2024-08-01

The Additive Effect of Neuromuscular Electrical Stimulation on Resistance Training Induced Adaptations in Glycemic Control, Muscle Mass and Muscular Strength

Gabriel Narvaez
University of Texas at El Paso

THE ADDITIVE EFFECT OF NEUROMUSCULAR ELECTRICAL STIMULATION ON RESISTANCE TRAINING INDUCED ADAPTATIONS IN GLYCEMIC CONTROL, MUSCLE MASS, AND MUSCULAR STRENGTH

GABRIEL NARVAEZ

Master's Program in Kinesiology

APPROVED:

Sudip Bajpeyi, Ph.D., Chair

Jason B. Boyle, Ph.D.

Andrew McAinch, Ph.D.

Stephen L. Crites, Jr., Ph.D.
Dean of the Graduate School

THE ADDITIVE EFFECT OF NEUROMUSCULAR ELECTRICAL STIMULATION ON RESISTANCE TRAINING INDUCED ADAPTATIONS IN MUSCLE MASS, MUSCULAR STRENGTH, AND GLYCEMIC CONTORL

by

GABRIEL FERNANDO NARVAEZ, B.S.

THESIS

Presented to the Faculty of the Graduate School of

The University of Texas at El Paso

in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF SCIENCE

Department of Kinesiology

THE UNIVERSITY OF TEXAS AT EL PASO

August 2024

ACKNOWLEDGEMENTS

This thesis was made possible by the guidance of my committee Dr. Sudip Bajpeyi, Dr. Andrew McAinch, and Dr. Jason Boyle. Thank you all for providing me with valuable feedback and letting me know how I can improve in all aspects of research. Thank you all for your patience as well since my thesis came down to some of the very last days for submission.

The data collection process would not be possible without the assistance of my current lab mates Jehu Apaflo, Joshua Labadah, Zahra Fatahimeiabadi, Irene John Tomy and Ulices Villalobos and past lab mates Ali Mossayebi, Cassandra Barua Reyes, and Moses Jimenez. Thank you all for everything. I would also like to thank the interns and students that worked in the Ross Moore Building to train CHHP clients. We often worked around each other and made things as easy as possible without conflicting with each other or our participant's/client's training routines. I am thankful for receiving funding from the Dodson Research Grant and additional funding provided by Dr. Bajpeyi, which made the study possible.

I would also like to thank my girlfriend Daisy Lopez and all my family for providing unwavering support throughout my educational career. I would not have made it through my master's degree without them always being proud and providing encouragement whenever I needed it.

ABSTRACT

Background: Most adults do not reach the physical activity guidelines set by ACSM (>75%). Resistance training is well known to improve muscle mass, strength, and glycemic control. Neuromuscular electrical stimulation (NMES) is a mode of inducing involuntary muscle contractions. Previously, we have shown neuromuscular electrical stimulation is able to improve glycemic control. However, the effects of superimposing NMES while resistance training on glycemic control, substrate utilization and resting energy expenditure (REE) is unknown.

Purpose: To investigate the effects of 8 weeks of superimposed NMES on resistance training compared to resistance training for glycemic control, substrate utilization, REE, muscle mass and strength.

Methods: Sedentary, untrained participants with overweight to obesity (n=24; age-32.12±2.64 years; BMI-34.24±1.45 kg/m²) were randomized into a superimposed NMES on resistance training or resistance training group. All participants performed resistance training (24 sessions, 3x/week for 8 weeks) while also receiving bilateral quadricep stimulation using low intensity (minimum setting on device) or high intensity (maximum tolerable) NMES (50 Hz, 300μs pulse width). Insulin sensitivity was assessed by homeostatic model assessment of insulin resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI-IS), oral glucose tolerance test, and continuous glucose monitoring. REE and substrate utilization was measured by indirect calorimetry, with body composition measured by dual energy X-ray absorptiometry and strength by 1 repetition maximum.

Results: Both groups had comparable fasting glucose, glucose tolerance, substrate utilization, muscle mass, and strength at baseline ($p > 0.05$). 8 weeks of superimposed NMES on resistance training improved insulin sensitivity measured by HOMA-IR and QUICKI and trended to

improve glucose tolerance ($p<0.05$). REE increased in the resistance training group ($p<0.05$) while substrate utilization did not change in either group ($p>0.05$). Both groups similarly improved lower body strength ($p<0.05$) and body composition ($p<0.05$).

Conclusion: Superimposing NMES during resistance training results in greater improvement in insulin sensitivity compared to resistance training alone. Improvement in muscle mass and strength was comparable between the two groups.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Type 2 diabetes (T2D) is the most common form of diabetes in which there is increased insulin resistance in the body and/or pancreatic cell dysfunction, leading to insulin being ineffective in controlling blood glucose levels (Galicia-Garcia et al., 2020). An estimated 34.2 million individuals (approximately 10.5% of the population) (NIH, 2020) in the United States are living with diabetes, of which 90-95% have T2D (CDC, 2022c). Diabetes prevalence is expected to increase to approximately 39.7 million (13.9%) in 2030 and 60.6 million (17.9%) in the year 2060 (Lin et al., 2018). Hispanics which account for approximately 82.9% of the population in the border region of El Paso (Census, 2020), have 1.7 times the prevalence and 1.3 times the risk of death for diabetes compared to non-Hispanic Whites (HHS, 2021). Prevalence of diabetes in El Paso exceeds both the Texas and national average with diabetes related deaths being almost 50% higher (TTUHSC, 2023). The leading risk factor for diabetes is obesity (Barnes, 2011), which is classified as a body mass index (BMI) of 30 kg/m^2 or greater (CDC, 2022b). An alarming 72.6% of US adults are classified as overweight and 41.1% are classified as obese (CDC, 2022b). Among the Hispanic population, this risk is even greater as 47% are considered obese (Howell et al., 2022). Obesity has many detrimental health effects and significantly contributes to all causes of mortality (Flegal et al., 2013).

Obesity and T2D have been linked to many factors including physical inactivity and lack of exercise (HHS, 2022). It is recommended that adults perform 150 minutes of moderate intensity aerobic exercise and 2-3 days of strengthening exercise per week, however many people do not meet such recommendations (Liguori, 2021). In the United States, approximately 50% of adults meet the recommendation for aerobic exercise, 35% meet the guidelines for strengthening exercise, and only 23% meet both aerobic and resistance exercise

recommendations (CDC, 2019). This lack of exercise is even more prevalent in a Hispanic population as they have lower physical activity compared to other non-Hispanic ethnicities (CDC, 2022a). For people with obesity, exercise may be difficult to perform due to possible functional limitations and pain from excess weight in the muscles and joints (Eves & Plotnikoff, 2006). Although aerobic exercise is often recommended for the overweight to obese population, resistance exercise has been shown to have greater preference, tolerance and improvements in physical health status compared to aerobic exercise (Eves & Plotnikoff, 2006; Flack et al., 2017). This greater preference and tolerance is a significant aspect to consider for exercise adherence as people are more likely to perform exercise that they enjoy and be more consistent with exercising (Jekauc, 2015). There are many theories on how to maximize the improvements seen from resistance training. One novel strategy is superimposing neuromuscular electrical stimulation (NMES) during resistance training sessions. NMES is an efficient, affordable, and non-invasive way of invoking muscle contractions.

NEUROMUSCULAR ELECTRICAL STIMULATION BENEFITS

NMES, most used in rehabilitation settings, uses pulses of electricity to induce involuntary muscle contractions (Dehail et al., 2008). Like resistance training, NMES causes the generation of an action potential which leads to a change in membrane potential of muscle cells, resulting in the release of calcium and activation of the signaling cascade that results in a muscle contraction (Silverthorn DU, 2020). Resistance training follows the size principle in which motor units are recruited from the smallest and increasing in size until enough motor units are recruited for the amount of force generated for muscle contraction (Henneman et al., 1965). NMES tends to bypass the size principle and recruit larger motor units first (Dehail et al., 2008). This earlier

recruitment of larger motor units results in a relatively high force output with less effort (Dehail et al., 2008).

EFFECT OF NMES ON MUSCLE MASS AND STRENGTH

Skeletal muscle is highly metabolically active and is the main area for lipid and glucose metabolism (Koistinen & Zierath, 2002; Rasmussen & Wolfe, 1999; Stump et al., 2006). Hence, it is a primary area for investigating insulin sensitivity, obesity, and T2D (Koistinen & Zierath, 2002; Mizgier et al., 2014). Increases in muscle mass because of resistance training have been proposed to be the main regulator of increased glucose uptake and insulin sensitivity (Takala et al., 1999; Yki-Järvinen & Koivisto, 1983). NMES has shown the ability to increase muscle mass in therapeutic settings (Dal Corso et al., 2007). Increases and attenuation of the loss of muscle mass in critically ill patients has been shown because of NMES (Segers et al., 2021). In an elderly population, NMES has also been shown to increase muscle fiber cross sectional area (CSA) following 8 weeks of high frequency stimulation (Di Filippo et al., 2017). Increases in muscle mass may be due to increases in anabolic signaling pathways. It has been shown that following an acute bout of high frequency NMES, an increase in phosphorylation of mammalian target of rapamycin (mTOR) and S6K1 was found (Mettler et al., 2018). S6K1 and mTOR play vital roles in the maintenance and increase in muscle mass by relating muscle cell size and muscle protein synthesis respectively (Boluyt et al., 1997; Gonzalez et al., 2016). Another potential explanation could be increased satellite cell fusion in muscle fibers (Di Filippo et al., 2017). Satellite cell fusion assists in the contribution of new myonuclei in skeletal muscle fibers, assists in hypertrophy caused by overloading, and potentially supporting the repair of membrane damage and chronic myonuclear transcription output (Murach et al., 2021).

