 2 x 3 repeated measures ANOVA revealed a significant main effect for protocol (Table 2), F (1, 10) = 8.16, p = .017, $\omega^2 = .062$, a significant main effect for time, F (1.13, 12.7) = 68.4, p < .001, $\omega^2 = .678$, and a significant protocol x time interaction, F (2, 20) = 5.79, p = .010, $\omega^2 = .043$. Pairwise comparisons for the interaction are displayed in Figure 3. For RPE, the 2 x 5 repeated measures ANOVA revealed a significant main effect for protocol (Table 2), F (1, 10) = 8.48, p = .015, $\omega^2 = .0212$, and a main effect for time, F (4, 40) = 66.9, p < .001, $\omega^2 = .788$. Pairwise comparisons for the main effect for time are displayed in Table 3. A protocol x time interaction was not observed.

**Heart Rate**

For minimum HR, the 2 x 5 repeated measures ANOVA revealed a significant main effect for protocol (Table 2), F (1, 10) = 16.1, p = .002, $\omega^2 = .059$, a significant main effect for time, F (4, 40) = 37.6, p < .001, $\omega^2 = .179$, and a protocol x time interaction, F (4, 40) = 6.39, p < .001, $\omega^2 = .016$. Pairwise comparisons for the interaction are displayed in Figure 4. For maximal HR, the 2 x 5 repeated measures ANOVA revealed a significant main effect for protocol (Table 2), F (1, 10) = 78.4, p < .001, $\omega^2 = .303$, and a main effect for time, F (4, 40) = 80.6, p < .001, $\omega^2 = .260$. Pairwise comparisons for the main effect for time are displayed in Table 3. A protocol x
time interaction was not observed. Moreover, a paired samples t-tests revealed that average HR was higher during TRAD (Table 2).

**Muscle Oxygenation**

For minimum TSI, the 2 x 5 repeated measures ANOVA revealed no significant main effects for protocol, time, or group x time interaction. For delta TSI, the 2 x 5 repeated measures ANOVA revealed no significant main effect for protocol or group x time interaction. However, a main effect for time was observed, F (2.10, 21.0) = 4.65, p = .020, \( \eta^2 = .014 \), and significant pairwise comparisons are displayed in Table 3.

**Discussion**

The major finding in this study is that when TUT (60 seconds) is matched, blood lactate, HR and RPE were all significantly higher during RT with TRAD tempo. In addition, the present study demonstrated that TVL was higher during TRAD, but external load and IMP were higher during SLOW. Muscle oxygenation, measured as minimum TSI and delta TSI, were not different between TRAD and SLOW.

**External Load**

In the present study, data revealed that the average external load was 8% higher during SLOW, meaning our hypothesis that external load would not be different between conditions was not supported. Based on post-hoc testing (Figure 1), it is evident that the external load during SLOW was greater than TRAD during sets 3, 4, and 5. This reflects the stated purpose of the research as we attempted to keep TUT and proximity to concentric muscular failure similar between conditions. If we decided to match external load, proximity to concentric muscular
failure would have been greater for TRAD, which may have confounded our data. It is tempting to conclude that external load was greater during SLOW because there is general agreement that lifters can exert more force, and are therefore stronger, during eccentric muscular contractions (47, 48). Although the eccentric duration was two times greater per repetition during SLOW (4 vs. 2 sec), the matched-TUT design resulted in a total of 40 seconds of eccentric contractions for both protocols. This suggests that the physiological differences between contraction types does not explain the disparate outcomes. Above all, practical significance should be considered, because when expressed relative to 1-RM, the average external load was 53 and 49% for SLOW and TRAD, respectively. In other words, both protocols would be considered low-intensity, high-volume training that generally leads to increased local muscular endurance and hypertrophy (17, 19), although some have reported such intensities stimulate increased maximal strength (39, 49). Therefore, while the difference in average external load was statistically significant, it may not be of practical importance.

**Total Volume Load and Impulse**

Total volume load is commonly used to quantify the work performed during sessions of RT (42). The present results indicate that TVL was 45% higher during TRAD, which supported our hypothesis that TVL would be lower during SLOW. Although lower external loads were used, it is logical that TVL was greater during TRAD because the repetition volume was 50% higher during these training sessions (100 vs. 50 total repetitions). These data generally agree with previous research that slower tempos result in fewer repetitions per set and lower TVL (23, 30, 50). In turn, previous authors have suggested that because slower tempo training results in fewer repetitions (e.g., external load is matched), scientists should use TUT as a metric for volume when comparing RT with different tempos (18, 50). The current results corroborate this
logical suggestion. In addition to TUT, IMP has also been used as a training volume metric to quantify the total work performed during sessions of RT with various intensities and tempos (32, 50). The current study demonstrates that IMP was 8.6% higher during SLOW, which implies that overall work may have been higher during these sessions. Similarly, with intensity matched at 80% 1-RM, Arazi et al. (50) reported that faster tempos (1:1 sec) led to higher TVL, but lower IMP, when compared to slower tempos (4:2 sec). Indeed, longitudinal studies are necessary to confirm if the difference in IMP leads to divergent adaptations between SLOW and TRAD, but the present data suggest that it may be a more accurate quantification of training volume when comparing RT sessions with different tempos.

**Blood Lactate**

Data from the majority of research studies that have compared different tempos and TUT suggest that blood lactate, a proxy measure for metabolic stress, typically increases with set duration (i.e., TUT) (11-14, 22, 23). More specifically, researchers have consistently shown that when relative intensity is matched, slower tempos result in greater blood lactate, which is likely caused by longer TUT per set (20, 22, 23). However, as pointed out by Lacerda et al. (28), it is difficult to attribute greater metabolic stress to longer eccentric contractions (i.e., slower repetition tempos) if TUT is not matched. Accordingly, the current study demonstrates that blood lactate was significantly higher during TRAD, which confirms our hypothesis that metabolic stress would be significantly greater with faster tempos. This result supports previous research where faster tempos led to greater blood lactate concentration than slower tempos when TUT was matched at 36 seconds (28) and 60 seconds (29). Although speculative, it is possible that RT with more repetitions (20 vs. 10) with shorter concentric phases (1 vs. 2 seconds) involves more frequent and forceful contractions that recruit higher-threshold motor units with more glycolytic
fibers (i.e., more anaerobic byproducts) (20, 28, 51, 52). This speculation is further supported by evidence that RT with faster tempos resulted in greater motor unit recruitment, as indicated by higher electromyographic responses (28) and higher energy expenditure (52). Alternatively, because TRAD involved twice the number of repetitions, this means that twice the mechanical work (Force x Distance) was performed during these sessions because the distance traveled (i.e., the full range of motion for the squat) was two times greater. This is important, because previous studies have concluded that RT protocols with higher mechanical work result in a more robust metabolic (i.e., blood lactate) response (28, 53).