Similarly, for muscle strength, NMES has shown significant improvements (Stevens-Lapsley et al., 2012). A meta-analysis that compared strength increases in resistance training and neuromuscular electrical stimulation found that when volume is matched, both modes of exercise/muscle contraction result in similar increases in muscle strength (Happ & Behringer, 2021). The strength increases from NMES may be attributed to synchronous motor unit depolarization in contrast to the oscillation of motor units seen in voluntary contractions as well as constant, higher intensity firing rates of motor units leading to greater force production (Dehail et al., 2008). As previously mentioned, in an elderly population, NMES increased muscle CSA (de Oliveira Melo et al., 2013; Di Filippo et al., 2017; Esteve et al., 2017; Langeard et al., 2017). In the same study, average force significantly increased following 8 weeks of high frequency stimulation as well (Di Filippo et al., 2017). In critically ill patients, following cardiothoracic surgery, an NMES intervention with a median duration of four days lead to 4.5 times faster return to preoperative strength compared to those that recovered normally (Fischer et al., 2016). For those who may not be able to perform conventional exercise such as those individuals with osteoarthritis or spinal cord injury, NMES has been shown to increase muscle strength and functional performance (De Freitas et al., 2018; Melo et al., 2012; Stevens-Lapsley et al., 2012; Talbot et al., 2003). When it comes to healthy able-bodied participants, a review reported that for young adults, NMES has shown to provide significantly greater improvements in muscle strength compared to control groups (Rahmati et al., 2021). There is evidence that NMES is effective in the improvement of muscular strength and muscle mass in able bodied, functionally impaired, and elderly populations (De Freitas et al., 2018; Melo et al., 2012; Rahmati et al., 2021).

EFFECT OF NMES ON SUBSTRATE UTILIZATION

Substrate utilization is assessed using indirect calorimetry in which the ratio of one's carbon dioxide production and oxygen consumption (known as respiratory quotient (RQ) is calculated (Patel et al., 2023). In theory, RQ ranges from 0.7 to 1.0 indicating utilization of 100% fats and carbohydrates respectively (Mcclave et al., 2003). However, RQ is limited in that it excludes protein oxidation which influences the value obtained through indirect calorimetry (Mcclave et al., 2003). Defects in substrate utilization have been identified as a major consequence of obesity and T2D (Borghouts et al., 2002; Kelley et al., 1999). T2D is characterized by reduced effectiveness of insulin in transporting glucose inside cells (Rachdaoui, 2020). Reductions in insulin stimulated glucose transport and metabolism in body fat and skeletal muscle cells demonstrate insulin resistance in those with obesity and/or T2D (Maeda et al., 2002). People with obesity and T2D have been shown to rely less on fat oxidation while fasting and an insufficient ability to switch to carbohydrate oxidation after a meal or in an insulin stimulated condition compared to those that are more metabolically healthy (Galgani et al., 2008). It has been shown that individuals with obesity had no change in RQ from a fasting to insulin stimulated condition, known as metabolic inflexibility (Kelley et al., 1999). However, after a 4-month weight loss intervention, insulin stimulated RQ was significantly greater indicating greater carbohydrate/glucose utilization (metabolic flexibility) (Kelley et al., 1999).

When examining RQ during the application of NMES, following an acute bout of high frequency NMES (75 Hz) applied to the quadriceps muscles, an increase in RQ was found (Hamada et al., 2003), indicating increased reliance on anaerobic metabolism and use of intracellular glycogen stores of the recruited muscle fibers (Theurel et al., 2007). Following an acute bout of low intensity NMES at 5 Hz applied to the quadriceps and hamstrings, increases in

RQ, oxygen uptake, energy expenditure, lactate production, heart rate, and carbohydrate oxidation in a population with obesity were seen (Grosset et al., 2013). Similarly, greater oxygen uptake and carbohydrate utilization were seen following one bout of NMES set at 20 Hz applied to the lower leg and thigh muscles (Hamada et al., 2004). Contrary to increased carbohydrate utilization during/after an acute bout of NMES, longitudinal studies have shown no changes. Following 4 weeks of NMES, substrate utilization showed no significant difference compared to baseline (Galvan et al., 2022). Similarly, in those with SCI, following 12 weeks of NMES there was also no change in substrate utilization (Gorgey et al., 2021). While no changes were found in substrate utilization following NMES interventions, studies on the topic are limited. In summary, NMES has been shown to increase oxygen uptake and carbohydrate oxidation during an acute bout indicating increased use of anaerobic metabolism during NMES, with no significant changes in resting substrate utilization after NMES interventions.

When examining energy expenditure in an acute setting, NMES application to the lower body has been shown to increase energy expenditure, while also increasing carbohydrate oxidation (Chen et al., 2022). When applied across the whole body, high frequency (85 Hz) NMES during low intensity resistance training demonstrated significant increases in energy expenditure compared to the resistance training performed alone in moderately trained men (Kemmler et al., 2012). Longitudinally, following 4 weeks of high frequency NMES, there was no change in resting energy expenditure (Galvan et al., 2022). In those with SCI, following 12 weeks of NMES, there was also no change in resting energy expenditure nor substrate utilization (Gorgey et al., 2021). However, following 14 weeks of whole-body electrical stimulation along with exercise training in postmenopausal women, resting metabolic rate (synonymous with resting energy expenditure), was maintained while those not utilizing electrical stimulation had a

reduced resting metabolic rate (Kemmler et al., 2010). These findings indicate increased energy expenditure during a bout of NMES with no significant improvement in resting energy expenditure when performed for longer periods of time.

EFFECT OF NMES ON GLYCEMIC CONTROL

On a cellular level, in vitro studies have shown that electrical stimulation (ES) performed on rat muscle cells has an additive effect on glucose uptake in insulin stimulated conditions (Nesher et al., 1985; Ploug et al., 1987). In human muscle cells, Nikolic et al utilized both high and low frequency ES and found that glucose uptake and lactate production increased in the high frequency group, while the low frequency group demonstrated increased oxidative capacity and mitochondrial content (Nikolić et al., 2017). ES has also shown increased insulin-stimulated glycogen synthesis and glucose oxidation (Feng et al., 2015; Lambernd et al., 2012; Nikolić et al., 2017).

In vivo studies have reported comparable results. In an acute setting, NMES has been shown to decrease plasma glucose levels, increase blood lactate, and increase glycogen depletion both immediately following stimulation (Hioki et al., 2021; Hoshiai et al., 2021; Johnson et al., 2003) and in the 24 hours post stimulation (Tsurumi et al., 2022). Similarly, following only one week of NMES, insulin sensitivity measured by hyperinsulinemic euglycemic clamp was significantly increased with a subset of the participants with greater insulin resistance demonstrating even greater improvements (Joubert et al., 2015). After 2 weeks of quadriceps stimulation at 50 Hz, an increase in insulin response was reported in individuals with T2D (Deepshikha Sharma, 2010). A recent study performed in our lab found that following 4 weeks of NMES performed 3 times per week for 30 minutes each session, glucose tolerance was

significantly improved (Galvan et al., 2022). In a longitudinal study with patients with spinal cord injury, both insulin sensitivity determined by hyperinsulinemic euglycemic glucose clamp and 2-hour blood glucose during an OGTT were significantly improved following 8 weeks of electrical stimulation assisted cycling intervention (Jeon et al., 2002). Further, following 10 weeks of NMES, fasting blood glucose and HbA1C were reduced with no changes in either body weight or bodyfat percentage (van Buuren et al., 2015). Lastly, in a meta-analysis NMES was shown to be an effective strategy to improve glycemic control in those with T2D, obesity, and spinal cord injuries (Sanchez et al., 2023). Collectively, the existing literature indicates that NMES can be used to improve glycemic control in healthy and metabolically impaired populations.

RESISTANCE TRAINING BENEFITS

Resistance training (RT) defined as periodic exercise whereby external weights provide progressive overload to skeletal muscles to make them stronger and often result in hypertrophy (Phillips & Winett, 2010). RT has long been shown to improve body composition (Candow & Burke, 2007), and is effective in the prevention of diabetes by improving glycemic control in both a healthy and a population with overweight/obesity (Croymans et al., 2013; Williams et al., 2007). As previously mentioned, in a population with overweight/obesity, resistance training has the advantage of being more tolerable, preferential, and better able to increase self-reported physical health status utilizing the Medical Outcomes Trust Short-Form 36-item version (SF-36) questionnaire compared to aerobic training (Flack et al., 2017; Reid et al., 2010). While aerobic exercise is highly effective towards improving cardiovascular health and all-cause mortality (Agarwal, 2012; Brellenthin et al., 2019; Lavie et al., 2015; Swain & Franklin, 2006), resistance

training has demonstrated similar benefits to those seen in aerobic training such as increased skeletal muscle mitochondria content and function (Frank et al., 2016; Groennebaek & Vissing, 2017), and insulin sensitivity (Evans et al., 2019; Frank et al., 2016). However, resistance training has additional benefits that aerobic training does not offer including reduced musculoskeletal pain (Andersen et al., 2011; Babatunde et al., 2017; Jackson et al., 2011), anxiety and depression (Gordon et al., 2018; LeBouthillier & Asmundson, 2017; Reid et al., 2010), and increased bone strength which reduces the risk of osteoporosis and fractures (Beck et al., 2017).

EFFECT OF RESISTANCE TRAINING ON MUSCLE MASS AND STRENGTH

Skeletal muscle is one of the most metabolically active tissues in the body and is the main site for lipid and glucose metabolism and as such it is the primary area for investigating insulin sensitivity, obesity, and type 2 diabetes (Jordy & Kiens, 2014; Merz & Thurmond, 2020; Stump et al., 2006). Short term studies have shown increases in muscular strength in as little as 2 weeks (Abe et al., 2000), with similar results extending to 4 (Boone et al., 2015), 6 (Scanlon et al., 2014), and 9 week interventions (Anderson & Kearney, 1982). In a 16-week study with resistance training performed 3 times per week, increased strength in bench press, row, and leg press was reported with improvement in glycemic control in a population with obesity and T2D (Cauza et al., 2005). Multiple studies incorporating resistance training show increases in muscle mass, strength, and insulin sensitivity at a variety of exercise doses and durations (Brooks et al., 2007; Dunstan et al., 2002; Ibañez et al., 2005; Misra et al., 2008; Van Der Heijden et al., 2010). In a study examining women specifically, it was determined that resistance training improved strength, power, endurance, and physical performance in untrained young women (Kraemer et

al., 2001). Similarly, improvements in muscle strength for both high and moderate load resistance training were observed in older adults (Kalapotharakos et al., 2004).