*Ratings of Perceived Exertion*

Proximity to concentric muscular failure (27) is an important component of RT to measure because it allows researchers to compare the effect of different volumes, intensities, and tempos when effort is matched. In lieu of quantitative measurements of concentric muscular failure, such as velocity-loss during sets of RT (14), researchers and practitioners can use RPE and repetitions-in-reserve (RIR) scales to monitor fatigue (54). As previously described by Grieg et al. (40), we taught the lifters to relate their RPE response to the RIR scale so that RPEs of 8, 9, and 10 would correspond with RIRs of 2, 1, and 0. Indeed, researchers have concluded that lifters are typically incapable of using the RIR scale with 100% accuracy (54, 55), but the current repeated-measures design compensates for this limitation because each subject served as their own control. Although we attempted to match RPE between conditions, data revealed a significant difference between TRAD (RPE = 9.2) and SLOW (RPE = 8.8). If we applied these results to the RIR scale, lifters felt as if they were 0.8 and 1.2 repetitions shy of concentric muscular failure for TRAD and SLOW, respectively. In our opinion, these values represent a rounding error because it is unlikely that lifters can estimate their RIR to a decimal point.
Instead, we submit that both protocols resulted in RPEs of ~9. Regardless, the fact that TRAD led to slightly higher RPE than SLOW is intriguing because similar results were reported by Vargas-Molina et al. (29) even though they reported that their lifters performed sets to concentric muscular failure during both conditions. Taken together, our study and Vargas-Molina et al. (29) suggest that when intensity is low (~50% 1-RM), RPE is lower when performing slower-repetition tempos. Because lifters report higher discomfort during low-intensity (i.e., high-repetition) RT (56), performing low-intensity RT with fewer, slower repetitions could be a strategy to circumvent this issue.

**Heart Rate**

Heart rate increases during sessions of RT (8), which may stimulate cardiovascular adaptations by applying stress to the myocardium via greater venous return and cardiac output (57). In the present study, HR was significantly greater during TRAD, which confirmed our hypothesis that TRAD would elicit greater cardiovascular stress than SLOW. Similar results were reported by Hunter et al. (53) who reported that traditional training (~1:1 sec) led to significantly greater HR, oxygen consumption, and energy expenditure compared to super-slow training (10:5 sec). In contrast, Barreto et al. (58) reported no differences in ventilation, energy expenditure, or oxygen consumption between slow (2:2 sec) and fast (1:1 sec) tempos. However, these results should be interpreted with caution because repetition number (10 reps) and relative intensity (70% 1-RM) were matched between conditions, meaning that TUT, effort, and proximity to failure were likely greater during the slow tempo condition. More research is needed, but the current data suggest that when TUT is matched, cardiovascular stress (i.e., HR) is greater during TRAD when more repetitions are performed per set. Although speculative, the higher cardiovascular drive during TRAD may be related to the greater blood lactate response.
during TRAD, as the accumulation of metabolites during exercise increases HR through the stimulation of Group III/IV afferents (59).

**Muscle Oxygenation**

Some have postulated that SLOW is a natural form of blood-flow restriction training (25, 26) because the constant muscular tension leads to sustained restriction of blood flow (i.e., restricted oxygen delivery) during exercise (11, 20, 38, 50). Whether it was expressed as minimal or delta values, the current data reveal that muscle oxygenation was not significantly different between conditions, which was contrary to our hypothesis that TRAD would result in lower muscle oxygenation. With external loads matched (55-60%), previous researchers reported that slower tempo (7 sec) led to greater decreases in muscle oxygenation than a faster tempo (3 sec) (11). However, because repetition volume was matched (8 reps), and TUT was not (24 vs. 56 seconds), effort and proximity to failure were significantly higher during the slower tempo sessions. In a follow-up study, the same group of researchers again concluded that the slower tempo (7 sec) led to greater decreases in muscle oxygenation than the faster tempo (3 sec) (38). Because intensity (55-60 vs. 80% 1-RM) and TUT (24 vs. 56 seconds) were not matched between conditions, it is difficult to isolate the effect of tempo on muscle oxygenation with their design (38). More research is needed in this area, but the current study suggests that when TUT (~60 sec), relative intensity (~50% 1-RM), and effort (~9 RPE) are matched, muscle oxygenation is similar between SLOW and TRAD. For practical application, there is evidence that local hypoxia is greater during sets of RT with higher TUT (60), which could potentially lead to traditionally aerobic adaptations such as increased capillary and mitochondrial density (25, 26).
**Limitations**

Several limitations should be considered when interpreting the current results. For example, the data were collected on young, resistance-trained females and males who were unfamiliar with low-intensity, high-volume RT. The results should be applied to populations with different ages and training statuses with caution. Also, we operationalized SLOW and TRAD tempos as 6 and 3 seconds, respectively, meaning that the results should not be extrapolated to slower (> 6 seconds) or faster (< 3 seconds) repetition tempos or to any repetition tempo within that range (4-5 seconds). It is also important to acknowledge the limitations of the measurement tools that were used to acquire data for the dependent variables in this study. First, blood lactate concentration provides a systemic measurement for this anaerobic metabolic byproduct and does not perfectly reflect the metabolic stress occurring at the skeletal muscle. Second, the near-infrared spectroscopy (NIRS) device provides information about oxygen concentration at one part (medial) of one muscle (vastus lateralis) and does not perfectly reflect deoxygenation of the entire lower body musculature.

**Conclusion**

The present study suggests that when TUT is matched, TRAD leads to significantly greater TVL, blood lactate, and RPE compared to SLOW. In contrast, SLOW leads to significantly greater external load and IMP. Surprisingly, muscle oxygenation was not different between conditions, which implies that when relative intensity is low, local hypoxia is similar between tempos when TUT is matched. In the future, studies should be designed to continue to isolate the true effect of repetition tempo on acute physiological variables by matching various TUT (e.g., 30, 60, or 90 sec) and using a variety of tempos (e.g., 2:1, 4:2, 6:4 sec). Longitudinal
studies are needed to see if the current protocols would lead to disparate neuromuscular (e.g., hypertrophy) or cardiovascular (e.g., cardiac output) outcomes.
Tables and Figures

Table 1. Demographic, descriptive, and strength data with sexes combined and with between-sex comparison. Data are displayed as mean ± standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>Combined (n = 11)</th>
<th>Male (n = 6)</th>
<th>Female (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.5 ± 4.4</td>
<td>25.0 ± 3.7</td>
<td>26.0 ± 5.5</td>
</tr>
<tr>
<td>RT Experience (years)</td>
<td>6.5 ± 2.1</td>
<td>7.5 ± 2.3</td>
<td>5.4 ± 1.1</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.3 ± 9.6</td>
<td>175.9 ± 4.3*</td>
<td>161.4 ± 8.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.6 ± 16.7</td>
<td>87.4 ± 11.5*</td>
<td>61.4 ± 8.6</td>
</tr>
<tr>
<td>BF%</td>
<td>15.2 ± 6.0</td>
<td>11.0 ± 4.1</td>
<td>20.3 ± 3.4</td>
</tr>
<tr>
<td>1-RM (kg)</td>
<td>129.3 ± 41.6</td>
<td>162.9 ± 16.9*</td>
<td>89.1 ± 16.0</td>
</tr>
<tr>
<td>10-RM (kg)</td>
<td>62.4 ± 19.0#</td>
<td>75.4 ± 15.1*</td>
<td>46.8 ± 8.1</td>
</tr>
<tr>
<td>% of 1-RM</td>
<td>48.3 ± 6.8</td>
<td>46.2 ± 5.1</td>
<td>52.5 ± 4.0</td>
</tr>
<tr>
<td>20-RM (kg)</td>
<td>60.1 ± 20.9</td>
<td>74.6 ± 14.1*</td>
<td>43.2 ± 7.9</td>
</tr>
<tr>
<td>% of 1-RM</td>
<td>46.4 ± 6.7</td>
<td>45.8 ± 5.8</td>
<td>48.5 ± 4.8</td>
</tr>
</tbody>
</table>

N = 11 *Significant difference between male and female subjects, p ≤ .05. #Significantly higher than 20-RM, p ≤ .05. cm = centimeters; kg = kilograms; RM = repetition maximum; BF% = body fat percentage.
Table 2. Mean values for all dependent variables measured during RT sessions.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Slow Tempo</th>
<th>Traditional Tempo</th>
<th>p-value</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>External load (kg)</td>
<td>68.7 ± 20.5*</td>
<td>63.2 ± 20.4</td>
<td>0.030</td>
<td>1.196</td>
</tr>
<tr>
<td>TVL (kg)</td>
<td>687.2 ± 205.6</td>
<td>1256.1 ± 391.9*</td>
<td>&lt; .001</td>
<td>-2.876</td>
</tr>
<tr>
<td>IMP (kg x sec)</td>
<td>4123.1 ± 1233.1*</td>
<td>3768.1 ± 1175.6</td>
<td>0.002</td>
<td>1.235</td>
</tr>
<tr>
<td>TUT (sec)</td>
<td>59.3 ± 1.0</td>
<td>59.6 ± 0.9</td>
<td>0.166</td>
<td>-0.451</td>
</tr>
<tr>
<td>Lactate (mmol/l)</td>
<td>4.7 ± 1.7</td>
<td>5.7 ± 1.9*</td>
<td>0.017</td>
<td>-0.862</td>
</tr>
<tr>
<td>RPE</td>
<td>8.8 ± 0.3</td>
<td>9.2 ± 0.3*</td>
<td>0.015</td>
<td>-0.878</td>
</tr>
<tr>
<td>Average HR (bpm)</td>
<td>122.4 ± 18.1</td>
<td>136.9 ± 15.0*</td>
<td>&lt; .001</td>
<td>-2.446</td>
</tr>
<tr>
<td>Max HR (bpm)</td>
<td>140.8 ± 16.6</td>
<td>160.2 ± 12.4*</td>
<td>&lt; .001</td>
<td>-2.670</td>
</tr>
<tr>
<td>Min HR (bpm)</td>
<td>107.5 ± 17.2</td>
<td>116.1 ± 15.8*</td>
<td>0.002</td>
<td>-1.211</td>
</tr>
<tr>
<td>Minimum TSI</td>
<td>32.0 ± 28.3</td>
<td>36.8 ± 29.2</td>
<td>0.140</td>
<td>0.416</td>
</tr>
<tr>
<td>Delta TSI</td>
<td>52.6 ± 23.2</td>
<td>51.2 ± 21.1</td>
<td>0.460</td>
<td>0.231</td>
</tr>
</tbody>
</table>

Values for external load, TVL, IMP, TUT, and RPE were averaged across sets 1-5, while the values for lactate were averaged across three time points: baseline, post, and 10 minutes post-exercise. Average HR is the mean of all recorded heart rates during the entire lifting session, which includes the rest intervals. Max HR is the average of the highest HR recorded during sets 1-5 while Min HR is the average of the lowest HR recorded during sets 1-5 (i.e., immediately before the first repetition was performed). Data are displayed as mean ± standard deviation. N = 11; *Significant difference between slow and traditional tempo, p ≤.05. kg = kilograms; TVL = total volume load; IMP = impulse, sec = second; TUT = time under tension; mmol = millimoles; l = liter; RPE = ratings of perceived exertion; HR = heart rate; bpm = beats per minute.
Table 3. Display of set-by-set data for main effect on time for ratings of perceived exertion (RPE), maximum heart rate (Max HR), and delta tissue saturation index (TSI). Values for slow-(4:2 seconds) and traditional- (2:1 seconds) repetition tempo protocols have been combined for each set. Data are displayed as mean ± standard error.

<table>
<thead>
<tr>
<th></th>
<th>Set 1</th>
<th>Set 2</th>
<th>Set 3</th>
<th>Set 4</th>
<th>Set 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPE</td>
<td>7.8 ± 0.12</td>
<td>8.6 ± 0.12*</td>
<td>9.3 ± 0.12#</td>
<td>9.5 ± 0.12#</td>
<td>9.9 ± 0.12‡</td>
</tr>
<tr>
<td>Max HR (bpm)</td>
<td>136.8 ± 4.4</td>
<td>144.9 ± 4.4*</td>
<td>153.0 ± 4.4#</td>
<td>157.1 ± 4.4#</td>
<td>160.8 ± 4.4‡</td>
</tr>
<tr>
<td>Delta TSI (%)</td>
<td>46.0 ± 6.8</td>
<td>52.1 ± 6.8</td>
<td>53.6 ± 6.8*</td>
<td>54.4 ± 6.8*</td>
<td>53.6 ± 6.8*</td>
</tr>
</tbody>
</table>

N = 11; *Significantly greater than Set 1, p ≤ .05; #Significantly greater than Sets 1 and 2, p ≤ .05; significantly greater than Sets 1, 2, and 3, p ≤ .05; bpm = beats per minute.
Figure 1: Set by set comparison of the external load used during five sets of SLOW (4:2 sec) and TRAD (2:1 sec) training. *Significantly greater than Set 1 for SLOW training, p ≤ .05. #Significantly greater than TRAD training during that specific set of exercise, p ≤ .05. N = 11.
Figure 2: Set-by-set comparison of the impulse (IMP, repetitions x external load x repetition tempo) performed during five sets of SLOW (4:2 sec) and TRAD (2:1 sec) training.