Among older adults, resistance training has also been shown to benefit muscle mass. Following a 12-week training program, RT was shown to decrease fat mass while maintaining muscle mass (Campbell et al., 1994). Other studies have shown more positive results leading to increases in muscle mass with a variety of training durations in older adults (Bamman et al., 2003; Fiatarone et al., 1990; Häkkinen et al., 2001; Trappe et al., 2001). Similarly, in a population with T2D, RT interventions have led to increased muscle mass, decreased fat mass, and overall decrease in bodyweight (Brooks et al., 2007; Dunstan et al., 2002). In a normoglycemic overweight population, following 12 weeks of RT, while bodyweight increased, it was largely attributed to significant increases in muscle mass (Van Der Heijden et al., 2010). In young healthy adults, increases in muscle mass demonstrate similar findings in both males and females (Candow & Burke, 2007; Chilibeck et al., 1997; Morton et al., 2018). Meta-analyses have also demonstrated that resistance training improves both muscle mass and strength in both young and elderly adults with various intensities and training volumes (Csapo & Alegre, 2016; Schoenfeld et al., 2017). RT is therefore a feasible and effective means of improving muscle mass and strength in healthy and especially populations with obesity and/or T2D.

EFFECT OF RESISTANCE TRAINING ON SUBSTRATE UTILIZATION

Resistance training has shown to affect substrate utilization in an acute setting by increasing glucose utilization measured by increased RER during exercise, followed by a slowly declining RER to lower than baseline levels post-exercise (Farinatti et al., 2016). Similarly, at 30 and 60 minutes following an acute high intensity resistance training session, significantly

decreased RER along with increased REE was found (Wingfield et al., 2015). When tracked longer after training, following one bout of RT performed for 60 minutes, decreased RQ and increased REE have been shown at 10 and 24 hours proceeding the bout of exercise (Jamurtas et al., 2004). Similarly, high intensity interval resistance training decreased RQ 22 hours following an acute exercise session along with an increased REE (Paoli et al., 2012). When measured during and after an acute resistance training session, RER has been shown to increase above baseline values, remain elevated throughout the training session and the initial recovery period until reducing to levels below baseline levels (Haddock & Wilkin, 2006). In the same study, energy expenditure demonstrated comparable results with increases seen during and after the session however, energy expenditure remained elevated following a 120-minute recovery period (Haddock & Wilkin, 2006). When tracked for a longer period, in the three days following an acute resistance exercise session, REE remained elevated at 24, 48, and 72 hours postexercise while RER showed no change post exercise (Heden et al., 2011). In summary, an acute bout of resistance exercise can improve substrate utilization and energy expenditure both during and after the bout of exercise.

Improved substrate utilization has been found following longitudinal interventions as well. Following a 16-week resistance training intervention, 24-hour RQ decreased, indicating increased fat oxidation throughout the day (Treuth et al., 1995). Following 9 months of resistance training, patients with T2D increased fat oxidation at rest with increased mitochondrial content as well (Sparks et al., 2013). This is significant as those with T2D typically have altered lipid metabolism on top of the more well-known dysfunctional glucose metabolism (McGarry, 1992). In a healthy population, improvement in glucose oxidation was evident in response to a mixed meal tolerance test following 12 weeks of whole-body resistance training (Alkhayl et al.,

2022). This indicates greater metabolic flexibility due to the increased carbohydrate utilization in response to a standard meal. Additionally, following 6 months of resistance training, respiratory quotient (analogous to RER) decreased at rest and while sleeping, indicating greater fat oxidation and improved substrate utilization over the course of the day (Kirk et al., 2009).

Increased REE has also been found following long-term resistance training interventions. In older women, after a period of 16 weeks, resting energy expenditure increased compared to pretraining levels (Treuth et al., 1995). After a longer period of 6 months of a minimal volume resistance training program, 24-hour, resting, and sleeping energy expenditure all increased compared to pretraining levels indicating greater caloric expenditure over the course of the day in an untrained overweight population (Kirk et al., 2009). As previously mentioned, a population with overweight/obesity is at an increased risk of all-cause mortality (Flegal et al., 2013). Increased 24-hour energy expenditure may result in a negative energy balance, therefore preventing gains in body weight and the subsequent detrimental health effects associated with obesity (Lemmer et al., 2001; Pratley et al., 1994; Treuth et al., 1995).

Like populations with overweight/obesity, among a healthy population, increases in REE following resistance training have been found. Following a whole body 24-week resistance training protocol, increased resting metabolic rates were seen in both older and younger men and women with similar increases seen in both age groups (Lemmer et al., 2001). Older adults specifically have been shown to have similar outcomes with increases in both resting and total energy expenditure (Lemmer et al., 2001). Younger adults as well have been shown to increase REE with increases in FFM following resistance training interventions in both untrained and trained populations (Hackney et al., 2008; Paoli et al., 2012; Poehlman et al., 2002). Resistance training can be beneficial for increasing resting energy expenditure through increases in muscle

mass (Lemmer et al., 2001; Webb, 1981). This increased muscle mass is important as skeletal muscle is the highly metabolically active and has the greatest effect on one's metabolism (Jordy & Kiens, 2014; Merz & Thurmond, 2020; Stump et al., 2006).

EFFECT RESISTANCE TRAINING ON GLYCEMIC CONTROL

Resistance training induced increases in muscle mass is often accompanied by improvement in insulin sensitivity and glycemic control (Takala et al., 1999; Yki-Järvinen & Koivisto, 1983). Following an acute resistance exercise session, decreases in blood glucose were seen immediately after, 10-, 20- and 30-minutes post-exercise at low, moderate, and high intensities of resistance training (Silveira et al., 2014). Similarly, blood glucose decreased following an acute resistance exercise session, with glucose remaining lower 60 minutes following the bout of exercise (Yardley et al., 2013). When given a standard 75-gram glucose drink before a resistance exercise session, decreases in glucose AUC were found in the two hours after exercise in a variety of resistance training protocols with equal volumes (Aguiar et al., 2018).

Similarly, improvements in glycemic control have also been found following longitudinal resistance training interventions. In a 12-week whole-body resistance training intervention in population with prediabetes, while fasting blood glucose did not decrease, blood glucose levels were significantly lower during minute 120 of an OGTT (Eikenberg et al., 2016). Effects of resistance training in participants with diabetes produced comparable results. Following a 22-week resistance training intervention, a significant decrease in HbA1C was found, with greater reductions seen in those with HbA1C levels $\geq$ 7.5% at baseline (Sigal et al., 2007). Similar results were found following a 6-month intervention with reductions in HbA1C and a trend in

reduced fasting blood glucose (p= 0.06) along with decreased bodyweight, waist circumference, fat mass, and resting blood pressure (Dunstan et al., 2002).

While the previous studies assessed insulin sensitivity with other valid measures, the gold standard for measuring insulin sensitivity in vivo is the hyperinsulinemic euglycemic glucose clamp. During the clamp, a participant is infused with a steady rate of insulin while glucose is infused at the rate to maintain a constant level of blood glucose (DeFronzo & Beckles, 1979; Kim, 2009; Shen et al., 1970). Utilizing this technique, several studies have found improvements in insulin sensitivity following a resistance training intervention (Bacchi et al., 2013; Bacchi et al., 2012; Ishii et al., 1998). In a population with diabetes, following whole-body resistance training, glucose disposal rate increased while HbA1c decreased, indicating improvement in insulin sensitivity (Bacchi et al., 2013; Bacchi et al., 2012; Ishii et al., 1998; Miller et al., 1994; Poehlman et al., 2000). When examining a healthy population, following a 16-week resistance training protocol, glucose infusion rate increased under both high and low insulin clamp conditions (Miller et al., 1994; Poehlman et al., 2000). Along with these results, fasting insulin, and insulin during an OGTT were reduced, indicating improvement in insulin sensitivity and glucose metabolism with resistance exercise training (Miller et al., 1994). When resistance training was performed for a longer period, an increase in insulin sensitivity and was found after 6 months of resistance training (Poehlman et al., 2000). Other studies utilizing the clamp technique demonstrated similar findings with increased glucose infusion rates, as well as reductions in homeostatic model assessment for insulin resistance and HbA1C as well (Bacchi et al., 2013; Jiahao et al., 2021; Kitamura et al., 2003; Tokudome et al., 2004). In summary, resistance training can aid in the improvement of glycemic control in both healthy and diabetic

populations through a variety of assessment methods, along with improved substrate utilization, energy expenditure, muscle mass and strength.

SUPERIMPOSED NMES ON RESISTANCE TRAINING BENEFITS

As discussed in the above sections, NMES and resistance training have both been shown to effectively improve glycemic control, muscle mass, and muscular strength when used independently. To date, there have been few studies that investigated the additive effects of superimposing NMES on resistance training for muscle mass, strength, glycemic control, resting energy expenditure and substrate utilization. Most studies have primarily focused on muscular strength while a few studies investigated the influence of superimposed NMES on resistance training on muscle mass.

EFFECT OF SUPERIMPOSED NMES ON RESISTANCE TRAINING ON MUSCLE MASS AND STRENGTH

In a 2-week study comparing conventional resistance training to superimposed NMES on resistance training, increases in muscle mass and strength were found with no differences between two groups (Abulhasan et al., 2016). While there were increases in muscle mass as determined by muscle thickness in the previously mentioned study, it is proposed that initial increases in muscle mass may be attributed to damage induced edema and swelling of the worked muscle/s (Damas et al., 2018; Defreitas et al., 2011). Longer intervention durations could be necessary to see true increases in muscle mass with a proposed minimum duration of 3-4 weeks (Defreitas et al., 2011). Following 4 weeks of training, similar but not significantly different increases in muscle strength for both superimposed NMES on resistance and

conventional resistance training were found (Dörmann et al., 2019). At a slightly longer duration of 6 weeks, while there was not a significant difference, there was a medium effect size difference favoring a superimposed NMES on resistance training group for muscular strength improvements compared to a resistance training group (Wirtz et al., 2016). Significant differences can be seen in studies of 8 weeks duration. Following 8 weeks of whole body superimposed NMES on resistance training, a significantly greater increase in both muscle mass and strength were reported in a superimposed NMES on resistance training group compared to a resistance training group (Evangelista et al., 2019; Ludwig et al., 2020; Micke et al., 2018).

To thoroughly understand the benefits of superimposed NMES during resistance training on muscle mass and muscle strength, we conducted a systematic review and meta-analysis. A thorough literature review was performed using the following databases: Google Scholar, EBSCO, PubMed, and ResearchGate. Search terms included various combinations of the following key words: neuromuscular electrical stimulation, NMES, electrical stimulation, superimposed neuromuscular electrical stimulation, superimposed NMES, resistance training, resistance exercise, strength training, weight lifting, or voluntary contraction. Data extracted included the following: 1. author name, 2. age of participants, 3. description of the study population, 4. gender distribution, 5. study duration, 6. days of training performed per week, 7. NMES protocol, 8. RT protocol, and 9. methods used to assess muscle strength and muscle mass. A risk of bias was performed using Cochrane Collaboration's Risk of Bias Tool (RoB2) (Higgins et al., 2011). Risk of bias assessment included the following criteria: 1. random sequence generation, 2. allocation concealment, 3. blinding participants, 4. blinding of outcome assessment, 5. incomplete data reporting, and 6. selective reporting. Statistical analyses included random effects models being used to combine data in R (version 4.2.2). Statistical heterogeneity

among studies was assessed using I^2 Statistics. I^2 values 25-50% were considered indicative of low heterogeneity, 50-75% were considered moderate heterogeneity, and values above 75% were considered to have a high degree of heterogeneity. Sensitivity analysis was performed using a Q test for moderators in the random effect meta-analysis model. A p-value of <0.05 was considered significant.

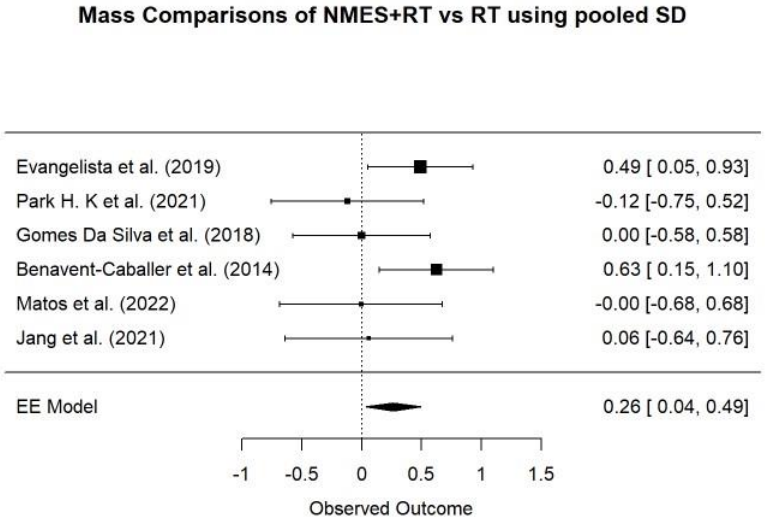

Figure 1. Meta-analysis results for muscle mass. Abbreviations- NMES+RT- superimposed NMES on resistance training; RT- resistance training; SD- standard deviation; EE- experimental effects.

The meta-analysis for muscle mass included 6 studies with results indicating a favorable effect for superimposed NMES on resistance training (**Figure 1**). The meta-analysis for muscle strength included 13 studies and demonstrated a favorable effect towards superimposed NMES on resistance training (**Figure 2)**. The results were also substantiated by the systematic review in which 5 studies reported significant differences in favor of superimposed NMES on resistance training with an additional study finding that while there was no significant difference, there was a medium effect size difference favoring superimposed NMES on resistance training as well.

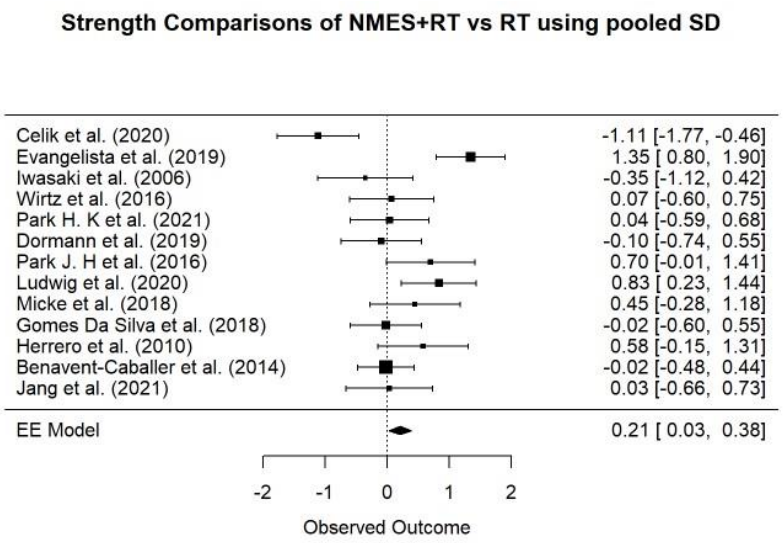

Figure 2. Meta-analysis results for muscular strength. Abbreviations- NMES+RT- superimposed NMES on resistance training; RT- resistance training; SD- standard deviation; EE- experimental effects.

While the effects of superimposed NMES on resistance training on muscle mass and strength have been investigated to some extent, the effect on glycemic control is much less understood. A pilot study (n=6) performed by Holzer et al. investigated the effects of acute superimposed NMES on resistance exercise compared to resistance exercise, aerobic exercise, and an inactive control for postprandial glucose responses monitored by a continuous glucose monitor in a population with diabetes (Holzer et al., 2021). In the study, participants performed either a whole-body resistance exercise session with NMES, resistance exercise without NMES, or 20 minutes of moderate intensity aerobic exercise done in a randomized crossover fashion. Postprandial glucose response, time to baseline glucose, glucose AUC, time in target range (70-180 mg/dL) and time above target range (≥180 mg/dL) showed no significant differences between exercise modes. However, the NMES protocol was relatively low in intensity with participants asked to increase until a RPE of approximately 4-5 out of 10. Additionally, the resistance training protocol was also relatively low in intensity with many exercises being done using only bodyweight, with some exercises incorporating an elastic band for external resistance

and intensity being moderate with participants instructed to perform each set to 3-4 repetitions away from muscular failure. While this study did not show significant differences between superimposed NMES on resistance and conventional resistance exercise in an acute setting among a population with diabetes, literature investigating effects of superimposed vs conventional resistance training on glycemic control longitudinally are quite limited. Studies investigating an at-risk population with overweight/obesity are also limited. To our knowledge there are no longitudinal studies that investigated the effect of superimposed NMES on resistance training compared to conventional resistance training for glycemic control, substrate utilization muscle mass, and muscular strength in an at-risk population with overweight/obesity.

PURPOSE

The primary purpose of this study is to determine if superimposing NMES on resistance training leads to additive improvements in glycemic control, energy metabolism and muscle mass and strength in an at-risk population with overweight/obesity.

***Specific Aim 1*:** To determine the effects of 8 weeks of superimposed NMES on RT on glycemic control measured by oral glucose tolerance test, continuous glucose monitoring, and hemoglobin A1C in a sedentary to moderately active population with overweight/obesity.

***Specific Aim 2*:** To determine the effects of 8 weeks of superimposed NMES on RT on substrate utilization and energy metabolism (resting metabolic rate and respiratory quotient in a fasting condition prior to the oral glucose tolerance test) via indirect calorimetry in a sedentary to moderately active population with overweight/obesity.

***Specific Aim 3*:** To determine the effects of 8 weeks of superimposed NMES on RT on body composition and muscle strength by dual energy x-ray absorptiometry, 1 repetition maximum, and total grip strength in a sedentary to moderately active population with overweight/obesity.

METHODS

24 participants with overweight/obesity between the ages of 18 and 65 were recruited to this study and randomized into two groups (resistance- 13, superimposed NMES on resistance- 11). All study protocols were approved by the Institutional Review Board of the University of Texas at El Paso. Each participant provided informed consent following explanation of the study procedures. All participants were sedentary to moderately active as determined by an accelerometer and untrained for resistance training (i.e., not engaged in a structured resistance exercise regimen consistently within the past 6 months).

Participants were screened either over the phone or via an in-person interview using a standard questionnaire to determine eligibility (Appendix 1). If participants met the basic inclusion criteria of being of adult age, with self-reported height, weight, BMI of ≥ 25 kg/m^2, and untrained status (**Table 1**), a meeting was scheduled to provide information about the study, informed consent was obtained, and further screening was completed (**Table 2**). All pre- and postintervention variables are stated in **Table 3**.