*Significantly greater than Set 1 for SLOW training, $p \leq .05$. #Significantly greater than TRAD training for that specific set, $p \leq .05$. N = 11.
Figure 3: Blood lactate, quantified as millimoles per liter (mmol/L), was measured at baseline, immediately after exercise (post), and 10 minutes after exercise (10-min post) for SLOW (4:2 sec) and TRAD (2:1 sec) training. *Significantly greater than baseline during SLOW training, p ≤ .05. **Significantly greater than baseline during TRAD training, p ≤ .05. #Significantly greater than SLOW training at the 10-min post time point, p ≤ .05. N = 11.
**Figure 4:** Minimum heart rate (HR) was recorded as the first measured HR at the beginning of each set of exercise during SLOW (4:2 sec) and TRAD (2:1 sec) training. *Significantly greater than Set 1 for that specific protocol, p ≤ .05. **Significantly greater than Sets 1 and 2 for that specific protocol, p ≤ .05. ***Significantly greater than Sets 1, 2, and 3 for that specific protocol, p ≤ .05. #Significantly greater than SLOW training for that specific set of exercise, p ≤ .05. N = 11.
References


CHAPTER IV: Summary, Conclusion and Recommendations

Summary

As analyzed in Chapter 1, skeletal muscle adaptations to exercise are often viewed through a dichotomous lens where RT leads to increases in hypertrophy and strength while AT leads to increases in capillary and mitochondrial density. Recently, there has been evidence that RT leads to traditional adaptations to AT (e.g., increased mitochondrial quantity and quality), especially when TUT is higher during sets of RT. The concept of using RT with high-TUT is intriguing because it may lead to increased hypertrophy, strength, and oxidative capacity, all of which are independent predictors for cardiometabolic health and longevity. Time under tension is determined by the number of repetitions per set and the tempo of each repetition within each set of exercise, and little is known about the effect of repetition tempo when TUT is matched. It was speculated that metabolic stress (e.g., higher lactate and lower oxygenation) would be greater when faster repetitions are performed at a greater frequency (e.g., 20 reps with 2:1 sec tempo vs. 10 reps with 4:2 sec tempo), which would ultimately result in greater upregulation and gene expression for proteins involved the mitochondrial biogenesis signaling cascade.

In Chapter 2, the literature review outlined the PGC-1α signaling cascade, which stimulates several peripheral aerobic adaptations to exercise such as angiogenesis and mitochondrial biogenesis and is generally upregulated by metabolic perturbations (e.g., local energy turnover, blood lactate, and hypoxia). Although the preponderance of available data have come from cell and rodent studies, there is evidence that lactate upregulates the PGC-1α signaling cascade via increased activation of AMPK, ROS, and GRP-81. Because there is a
direct relationship between TUT and blood/muscle lactate concentration, it is logical to speculate that RT with high-TUT may lead to peripheral aerobic adaptations via PGC-1α. More research is necessary, but it is possible that slow-repetition tempo, traditional high-volume, and drop-set RT are all beneficial applications of RT with high-TUT that may lead to aerobic adaptations.

As portrayed in Chapter 3, the experimental portion of the current manuscript involved a repeated-measures design in which 11 recreationally-trained lifters performed two sessions of low-intensity RT with TUT matched at 60 seconds: SLOW (10 reps; 4:2 sec) and TRAD (20 reps; 2:1 sec). A commercially available belt squat apparatus was the exercise used for the experiment, and subjects performed five sets close to concentric muscular failure with three minutes of rest between each set. Data revealed that TVL, HR, lactate, and RPE were significantly greater during TRAD while external load and IMP were significantly greater during SLOW. No differences were detected between protocols for muscle oxygenation. These results suggest that metabolic stress, cardiovascular stress, and perception of effort are higher during faster-repetition tempos when TUT is matched at 60 seconds.

Conclusion

When TUT is matched, TRAD leads to significantly greater TVL, blood lactate, and RPE compared to SLOW. In contrast, SLOW leads to significantly greater external load and IMP. Although speculative, it is possible that cardiorespiratory drive and local metabolic stress were greater during TRAD because this session involved twice the number of repetitions and therefore required twice the mechanical work. More research is needed to corroborate these findings, but it seems that central and local stress are greater when more frequent, forceful repetitions are performed during low-intensity, high-TUT RT.
Recommendations

Future researchers should replicate our design and provide data for acute molecular signaling within skeletal muscle samples to determine if SLOW and TRAD lead to different upregulation of PGC-1α and mTORC1. From there, training studies are necessary to see if repeated bouts of SLOW and TRAD lead to divergent outcomes for muscular endurance, hypertrophy, strength, and measures of aerobic fitness (e.g., VO₂max test or time trial). To isolate the true effect of repetition tempo on skeletal muscle adaptations, it would be beneficial to match TUT with higher relative intensities (e.g., 30 seconds) and perform different combinations of repetition number and tempo (e.g., 10 reps, 2:1 sec vs. 5 reps, 4:2 sec vs. 3 reps, 6:4 sec). The fact that RPE was lower during SLOW bears practical significance because higher perceptions of pain and effort may deter lifters from performing low-intensity, high-TUT RT. In turn, a simple follow-up study would be to match TUT (60 seconds) and external load (~50% 1-RM) and assess the effect of 2:1, 4:2, and 6:4 sec tempos on perceived motivation, demotivation, and enjoyment.
APPENDICES

Appendix A

Informed Consent

The effect of repetition duration on lactate metabolism and markers of mitochondrial biogenesis during resistance exercise.

Consent to Participate in Research

3/25/2021

Purpose of the research: You are being asked to participate in a research project that is being done by

Key information for you to consider:

- General description: the research study is investigating the effect of slow tempo resistance training (5 sets, 10 repetitions, 6 second contractions) vs. traditional tempo resistance training (5 sets, 20 repetitions, 3 second contractions) on lactate (i.e., a molecule muscles make when they work hard), oxygen in the muscles, and mitochondria (i.e., where your cells make energy) while using a belt squat machine.
- Major requirements of the research: you are being asked to come to the exercise physiology lab 4 times. First, we will determine how much weight you can lift 1 time, 10 times, and 20 times (i.e. 1-RM, 10-RM, and 20-RM) for the belt squat exercise. Second, you will repeat the 1-RM, 10-RM, and 20-RM to confirm your maximal strength, and you will be familiarized with the two exercise tempos (e.g., 3 and 6 second repetitions). For your third and fourth visits, you will perform 5 sets of belt squat with the previously mentioned repetition tempos.
- The most important risks include dizziness, nausea or lightheadedness with the exercise tests, discomfort with the pinprick for blood lactate, discomfort/soreness from the muscle biopsies, or possible loss of privacy and confidentiality associated with participating in this study. Also, you have increased risk of exposure to COVID-19 because of your participation in this study.
- The most important benefits include gaining information specific to your fitness: 1-RM result, percent body fat results, and lower body muscular performance. These data can help with exercise programming.
- Time commitment: taking part in this project will take a total of 10-12.5 hours (4 visits to the exercise physiology lab) over a period of 4 weeks.