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• $18 \leq$ Age ≤ 65 years old • $25 \leq$ BMI kg/m^2 • Sedentary to Moderately Active ❖ Less than 150 minutes of voluntary moderate to vigorous physical activity per week • Untrained Status (no consistent structured resistance training in the previous 6 months)	• Anyone taking antihypertensive, lipid lowering, or insulin sensitizing medications • Smoking • Excessive Drinking • Pregnant Women • Musculoskeletal Injury • Unwilling to adhere to intervention

Abbreviations- BMI- body mass index; kg- weight in kilograms; m^2- height in meters squared

Table 2. Screening Measurements

Measurement	Method
Physical Activity Level	Accelerometer
Random Blood Glucose	Blood sample via lancet stick Analysis via Contour Next Glucometer
Blood Pressure	Automated Blood Pressure Device
Resting Heart Rate	Automated Blood Pressure Device
Body Mass Index (BMI)	Height and Weight Measurements
Medical History	Questionnaire

Table 3. Study Variables

Study Variables	Assessment Method
Body Composition	Dual Energy X-Ray Absorptiometry Anthropometrics
Strength	1 Repetition Maximum Handgrip Dynamometer Isokinetic Dynamometer
Aerobic Capacity	Treadmill Graded Exercise Test
Resting Metabolic Rate	Indirect Calorimetry
Substrate Utilization	Indirect Calorimetry
Glycemic Control	Dexcom G6 CGM System
Glycemic Control	Oral Glucose Tolerance Test
Glycemic Control	Glycated Hemoglobin
Fasting Insulin	Laboratory Corporation of America ©
Fasting C-Peptide	Laboratory Corporation of America ©
Fasting Blood Glucose	Laboratory Corporation of America ©
Insulin Sensitivity	Homeostatic Model Assessment of Insulin Resistance
Insulin Sensitivity	Quantitative Insulin Sensitivity Check Index

Abbreviations- CGM- continuous glucose monitor; ©- copyright

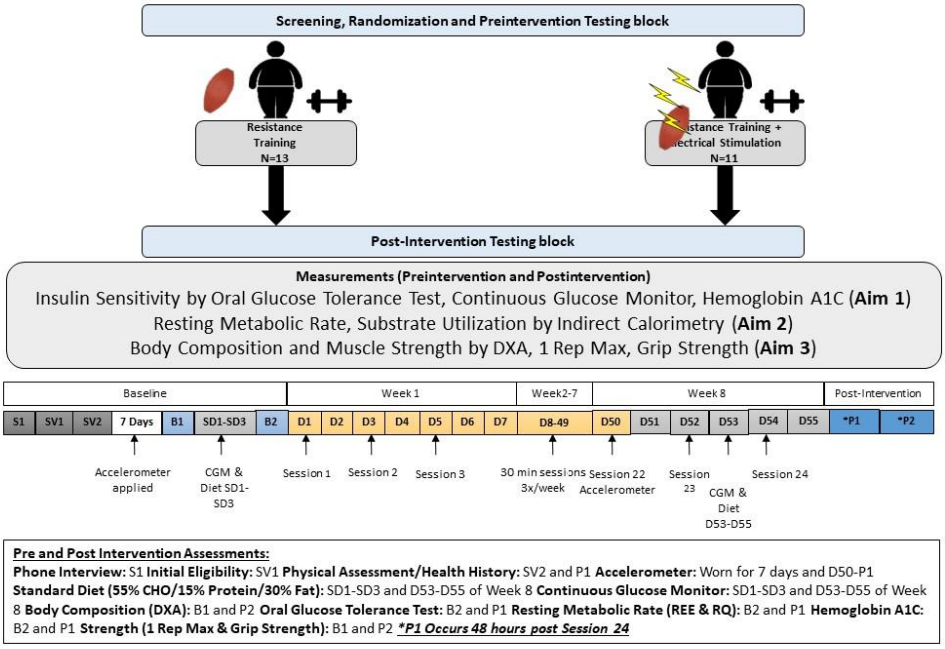

Figure 3. Study Design

PHYSICAL ACTIVITY

Once eligibility was confirmed, participants were issued an accelerometer to confirm sedentary to moderate physical activity status. The accelerometer used was the ActiGraph wGT3X-BT physical activity monitor (Pensacola, FL) and was attached to an elastic belt worn at the waist on the side of the dominant leg for 7 consecutive days with removal only when bathing. After return of the accelerometer, a compliance of 90% wear time was confirmed, and physical activity levels were calculated utilizing Microsoft Excel (Redmond, WA) utilizing Freedson cut points (Freedson et al., 2012) as recommended by ActiGraph.

BLOOD PRESSURE

Once consent was received, participants were screened for blood pressure and resting heart rate. Following a 5-minute rest period, blood pressure was obtained using an OMRON Professional

Intellisense® HEM-907XL automated blood pressure monitor (Shimogyō-ku, Kyoto, Japan). Blood pressure was measured twice on each arm with the highest pressure being used if there is a consistent difference between arms. Resting heart rate was also obtained using the automated device using the same protocol. Participants with a blood pressure of 140/80 mmHg or less and resting heart rate of less than 100 beats per minute were included in the study.

RANDOM BLOOD GLUCOSE

Once consent was received, participants were screened for random blood glucose. Blood glucose was obtained using a CONTOUR® NEXT One, Ascensia Diabetes Care handheld glucometer (Parsippany, NJ). Participants with a blood glucose level of 140 mg/dL or less were included in the study.

ANTHROPOMETRIC MEASUREMENTS

Height (cm) and body mass (kg) measurements were obtained to calculate BMI for the purpose of confirming that the participants meet the overweight (BMI $\geq$ 25.0-29.9 kg/m^2) or obese (BMI $\geq$ 30.0 kg/m^2) criteria. Additional measurements were taken including waist, hip and thigh circumference measurements following the protocols set by ACSM (Liguori, 2021). Waist circumference (cm) was taken at the level of the narrowest circumference of the torso superior to the iliac crest while the participant stood with arms outstretched and feet together. Hip circumference (cm) was taken at the maximal circumference of the hip at the midpoint of the inguinal crease; thigh circumference (cm) was taken with the participant standing with one foot on a chair/bench with the knee at approximately 90° with measurement taken midway between the inguinal crease and the proximal border of the patella. Each circumference measurement was

performed 3 times, and the mean of each measurement was calculated. Utilizing mean waist and hip circumference, waist to hip ratio (WHR) was also calculated by dividing the mean waist by the mean hip circumference measurements.

DUAL ENERGY X-RAY ABSORPTIOMETRY (DEXA)

Participants were placed supine on the padded surface of the scanner table of a GE Medical Systems Lunar iDXA Dual Energy X-Ray Absorptiometer (Madison, WI). Participants were instructed to lie with both arms at the sides with palms flat to the scanner table and positioned within the outlined measurement area of the scanner table. Ankles were fastened together with a Velcro strap to eliminate movement during the scan and to standardize positioning. The scanner arm moved downward starting from the head to the toes, taking approximately 7-14 minutes depending on the participant's body size. Measurements of total lean mass, fat free mass, total fat mass, fat mass %, leg fat mass, leg fat %, leg lean mass, leg lean %, android fat %, gynoid fat % and android to gynoid ratio were performed.

1 REPETITION MAXIMUM (1RM)

A 1 repetition maximum test following the NSCA guidelines (Haff & Triplett, 2021) was performed utilizing a Magnum Fitness Systems leg extension machine (Milwaukee, WI) located in the UTEP Fitness Research Facility (Ross Moore Building). A dynamic warm up was performed consisting of 5 minutes of low intensity aerobic exercise on a Life Fitness 95Ci stationary bicycle (Franklin Park, IL) followed by dynamic stretches of the lower body to activate the quadriceps, hamstrings, and gluteal musculature. Following the dynamic warm up, each participant was seated on the machine with the machine set to begin at approximately a 90°

knee angle and the back rest positioned to align the participant's knee with the axis of rotation of the machine. The participant was asked to fully extend the knee and return the weight to the starting position in a controlled manner following a 2:0:2:0 (eccentric: isometric: concentric: isometric) repetition tempo. A low intensity warm up set was performed for 10 repetitions to gauge the participants strength. A second warm up with a 10-20% load increase was performed for 5 repetitions. A final warm up set of 2 repetitions with another 10-20% load increase was performed. Following completion of the final warm up set, the load was increased by 5-10% and the first 1 repetition maximum attempt was performed. If successful, following a 2–3-minute rest period, load was increased 5-10% and another attempt was performed until the participant reached the highest load they can successfully lift utilizing the previously mentioned tempo. 1 repetition maximum testing was performed preintervention and postintervention.

GRIP STRENGTH

Grip strength was assessed using a Takei Handheld Dynamometer (Tokyo, Japan) following the ACSM protocol (Liguori, 2021). For measurement, participants stood with the testing arm straight at their side with the elbow straight. The dynamometer was held in the most comfortable hand position determined by the participant. Measurement consisted of a 5 second maximal squeeze of the hand beginning with the dominant hand then repeated on the nondominant side. Participants were provided with 2 minutes rest and measurements were repeated 2 times. The highest measurement for each hand was determined and summed together to provide total grip strength. Grip strength was measured both pre- and post-intervention.

AEROBIC CAPACITY

Aerobic capacity was assessed pre and postintervention using a standard graded protocol on a TrackMasterTMX58 treadmill (Full Vision Incorporated, Newton, KS). Analysis of ventilatory expired gas was performed using a ParvoMedics TrueOne metabolic cart (ParvoMedics, Salt Lake City, UT). Before each test, standardized calibration gases were used to calibrate the metabolic cart according to the manufacturer's instructions. A Polar H10 heart rate monitor was provided to participants for the measurement of heart rate during the exercise test (Polar Electro, Kempele, Finland). Prior to exercise, participants were asked to rest for 5 minutes while expired gas was collected. Exercise began with a 3-minute warm up at a speed of 3 miles per hour and incline of 3.5%. After the warm up, the treadmill was set to a self-selected speed for each participant with an incline of 0% for 1 minute. Each minute thereafter, the incline increased 1% while speed remained constant until volitional exhaustion. Following exercise, a 5-minute cooldown was performed at a speed of 3 miles per hour and 0% incline. During each minute of exercise, rating of perceived exertion (RPE) was assessed using the Borg RPE scale (Williams, 2017). Exercise testing ended when RPE reached a value of 18 or more. Aerobic capacity was validated using secondary criteria including RPE >17, respiratory exchange ratio ≥1.1,and/or max heart rate within 10 beats per minute of age predicted heart rate maximum (208 – [0.7 * age]) (Tanaka et al., 2001). Aerobic capacity was considered valid when two or more criteria were met.

DIETARY CONTROL

Participants were provided with all food for the three days preceding insulin sensitivity and substrate utilization measurements to eliminate dietary influence on insulin sensitivity, substrate

utilization, and blood profiles. Meals were designed to comply with the USDA 2015-2020 Dietary Guidelines for Americans and individualized to participants preferences and/or food allergies. The standard diet consisted of 55% carbohydrates, 15% protein, and 30% fat. Caloric requirements were calculated using the Mifflin St. Jeor equation (Mifflin et al., 1990) to match participant's energy requirements. The standardized diet was provided in the 3 days preceding metabolic testing with diet matched pre- and postintervention.

CONTINUOUS GLUCOSE MONITORING

When the participant arrived to pick up the prepared food for the first day of diet, a Dexcom G6 continuous glucose monitor (Dexcom Incorporated, San Diego, CA) was attached to their abdomen. Prior to attachment, the area was sanitized with an alcohol wipe followed by attachment of the CGM. Analysis included the 24-hour glucose average, standard deviation, minimum glucose, maximum glucose, glucose fluctuation (max-min), time above target range (>140 mg/dl) (Battelino et al., 2019), time below target range (<70 mg/dL) (Battelino et al., 2019), time in target range (minutes between ≥70 and ≤140 mg/dL) (Battelino et al., 2019), glucose management index (3.38 + 0.02345 × [mean glucose in mg/dL]) (GMI) (Bergenstal et al., 2018) and coefficient of variation (100*[glucose standard deviation/mean glucose in mg/dL]) (CV) (Yoo & Kim, 2020).

ORAL GLUCOSE TOLERANCE TEST (OGTT)

Participants were instructed to abstain from alcohol, smoking, and strenuous activity in the 24-48 hours preceding testing. Following an overnight fast, participants arrived at the UTEP Health Sciences and Nursing Building and were instructed to sit for approximately 5 minutes to

eliminate the influence of physical activity involved in arriving to campus. A fasting blood glucose sample was obtained at the end of the rest period. Following fasting glucose measurement, participants were provided with a drink containing 75 grams of glucose and instructed to consume it within 5 minutes. Once the drink is finished, blood glucose samples were taken at intervals of 15-, 30-, 60-, 90-, 120-, 150-, and 180-minutes following ingestion using a CONTOUR® NEXT One, Ascensia Diabetes Care handheld glucometer (Parsippany, NJ). Glucose tolerance was determined by calculating the glucose area under the curve (AUC) for all measurements up to 120 minutes and again with all measurements during the entire 180 minutes of testing. AUC was calculated using the trapezoid method (Sakaguchi et al., 2016). The oral glucose tolerance test was performed twice; pre- and postintervention.

HEMOGLOBIN A1C

On the same day as the oral glucose tolerance test hemoglobin A1C was measured. Measurements were performed via a drop of blood from a lancet stick. Blood samples were collected in an Afinion HbA1C test cartridge and analyzed using an Abbott Afinion 2 analyzer (Abbott Park, IL). Measurements were performed both pre- and postintervention.

BLOOD SAMPLE ASSAYS

On the same day as the OGTT, fasting blood samples were obtained via antecubital venipuncture for analysis of fasting glucose, insulin, and C-peptide levels. Blood sample assays were assessed by Laboratory Corporation of America (Burlington, NC). Blood sample assays were performed pre and postintervention.

INSULIN SENSITIVITY

Insulin sensitivity was determined via the results of fasting glucose and insulin using the formulas for both Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) (Gayoso-Diz et al., 2013) and Quantitative Insulin Sensitivity Check Index (QUICKI-IS) (Katsuki et al., 2002). HOMA-IR ([fasting insulin * fasting glucose]/22.5) and QUICKI-IS (1/[log of fasting insulin] + [log of fasting glucose]) were assessed pre and postintervention.

RESTING ENERGY EXPENDITURE AND SUBSTRATE UTILIZATION

Resting energy expenditure and substrate utilization were measured in a fasting condition via indirect calorimetry. Participants were placed in a supine position with a hood canopy over their head to obtain measurements of oxygen consumption and carbon dioxide production to estimate REE and RQ using Parvomedics TrueOne 2400 metabolic cart (Salt Lake City, UT). Participants were instructed to lie still and rest without sleeping. Data was collected for 30 minutes with the first 5 minutes being excluded to allow for stabilization. Once stabilized, RQ and REE data was averaged. REE values were also normalized to bodyweight and fat free mass in kilograms (Müller et al., 2018). Testing was performed both pre- and postintervention.

SUPERIMPOSED NMES ON RESISTANCE TRAINING PROTOCOL

All participants received training in the UTEP Fitness Research Facility (Ross Moore Building). Training was performed 3 days per week for approximately 30 minutes per session. Each session began with a dynamic warm up consisting of 5 minutes of low intensity aerobic exercise on a Life Fitness 95Ci stationary bicycle (Franklin Park, IL) followed by dynamic stretches of the lower body to activate the quadriceps, hamstrings, and gluteal musculature. Resistance training

consisted of 5 compound and isolation exercises chosen by the participant from a prescribed menu of exercises targeted to stimulate the major musculature of the lower body (i.e., quadriceps, hamstrings, glutes, and calves). Warm up sets for each exercise were performed for 1-3 sets to allow for sufficient motor unit recruitment. Each exercise was performed for 3 sets of 8 repetitions at a tempo of 2:0:2:0 (ecccentric: isometric: concentric: isometric) with a rest period of 90 seconds between each set and between exercises. In weeks 1 and 2, load was adjusted to yield an RPE of 12-14 to allow for a relatively challenging stimulus without overworking participants considering they were untrained. In weeks 3-8, the load was adjusted to yield an RPE of 14-16 to allow for a more challenging stimulus once participants were better acclimated to resistance training.

NEUROMUSCULAR ELECTRICAL STIMULATION

NMES was applied using a QuadStar® II Digital Multi-Modality Combo Device (TENS-INF-NMS) (BioMedical Life Systems, Vista, CA) and eight 2" x 2" square electrodes (BioMedical Life Systems, Vista, CA). Electrodes were placed bilaterally on the proximal and distal quadricep muscles in the location of the motor point (Botter et al., 2011; Gobbo et al., 2014; Weiss et al., 2018). The stimulation device was set to a cycled biphasic waveform with a pulse duration of 300 μs and frequency of 50 Hz. Each electrically stimulated contraction consisted of a 2 second ramp up in intensity, 10 seconds of stimulation, 2 second ramp down in intensity, and a 30 second off period. Participants in the superimposed NMES on resistance training group received stimulation up to their maximum tolerable intensity with visible muscle contraction while those in the resistance training group received stimulation at the lowest setting on the device.

STATISTICAL ANALYSIS

Statistical analyses were conducted using GraphPad Prism version 10.3 (GraphPad Software, La Jolla, CA) and Microsoft Excel (Redmond, WA). A two-way ANOVA with repeated measures were used to compare groups (superimposed and resistance training), time (before and after), and group by time effects. Unpaired t-tests were used to compare the superimposed NMES on resistance and resistance training groups for the degree of change (post-pre) for all parameters as well. For all comparisons, a $p<0.05$ is considered significant, and values are presented as mean ± SEM.

RESULTS

Participant baseline characteristics and outcomes following eight weeks of superimposed NMES on resistance and conventional resistance training are shown in **Table 4**. At baseline, age, weight, BMI, fasting glucose, RMR, body composition and strength were not significantly different between superimposed and resistance training groups.