Dr. Fabiano Amorim, the Principal Investigator and his associates from the Department of Health, Exercise and Sports Sciences at the University of New Mexico. The purpose of the research study is to investigate the effect of slow tempo resistance training (5 sets, 10 repetitions, 6 seconds per repetition) vs. traditional tempo resistance training (5 sets, 20 repetitions, 3 seconds per repetition) on lactate production (i.e., a molecule muscles make when they work hard), the amount of oxygen in your muscles, and proteins that help make energy in muscle cells (i.e., mitochondria). You are being asked to join because
you are between 18 and 35 years old, are a healthy individual who has engaged in lower body weight lifting 2 or more days per week for the past 12 months, and are familiar with moderate-heavy lifting during the squat, belt squat, or leg press exercise. Twelve people will take part in this study at the University of New Mexico. All study visits will take place in the exercise physiology lab at the University of New Mexico, as well as the weight room immediately next door to the exercise physiology lab. This form will explain what to expect when joining the research, as well as the possible risks and benefits of participation. If you have any questions, please ask one of the project researchers.

What you will do in the project:

After reading the consent form and discussing the details with the research team (on Zoom or via e-mail), if you decide to participate, you will be asked to fill out a health history/physical activity questionnaire and COVID-19 Symptoms Screening Checklist that will be sent to you via email. You will complete these questionnaires and send it back to the research team via email the day before your first visit. If you decide not to come to your first scheduled visit or do not sign the informed consent, your health history/physical activity questionnaire and COVID-19 symptoms Screening Checklist will be permanently destroyed (e.g., paper shredder) within 4 weeks of receipt.

If you agree to participate, you will be asked to sign this consent form during your first visit, and the following things will happen:

- You will be asked to visit the exercise physiology lab in Johnson Center at the University of New Mexico, Albuquerque, NM on four separate occasions.
- You will be asked to wear gym clothes and athletic shoes for each visit.
- All visits will be separated by a minimum of 2-days and a maximum of 14-days. You will complete all trials within a 4-week time frame.
- Prior to each visit, you will be asked not to perform any exercise 24 hours before the session, not ingest alcohol 24 hours prior to the session, and to consume at least a pint of water as well as a small meal 2-3 hours before the session.
- Visits will take between 1 to 5 hrs.

Before every visit, a research team member will contact you and inquire whether you have any COVID symptoms using the COVID-19 symptoms checklist. You will also be asked if you have been exposed to anyone with suspected or known COVID-19. You will be approved to come to the laboratory if you have no signs and symptoms of COVID-19 and if you have not been exposed to anyone who has COVID-19 symptoms or has tested positive for the virus. Prior to entering the lab, your body temperature will be measured by a no-touch forehead thermometer. If your temperature is over 37.5 °C (99.5 °F) you will not be allowed into the lab and the visit will be rescheduled unless you test positive for the coronavirus, in which case you will not be able to participate.

Visit 1: Paperwork, body composition, and strength testing

- Before your first visit, you will be asked to complete a health history/physical activity questionnaire and a COVID-19 Symptoms Screen via e-mail, which you will fill out and send back to the research team. You will only complete the health history/physical activity
questionnaire once, but as mentioned above, you will complete the COVID-19 Symptoms Screen via e-mail before every visit and research member will reach out to you via Zoom or telephone to inquire about COVID-19 related symptoms and/or exposure.

- When you arrive to the lab for your first visit, you will sit in a private room with only a research team member present where you can read the informed consent form and ask as many questions as you would like in order to understand the research protocols. If you agree to be a participant, you will sign the consent form, and become enrolled in the study.

- If you are a female, you will be required to perform a urine pregnancy test to ensure you are not pregnant. This test will be provided at no cost to you and will take place in a private restroom inside of the exercise physiology lab. You will interpret the test in the privacy of this restroom and will privately disclose the result (i.e., positive or negative) of the test to a researcher in another private room that is adjacent to the bathroom. If you test positive (i.e., you are pregnant), you will be referred to their own health care provider or one at SHAC to follow up with a confirming test and other follow-up health care as needed.

- Your height and weight will be measured, and body fat will be estimated via skinfold (SKF) measurements. The SKF measurements are done using a skinfold caliper to measure a double layer of skin and underlying (subcutaneous) fat. The SKF sites include the chest, abdomen and thigh for males and the triceps, top of hip joint (suprailiac) and thigh for females. The sum of the SKF measurements is used to estimate body density. The determined body density is used to estimate your percent body fat. The caliper measurements require a technician to pinch your skin two-three times at each site.

- You will then be asked to perform a one-repetition maximum (1-RM) strength test using the belt squat equipment. First, you will warm-up for 5-10 minutes as you typically would for your usual weightlifting session. Next, a member from our research team will demonstrate the proper lifting technique for the belt squat. From there, you will perform successive sets of 1 repetition until we determine the maximum intensity (e.g. how much weight is on the machine) that you can lift no more than 1 time. You will have 2-3 minutes to rest between sets and your 1-RM will be determined within 3-4 sets.

- After your 1-RM is determined, you will be given 5 minutes of rest, and the researchers will conduct 10-RM testing using the 7 second repetitions (i.e., slow tempo) paced with a metronome. The initial load will be ~40% of the previously determined 1-RM and the load will be increased by 5-10% per set until an 10-RM is determined (i.e., the maximal amount of weight that you can lift for no more than 8 consecutive repetitions). You will be given 2-3 minutes of rest between each set, and the 10-RM will be determined within 3-4 sets.

- After your 10-RM with 7 second repetitions is determined, you will be given 5 minutes of rest, and the researchers will conduct 20-RM testing using the 3 second repetitions (i.e., traditional tempo) paced with the metronome. The initial load will be ~40% of the previously determined 1-RM and the load will be increased by 5-10% per set until a 20-RM is determined (i.e., the maximal amount of weight that you can lift for no more than 20 consecutive repetitions). You will be given 2-3 minutes of rest between each set, and the 20-RM will be determined within 3-4 sets.
sets. **NOTE:** to reduce the influence of fatigue on your performance, the research team will randomize the order in which you do your 10-RM and 20-RM tests.

- This first visit will take 1-1.5 hours.

**Visit 2: Confirmation of 1-RM, 10-RM, and 20-RM and familiarization sets**

- Visit two will take place 2-3 days after visit one.

- You will repeat the procedures outlined above to determine 1-RM, 10-RM, and 20-RM for belt squat. We are doing this to confirm your maximal strength because we need to confirm these values to make a protocol that is individualized for you. As before, the order in which you perform your 10-RM and 20-RM tests will be randomized.

- After the replication of 1-RM, 10-RM, and 20-RM tests, you will perform 3 sets of belt squat to muscular fatigue (i.e. it would be too hard for you to do another repetition) with your 10-RM while using the slow tempo (i.e., 6 seconds per repetition). Muscular fatigue will be determined if one of three conditions occur: you voluntarily stop exercise, you break your form to complete another repetition, or you cannot keep pace with the metronome on two consecutive repetitions. 3-minutes of rest will be allowed between each set.

- After you complete your 2 sets of belt squat with 10-RM and slow tempo, you will rest for 3-5 minutes before performing 2 sets of belt squat to muscular fatigue with your 20-RM and the traditional tempo (i.e., 3 seconds per repetition).

- During this time, you will be familiarized with the “OMNI-RPE scale” which requires you to rate your physical exertion on a scale of 1-10 after each set of exercise.

- For the traditional tempo sets, a metronome will be used to ensure a 2:1 second ratio for each repetition. In other words, you will lower into a squat for 2 seconds, and stand up from the squat for 1 second. For the slow tempo sets, a metronome will be used to ensure a 4:2 second ratio for each repetition. In other words, you will lower into a squat for 4 seconds and stand up from the squat for 2 seconds.

- This visit should take 1-1.5 hours.

**Visit 3: Traditional Tempo Resistance Training Session**

- Visit three will take place 7 days after visit two.

- You will have done no exercise 24 hours before the session, consumed any alcohol 24 hours prior to the session, and consumed at least a pint of water and a small meal 2-3 hours before the session)
• Before data collection and exercise begin, you will fill out a 24-hour diet recall food log. This will be done so you can replicate your pre-exercise diet for the subsequent training session.

• Next, a small muscle tissue sample will be collected via biopsy taken from your upper leg/thigh area. To do so, you will be placed on an examination table lying down on your back (supine) so that the muscles of the leg are relaxed. The skin will be cleaned and prepared with surgical antiseptic after which a surgical cover will be placed around the sampling site. Your leg will be numbed with a local anaesthetic (Lidocaine). You may experience a slight pinching sensation while the anaesthetic is injected. Once the area has been completely numbed, a small incision will then be made in the skin overlying the muscle using a pilot needle that allows easier access of the biopsy needle. After this, the biopsy needle will be inserted into your leg, and a small sample (i.e., about the size of a sesame seed) will be taken.

• There may be some minimal bleeding. If you have a bleeding disorder or blood clotting problem, you will inform the lab personnel and not participate in the biopsy procedure. Sterile disposable instruments will be used for the preparation of the site and tissue sampling. Approximately 10 mg (size of a sesame seed) of skeletal muscle tissue will be removed. You may feel a brief sensation of pressure in the leg and potentially some moderate pain. This pain will quickly subside, and you will likely be able to perform exercise and normal daily activities unhindered.

• Following the biopsy, the incision will be cleaned, treated with a sterile dressing, and a bandage will be applied to apply pressure and minimize the possibility of a blood related infection. You will also be given instructions for the proper care of the biopsy site.

• You will then perform 5-10 minutes of a self-selected dynamic warm-up as you typically would before a session of lower body lifting.

• Two small electrodes will be placed on the outside of your thigh to measure the amount of oxygen that is being used during exercise. A researcher will clean the area with an alcohol wipe and may use a single blade razor to remove hair before placing the electrodes. You will also don a chest strap to measure your heart rate.

• Next, you will perform two warm-up sets of 10-12 repetitions with 30-40% of your one-repetition maximum (determined on visits one and two). The warm-up sets will be performed with the 2:1 second tempo as previously described.

• Then you will perform 5 sets of 20 repetitions with the 2:1 second tempo using the external load that corresponded to your 20-RM as determined during visits one and two. These sets will be performed to muscular fatigue, which will be determined if one of three conditions occur: you voluntarily stop exercise, you break form to complete another repetition, or if you cannot keep pace with the metronome on two consecutive repetitions. 3-minutes of rest will be allowed between each set.

• You will be asked to rate your exertion on a scale of 1-10 after each set.
• A metronome will be used to ensure the 2:1 second ratio for all repetitions.

• The researchers will measure your lactate (i.e. a molecule that your muscles produce when they work hard) at these time points: before exercise begins, immediately after the 5th set of exercise, and 5-minutes after the 5th set of exercise. To do this, a researcher will clean the site with alcohol and then puncture your ear lobe with a very small needle and take two blood samples that are about the size of a small bead.

• After the lactate sample is collected, the muscle biopsy procedure will be replicated as described above. After the second biopsy is taken, you will rest/recover in the exercise physiology lab for 3 hours before a third biopsy is taken following the same procedures described above. All three muscle biopsies will be conducted on the same muscle (i.e., thigh) of the same leg and will be performed in close proximity to each other (e.g., roughly 1 cm apart).

• This visit should take 4-5 hours including the 3 hour rest time.

**Visit 4: Slow Tempo Resistance Training Session**

• Visit four will take place 14 days after visit three.

• You will wear the same clothing and follow the pre-exercise guidelines as previously outlined in this document. Next, you will fill out another 24-hour diet recall to verify that you ate the same foods from the first session.

• All procedures, exercises, and measurements will be replicated from visit three. The only difference is that you will be performing slow tempo resistance training (defined below) instead of traditional tempo resistance training sets. The muscle biopsies will be performed on the same leg and on the same muscle, but the researchers will take the samples ~3 cm away from where they did during Visit 3.

• Next, you will perform two warm-up sets of 4-6 repetitions with 30-40% of your one-repetition maximum (determined on visits one and two). The warm-up sets will be performed with the 4:2 second tempo as previously described.

• Then you will perform 5 sets of 10 repetitions with the 4:2 second tempo using the external load that corresponded to your 10-RM as determined during visits one and two. These sets will be performed to muscular fatigue, which will be determined if one of three conditions occur: you voluntarily stop exercise, you break form to complete another repetition, or if you cannot keep pace with the metronome on two consecutive repetitions. 3-minutes of rest will be allowed between each set.

• This visit should take 240-300 minutes.
NOTE: Visits 3 and 4 will be randomized and counterbalanced, meaning that the order in which the sessions are performed will vary between participants. When you arrive to the lab for Visit 3, the researchers will inform you what order you will perform the training sessions.

Participation in this study will take a total of 10-12.5 hours over a period of 4 separate sessions. Each session will last between 1 and 5 hours. All visits are intended to be completed over a 4-week period.

**Risks:**

**COVID-19 exposure risks:**

There is risk of COVID-19 exposure due to your participation in this study as the visits involve face-to-face interaction with research personnel. In order to minimize the risk, we will take several precautions. You and research personnel will follow social distancing requirements (6 ft.) except for when it is necessary to collect data (i.e., skin fold, lactate). Research personnel will be screened for symptoms or exposure to COVID-19 positive individuals before they will be allowed to work with you. The lab area will be cleaned and disinfected regularly and between participants. Hand sanitizer will be available in the lab. All research personnel have been trained on any new procedures adopted to prevent exposure to COVID-19. There will be no more than 2 research team members working with you at a time. They will wear face masks at all times in the lab. You are also required to wear a mask in the lab except when you are exercising. When it is necessary for a research team member to touch your skin, such as skinfolds and muscle biopsy, research personnel will wear disposable gloves (sterile disposable gloves for biopsies). If you or a research team member reports exposure to, develops symptoms possibly associated with, or tests positive for COVID-19 within 14-days of a visit, the study will be paused and you will start a self-quarantine for at least 14 days. You will not be allowed to continue participating in this study unless you show no symptoms and test negative after the quarantine.