Table 4. Descriptive Characteristics

	Resistance Training (n=13; F-8 M-5)			Superimposed NMES on Resistance Training (n=11; F-7 M-4)						
	Pre Mean ± SEM	Post Mean ± SEM	p-value	Pre Mean ± SEM	Post Mean ± SEM	p-value	Baseline	Group	Time	Interaction
Age (years)	28.2 ± 2.8			36.8±2.7			>0.05			
Blood Pressure										
Systolic (mmHg)	111 ± 3	114 ± 3	>0.05	115 ± 4	111 ± 5	>0.05	>0.05	>0.05	>0.05	>0.05
Diastolic (mmHg)	73 ± 2	75 ± 2	>0.05	75 ± 3	71 ± 3	>0.05	>0.05	>0.05	>0.05	>0.05
Heart Rate (bpm)	69 ± 4	68 ± 3	>0.05	70 ± 2	66 ± 3	>0.05	>0.05	>0.05	>0.05	>0.05
Body Composition										
Height (cm)	164.1 ± 2.2			165.1 ± 1.9			>0.05			
Weight (kg)	93.25 ± 5.83	94.17 ± 5.76	>0.05	89.80 ± 5.25	90.43 ± 5.41	>0.05	>0.05	>0.05	>0.05	>0.05
BMI (kg/m²)	34.5 ± 1.9	34.9 ± 1.9	>0.05	33.0 ± 2.1	33.3 ± 2.1	>0.05	>0.05	>0.05	>0.05	>0.05
Waist (cm)	98.8 ± 3.98	97.2 ± 4.1	>0.05	97.5 ± 4.8	96.2 ± 4.1	>0.05	>0.05	>0.05	>0.05	>0.05
Hip (cm)	115.8 ± 4.0	114.3 ± 4.2	>0.05	109.1 ± 4.1	108.3 ± 3.6	>0.05	>0.05	>0.05	>0.05	>0.05
Waist to Hip Ratio	0.85 ± 0.02	0.85 ± 0.02	>0.05	0.90 ± 0.03	0.89 ± 0.03	>0.05	>0.05	>0.05	>0.05	>0.05
Thigh (cm)	58.5 ± 1.4	56.9 ± 1.7	>0.05	53.7 ± 2.4	54.2 ± 2.6	>0.05	>0.05	>0.05	>0.05	>0.05
Total Fat (%)	43.25 ± 3.06	42.33 ± 2.84	>0.05	38.33 ± 3.59	37.61 ± 3.71	**<0.05**	>0.05	>0.05	**<0.05**	>0.05
Fat Free Mass (kg)	49.22 ± 3.19	50.86 ± 3.32	**<0.05**	49.25 ± 2.80	50.00 ± 2.89	>0.05	>0.05	>0.05	**<0.05**	>0.05
Leg Fat Free Mass (kg)	18.25 ± 1.26	19.16 ± 1.39	**<0.05**	17.39 ± 1.07	18.02 ± 1.03	>0.05	>0.05	>0.05	**<0.05**	>0.05
Leg Fat (%)	40.78 ± 3.56	39.61 ± 3.35	**<0.05**	32.34 ± 3.78	31.27 ± 3.78	**<0.05**	>0.05	>0.05	**<0.05**	>0.05
Android Fat (%)	49.99 ± 3.45	49.17 ± 3.17	>0.05	45.88 ± 4.58	45.67 ± 4.76	>0.05	>0.05	>0.05	>0.05	>0.05
Gynoid Fat (%)	44.62 ± 3.17	43.28 ± 3.00	**<0.05**	36.06 ± 4.08	34.79 ± 4.09	**<0.05**	>0.05	>0.05	**<0.05**	>0.05
Substrate Utilization										
Respiratory Quotient	0.77 ± 0.02	0.77 ± 0.02	>0.05	0.77 ± 0.01	0.74 ± 0.02	>0.05	>0.05	>0.05	>0.05	>0.05
Resting Energy Expenditure (kcal/day)	1703 ± 83	1781 ± 95	**<0.05**	1808 ± 112	1861 ± 113	>0.05	>0.05	>0.05	**<0.05**	>0.05
REE/BW (kcal/kg/day)	18.4 ± 0.7	19.1 ± 0.7	>0.05	20.3 ± 0.9	20.9 ± 1.2	>0.05	>0.05	>0.05	>0.05	>0.05
REE/FFM (kcal/kg/day)	35.8 ± 0.8	36.3 ± 1.1	>0.05	36.4 ± 1.0	36.9 ± 3.3	>0.05	>0.05	>0.05	>0.05	>0.05
Glycemic Control										
Fasting Glucose (mg/dL) [OGTT]	94.0 ± 2.6	97.4 ± 2.2	>0.05	100.2 ± 6.2	97.4 ± 3.0	>0.05	>0.05	>0.05	>0.05	>0.05
120-Minute Glucose (mg/dL)	135.7 ± 8.4	133.5 ± 5.6	>0.05	164.2 ± 20.5	145.6 ± 14.1	>0.05	>0.05	>0.05	>0.05	>0.05
120-Minute AUC	285.93 ± 13.77	284.77 ± 7.81	>0.05	331.11 ± 27.35	313.37 ± 22.20	>0.05	>0.05	>0.05	>0.05	>0.05
180-Minute AUC	397.56 ± 16.39	395.29 ± 9.59	>0.05	461.46 ± 38.69	433.81 ± 27.89	>0.05	>0.05	>0.05	>0.05	>0.05
Hemoglobin A1C (%)	5.3 ± 0.1	5.2 ± 0.1	>0.05	5.6 ± 0.2	5.4 ± 0.2	>0.05	>0.05	>0.05	>0.05	>0.05
Fasting Glucose (mg/dL)	90.1 ± 2.4	91.9 ± 1.8	>0.05	97.4 ± 6.8	94.9 ± 3.1	>0.05	>0.05	>0.05	>0.05	>0.05
Fasting Insulin (µIU/mL)	12.2 ± 2.3	14.2 ± 2.1	**<0.05**	17.4 ± 5.2	17.7 ± 6.4	>0.05	>0.05	>0.05	>0.05	**<0.05**
C-Peptide (ng/mL)	2.8 ± 0.3	2.8 ± 0.3	>0.05	3.0 ± 0.6	3.1 ± 0.5	>0.05	>0.05	>0.05	>0.05	>0.05
HOMA-IR	2.79 ± 0.58	3.30 ± 0.54	>0.05	4.76 ± 1.81	3.08 ± 1.43	**<0.05**	>0.05	>0.05	>0.05	**<0.05**
QUICKI-IS	0.34 ± 0.01	0.33 ± 0.01	>0.05	0.33 ± 0.02	0.35 ± 0.01	**<0.05**	>0.5	>0.05	>0.05	**<0.05**
24-Hour Glucose (mg/dL) (RT-10 R+N-7)	116.7 ± 2.3	117.8 ± 3.7	>0.05	119.8 ± 3.2	127.9 ± 8.6	>0.05	>0.05	>0.05	**<0.05**	>0.05
Glucose Standard Deviation (mg/dL) (RT-10 R+N-7)	17.2 ± 0.7	17.0 ± 1.0	>0.05	17.2 ± 1.1	16.9 ± 1.8	>0.05	>0.05	>0.05	>0.05	>0.05
Minimum Glucose (mg/dL) (RT-10 R+N-7)	80.4 ± 3.0	82.7 ± 4.6	>0.05	84.1 ± 3.0	98.6 ± 10.2	>0.05	>0.05	>0.05	**<0.05**	>0.05
Maximum Glucose (mg/dL) (RT-10 R+N-7)	175.6 ± 6.2	174.8 ± 8.7	>0.05	177.0 ± 6.2	184.9 ± 11.9	>0.05	>0.05	>0.05	>0.05	>0.05
Glucose Fluctuation (mg/dL) (RT-10 R+N-7)	95.3 ± 7.1	92.1 ± 7.7	>0.05	92.9 ± 4.93	86.3 ± 8.0	>0.05	>0.05	>0.05	>0.05	>0.05
Time Above Range (mins) (RT-10 R+N-7)	149.1 ± 33.6	215.5 ± 72.1	>0.05	221.4 ± 50.0	348.6 ± 185.9	>0.05	>0.05	>0.05	>0.05	>0.05
Time Below Range (mins)	0.0 ± 0.0	2.7 ± 1.8	>0.05	0.0 ± 0.0	0.0 ± 0.0	>0.05	>0.05	>0.05	>0.05	>0.05

(RT-10 R+N-7)										
Glucose Management Index (%) (RT-10 R+N-7)	6.1 ± 0.1	6.1 ± 0.1	>0.05	6.2 ± 0.1	6.4 ± 0.2	>0.05	>0.05	>0.05	**<0.05**	>0.05
Coefficient of Variation (%) (RT-10 R+N-7)	14.7 ± 0.5	14.4 ± 0.8	>0.05	14.1 ± 0.6	13.6 ± 1.7	>0.05	>0.05	>0.05	>0.05	>0.05
Time in Range (min) (RT-10 R+N-7)	1294.1 ± 33.9	1216.8 ± 70.8	>0.05	1218.6 ± 62.0	1091.4 ± 185.9	>0.05	>0.05	>0.05	**<0.05**	>0.05
Exercise										
1 Repetition Maximum (kg)	83.04 ± 14.99	113.44±17.91	**<0.05**	97.16±9.70	119.19 ± 10.81	**<0.05**	>0.05	>0.05	**<0.05**	>0.05
1RM/BW (kg)	0.83 ± 0.17	1.14±0.20	**<0.05**	1.04±0.12	1.29 ± 0.15	**<0.05**	>0.05	>0.05	**<0.05**	>0.05
1RM/Total FFM (kg)	1.43 ± 0.22	1.97±0.25	**<0.05**	1.78±0.16	2.19 ± 0.18	**<0.05**	>0.05	>0.05	**<0.05**	>0.05
1RM/Leg FFM (kg)	3.88 ± 0.59		**<0.05**	5.09 ± 0.41		**<0.05**	>0.05	>0.05	**<0.05**	>0.05
Grip Strength (kg)	71.63 ± 6.73	72.54±7.01	>0.05	71.06±7.29	73.56 ± 7.15	>0.05	>0.05	>0.05	>0.05	>0.05
Aerobic Capacity (L/min)	2.45 ± 0.18	2.54±0.18	>0.05	2.19±0.34	2.54 ± 0.36	**<0.05**	>0.05	>0.05	**<0.05**	>0.05

Data are presented as Mean±SEM. Bold text represents significance ($p<0.05$). When the number of participants is less than the total, it is indicated under the title of the variable. Fasting blood glucose represents the value obtained via lancet prick. Fasting glucose [OGTT] represents glucose values measured by finger prick. Abbreviations: BMI- body mass index; mmHg- millimeters of mercury; bpm- beats per minute; cm- centimeters; kg- kilograms; kcal- kilocalories; mg- milligrams; dL- deciliter; µIU/mL- micro-international units per milliliter; ng- nanograms; mins- minutes; %- percentage- L- liters; REE- resting energy expenditure; BW- bodyweight; FFM- fat free mass; AUC- area under the curve; HOMA-IR- Homeostatic Model Assessment of Insulin Resistance; QUICKI-IS- Quantitative Insulin Sensitivity Check Index

8 WEEKS OF SUPERIMPOSED TRAINING LED TO GREATER IMPROVEMENTS IN INSULIN SENSITIVITY THAN RESISTANCE TRAINING

While fasting glucose (**Table 4**) and C-peptide remained unchanged (**Figure 4a**), change in C-peptide was significantly greater in the superimposed NMES on resistance training group (**Figure 4b).** Insulin levels significantly increased in the resistance training group compared to pre-training levels and compared to change in insulin levels between groups (**Figure 4c and 4d** respectively). HOMA-IR significantly decreased (**Figure 4e and 4f**) and QUICKI-IS significantly increased in the superimposed NMES on resistance training group compared to pre-training levels and compared to change in both HOMA-IR and QUICKI-IS levels between groups (**Figure 4g and 4h**) reflecting improvement in insulin sensitivity.