**Muscle Biopsy:**

The risks associated with a muscle biopsy include momentary discomfort or moderate pain during the time the needle is inserted. To minimize the occurrence of discomfort and pain, an effective numbing agent (Lidocaine) will be used to numb the area to be sampled. You will likely experience a brief and small pinching sensation while the numbing agent (Lidocaine) is injected. A minimal amount of muscle tissue (10 mg, 0.002 tsp) will be extracted from your leg. You may feel a brief sensation of pressure in the leg and potentially some moderate pain during the tissue sampling. This pain will quickly dissipate, and you will likely be able to perform exercise and normal daily activities unhindered. There is a risk that you may feel a sense of dizziness or feeling faint. Your leg may feel tight and you may feel a sensation of a deep bruise or “Charlie Horse” afterwards; however, this tightness in the muscle typically dissipates within 2 days and you may begin exercising immediately, and routinely begin exercising at normal capacity within 2 days. There is also a risk of the possible appearance of a scar, bruising or soreness, and infection. To limit the potential risks, only trained technicians wearing a mask, goggles and sterile gloves and using sterilized instruments will perform the biopsy procedure. Additionally, the sampling site will be sterilized prior to and after the procedure.

**Resistance Training:**
There are risks associated with maximal/submaximal weight lifting which include the following: brief feelings of nausea, lightheadedness, muscle cramps, dizziness, tiredness, soreness, or strains of muscles. If any of these symptoms arise, we can terminate the session and help make you feel as comfortable as possible. Risk for COVID-19 exposure is low during weight lifting exercise in our lab because we will maintain social distance (6 ft.) and researchers will be wearing a mask. All equipment will be sanitized before and after each lab visit, and the researchers will instruct you on which weights to add/take-off between your sets to minimize the number of people around the squat rack and touching the weights. You are encouraged to drink water as you wish, but we will ask you to bring your own water bottle to the gym.

**Lactate measurement:**

The risks associated with a pin prick for blood lactate may also include discomfort, infection, and bruising in the hours after the pin prick. The site will be sterilized before the pin prick to minimize risk of infection. To minimize risk for COVID-19 exposure, the researcher who collects this data will be wearing a mask, goggles, disposable gloves, and will minimize contact with your skin (i.e., they will only touch the ear lobe where the blood is being measured).

Every reasonable effort will be made to protect the information you give us. However, there is a risk of loss of privacy and/or confidentiality that may result in hardship or inconvenience. There are risks of stress, emotional distress, injury, inconvenience and possible loss of privacy and confidentiality associated with participating in this study. For more information about risks and side effects from participation in this study, ask the investigators.

**Benefits:** There is no direct benefit to you for participating in this study. However, you will receive the following information specific to your fitness: muscular strength results and body fat percentage results. This information is useful in determining your current level of physical fitness and planning exercise programs. In addition, it is anticipated information gained from this study will provide new information for exercise professionals to improve physical activity prescriptions to achieve specific training adaptations in healthy, physically active weight lifters.

**Confidentiality of your information:** All identifying information will be maintained in locked files, available only to authorized member of the research team for the duration of the study in order to schedule your appointments (including the COVID-19 screening sheets). In lieu of having your name written on any sheet of paper, you will be assigned a participant number (e.g., Subject #8), and the research team will record data and schedule appointments using this number instead of your name. For any information entered into a computer, the only identifier will be a unique study identification (ID) number. If you decide to withdraw from the study, all data which has been previously collected will be destroyed immediately. Any personal identifying information and any record linking that information to study ID numbers will be destroyed when the study is completed. Information resulting from this study will be used for research purposes and may be published; however, you will not be identified by name in any publications. We will take measures to protect the security of all your personal information, but we cannot guarantee confidentiality of all study data. The University of New Mexico Institutional Review Board (IRB) that oversees human subject research may be permitted to access your records. Your name will not be used in any published reports about this study.

**Research related injury:**

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There is a risk that you might need to be quarantined for 14 days if a research team member you interacted with tests positive for COVID-19. If you are injured or become sick as a result of this study, any emergency treatment will be at your cost. UNM makes no commitment to provide free medical care or money for injuries to you in this study.

It is important for you to tell the Principal Investigator immediately if you have been injured or become sick because of taking part in this study. Please also let someone from the research team know immediately if you show symptoms, are exposed to someone with the coronavirus, or test positive for COVID-19. If you have any questions about these issues or believe that you have been treated carelessly in the study, please contact the Office of the IRB at (505) 277-2644 for more information.

**Use of your information for future research:** Your information collected for this project will NOT be used or shared for future research, even if we remove the identifiable information like your name or date of birth.

**Payment:** You will be paid a total of $60 during this study in a prorated fashion (Day 1 = $10, Day 2 = $10, Day 3 = $20, Day 4 = $20).

**Right to withdraw from the research:** Your participation in this study is completely voluntary. You have the right to choose not to participate or to withdraw your participation at any point in this study without penalty. Any such data which may have been previously collected will be destroyed if you do decide to withdraw from the study, however you will be given your own test results up to that point.

If you have any questions, concerns, or complaints about the research, or if you contract COVID-19 (including showing symptoms or testing positive) within 14 days of a visit to the lab, please contact the principal investigator immediately:

Fabiano Amorim, Ph.D.
University of New Mexico Department Health, Exercise and Sport Sciences
Johnson Center, MSC04 2610
1 University of New Mexico
Albuquerque New Mexico 87131
(505) 277-4136
amorim@unm.edu

If you have questions regarding your rights as a research participant, or about what you should do in case of any harm to you, or if you want to obtain information or offer input, please contact the IRB. The IRB is a group of people from UNM and the community who provide independent oversight of safety and ethical issues related to research involving people:
CONSENT

You are deciding whether to participate in this research. Your signature below indicates that you have read this form (or the form was read to you) and that all questions have been answered to your satisfaction. By signing this consent form, you are not waiving any of your legal rights as a research participant. A copy of this consent form will be provided to you.

I agree to participate in this research.

______________________________    ________________________________
Name of Adult Participant          Signature of Adult Participant    Date

**Researcher Signature** (to be completed at time of informed consent)

I have explained the research to the participant and answered all of their questions. I believe that they understand the information described in this consent form and freely consents to participate.

______________________________    ________________________________
Name of Research Team Member       Signature of Research Team Member    Date
Appendix B

Health History and Physical Activity Questionnaire

HEALTH & PHYSICAL ACTIVITY QUESTIONNAIRE

Family history questions are included because certain conditions of your first-degree relatives can incur risk to you during maximal exercise.

Subject #__________________________ Date__/__/___

Phone (H or cell)___________________

Date of Birth__/__/___ Age_____ Gender_____ Ethnicity_______

Emergency contact (name, phone #)___________________________________________

MEDICAL HISTORY

Physical injuries (muscle, joint, other):________________________________________

(use back if needed)

Limitations_________________________________________________________________

Have you ever had any of the following cardiovascular problems? Please check all that apply.

Heart attack/Myocardial Infarction_____ Heart surgery _____ Valve problems _____

Chest pain or pressure _____ Swollen ankles _____ Dizziness _____

Arrhythmias/Palpitations _____ Heart murmur _____ Congestive heart failure _____

Shortness of breath _____
Have you ever had any of the following? Please check all that apply.

- High blood pressure
- Asthma
- Total cholesterol >200 mg/dl
- Diabetes (specify type)
- HDL cholesterol <35 mg/dl
- Emphysema
- Stroke
- LDL cholesterol >135 mg/dl
- Triglycerides>150 mg/dl

Do immediate blood relatives (biological parents & siblings only) have any of the conditions listed above? If yes, list the problem, and family member age at diagnosis.

Do you currently have any other medical condition not listed?
Details

Indicate level of your overall health. Excellent_____Good_____Fair_____Poor_____
Are you taking any medications, vitamins or dietary supplements now?  Y  N
If yes, what are they?

Are you allergic to latex?  Y  N

Have you ever experienced any adverse effects during or after exercise (fainting, vomiting, shock, palpitations, hyperventilation)?  Y  N  If yes, elaborate.

LIFESTYLE FACTORS

Do you now or have you ever used tobacco?  Y  N  If yes: type 

How long? ______  Quantity___/day  Years since quitting___________

EXERCISE

Aerobic training
Days per week:
Minutes per sessions:
How many years have you done such training:

Lower Body Resistance training
How many days per week:
How many exercises:
How many sets per exercise:
How many repetitions per set:
What is the typical tempo of each repetition:
How many year have you done such training:
Do you consistently perform sets to failure (i.e. until you can’t perform another rep):
Please list the lower body exercises that you are currently performing:
Appendix C

E-Mail Script for Potential Participants

My name is Zachary Mang and I am a researcher in the Health, Exercise and Sports Sciences department at the University of New Mexico. I am emailing to notify you of a research study we are conducting for which you may be an eligible participant. The research study is investigating the effect of slow tempo resistance training (5 sets, 10 repetitions, 6 second contractions) vs. traditional tempo resistance training (5 sets, 20 repetitions, 3 second contractions) on lactate production and oxygen consumption while using a belt squat machine. If you are a healthy male or female between the ages of 18-35 years old and have been engaging in regular lower body resistance training (>2-days/week for >12-months) you may be eligible to participate. We also ask that you consistently use a variation of squat, belt squat, or leg press exercise during your resistance training sessions program and are currently using moderate-heavy loads that you can only lift for 3-10 repetitions. During the study, you will have your blood lactate (i.e., a molecule that muscles produce when they are working hard) measured by a very small pin-prick of the ear (feels like a tiny pinch). You will also have a muscle biopsy (i.e., very small amount of muscle tissue removed from your quadriceps) performed before, immediately after, and 3-hours after each of the training sessions (i.e., 2 sessions, 6 biopsies). This study will require 4 visits to the research laboratory and require you to be at the laboratory a total of approximately 12 hours. Please be aware that participation in this study may increase your exposure to COVID-19, but you and all researchers will be screened for COVID-19 before entering the lab, and several precautions will be taken. Specifically, all equipment will be sanitized before and after each of your visits, you and all researchers will wear masks, researchers will wear goggles and gloves, and social distance (6 feet) will be maintained at all times. Please contact Zachary Mang at 505-412-3777 (zmang@unm.edu) or Dr. Fabiano Amorim, PhD at amorim@unm.edu if you are interested in participating and would like to learn more about the study.
Appendix D

Data Collection Sheets

Baseline/Demographic Data

Height (cm)

Weight (kg)

Chest/triceps skin fold (mm)

Abdomen/hip skin fold (mm)

Thigh skin fold (mm)

Day 1 Belt Squat 1-RM

Day 2 Belt Squat 1-RM

Day 1 Belt Squat 10-RM (4:2)

Day 2 Belt Squat 10-RM (4:2)

Day 1 Belt Squat 20-RM (2:1)

Day 2 Belt Squat 20-RM (2:1)
### Slow Tempo Resistance Training (5 sets; 10-RM; 4:2)

Resting lactate (before exercise begins) =

<table>
<thead>
<tr>
<th>Belt Squat</th>
<th>External Load</th>
<th>Repetitions completed</th>
<th>RPE (1-10)</th>
<th>Lactate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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<tr>
<td>Set #1</td>
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<td>Set #2</td>
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<td>Set #3</td>
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<td>Set #4</td>
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<td>Set #5</td>
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<tr>
<td>Post</td>
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<tr>
<td>10-minutes Post</td>
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</tbody>
</table>

### Traditional Tempo Resistance Training (5 sets; 20-RM; 2:1)

Resting lactate (before exercise begins) =

<table>
<thead>
<tr>
<th>Belt Squat</th>
<th>External Load</th>
<th>Repetitions completed</th>
<th>RPE (1-10)</th>
<th>Lactate</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>Set #1</td>
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<tr>
<td>Set #2</td>
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</table>
Figure 1: OMNI Perceived Exertion Scale for Resistance Exercise.
Appendix E

COVID-19 Symptoms Checklist

COVID-19 Symptom Screening Checklist

This checklist has been developed by Safety & Risk Services (SRS) with the guidance from the State of New Mexico and approval by the Office of the Vice President of Research. This document should be filled out every day before a research personnel and participant report to the lab.

Participant #: ___________________ Date: ___________________

<table>
<thead>
<tr>
<th>In the last 14 days have you had any of the following:</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td></td>
<td></td>
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<tr>
<td>Shortness of Breath or Difficulty Breathing</td>
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<tr>
<td>Fever</td>
<td></td>
<td></td>
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<tr>
<td>Chills</td>
<td></td>
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<tr>
<td>Muscle Pain</td>
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<tr>
<td>Sore Throat</td>
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<tr>
<td>New Loss of Taste or Smell</td>
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<tr>
<td>Nausea, Vomiting, or Diarrhea</td>
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<tr>
<td>Close contact with individuals diagnosed with COVID-19</td>
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</tbody>
</table>

If you answered yes to any of the above

1. Do not come to the lab
2. Go home and self-isolate
3. Please contact the principal investigator Dr. Fabiano Amorim (amorim@unm.edu)
4. Please contact the New Mexico Department of Health for testing by calling 855-600-3453 or visiting https://cv.nmhealth.org/
5. Report your symptoms or diagnosis to UNM here: http://www.unm.edu/coronavirus/