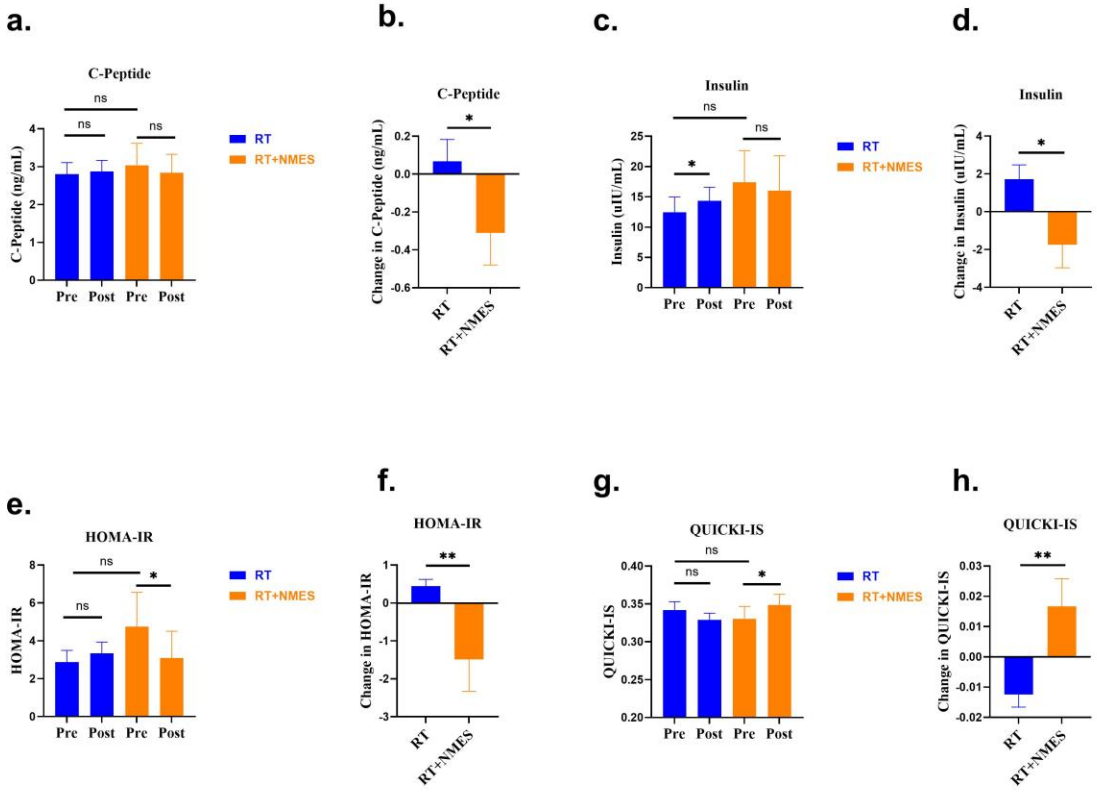

Figure 4. Insulin sensitivity following 8 weeks of training. Pre- and postintervention C-peptide (a) and (b), insulin (c) and (d), HOMA-IR (e) and (f), QUICKI-IS (g) and (h).*p<0.05, **p<0.01. Data are presented as mean ± SEM. Abbreviations- ng- nanograms; mL- milliliter; ns- not significant- µIU- micro international units; HOMA-IR- homeostatic model assessment of insulin resistance; QUICKI-IS- quantitative insulin sensitivity check index; RT- resistance training; RT+NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

The results of the OGTT curves showed that 90 minute blood glucose was significantly lower in the superimposed NMES on resistance group compared to pre-training levels (**Figure 5**).The results of the OGTT showed that while fasting blood glucose (OGTT) remained unchanged (**Figure 6a**), when changes in fasting glucose were compared, there was a trend for a greater decrease in fasting blood glucose (p= 0.09) in the superimposed NMES on resistance training group compared to resistance training group (**Figure 6b**). There was a trend for a lower 120-minute blood glucose for the superimposed NMES on resistance training group compared to pre-training levels while there were no changes in the resistance training group (**Figure 5 and 6c**) and no difference in the degree of change between groups (**Figure 6d**).

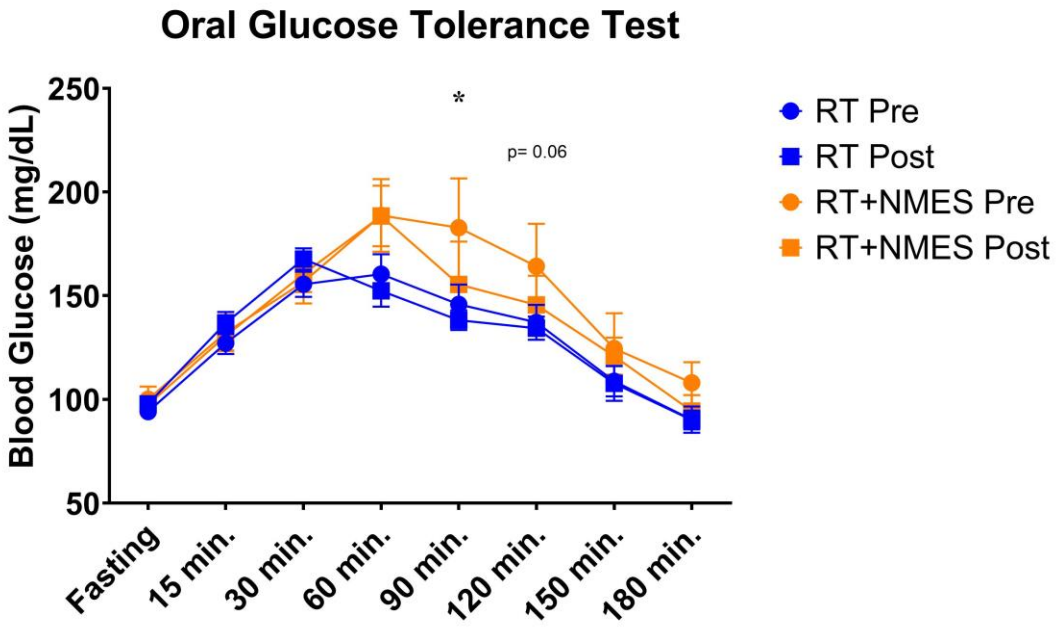

Figure 5. Oral glucose tolerance test curves for both groups pre- and post-training. *p<0.05. Data are presented as mean ± SEM. Abbreviations- mg- milligrams; dL- deciliter; min- minutes; RT- resistance training; RT+NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

Glucose AUC remained unchanged after 2 hours (**Figure 6e**) and 3 hours (**Figure 6g**) for both groups. Both groups also had no changes in HbA1c (p= 0.12; **Table 4**).

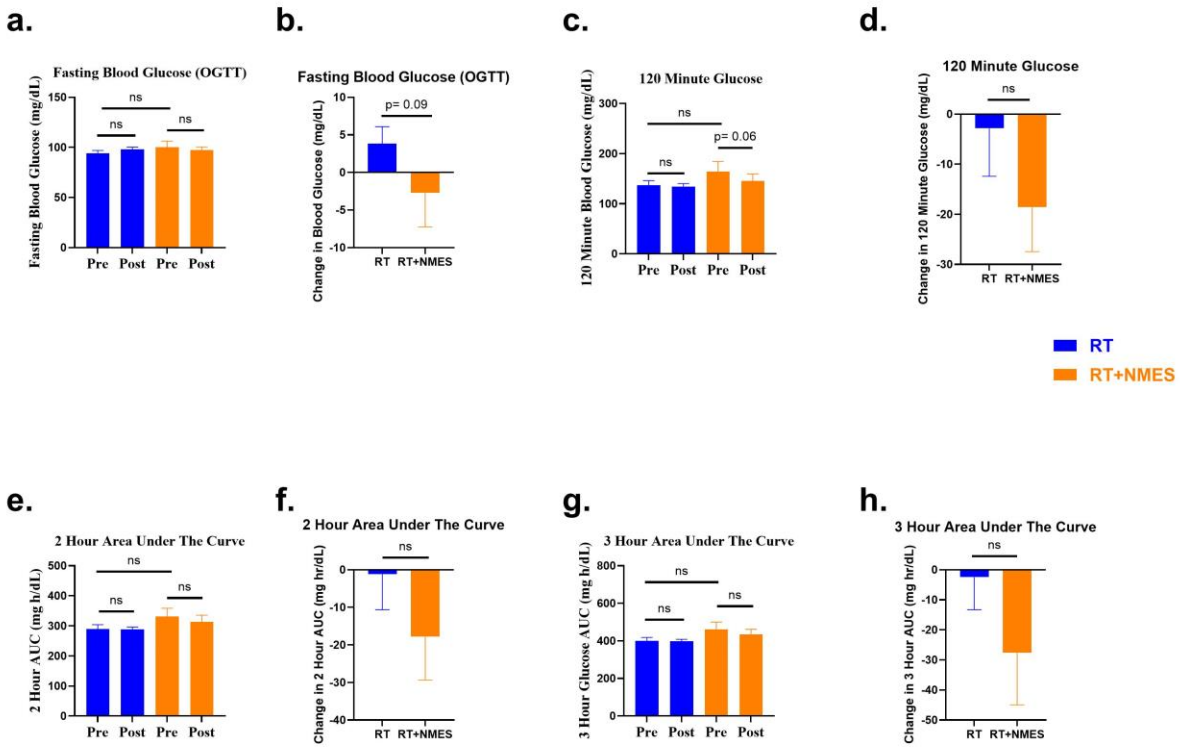

Figure 6. Oral glucose tolerance test results after 8 weeks of training. Pre- and postintervention fasting glucose (a) and (b), 120-minute glucose (c) and (d), 2-hour area under the curve (e) and (f), and 3-hour area under the curve (g) and (h). *p<0.05. Data are presented as mean ± SEM. Abbreviations- ns- not significant; mg- milligrams; dL- deciliter; AUC- area under the curve; RT- resistance training; RT+NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

There was no change in 24-hour glucose (**Figure 7a and b**), glycemic variability measured by glucose standard deviation (**Figure 7c and d**) and coefficient of variation (**Figure 7e and f**), glucose time in range (**Figure 7g and h**) nor minimum glucose, maximum glucose, glucose fluctuation, time above range, time below range, or glucose management index (**Table 4)**.

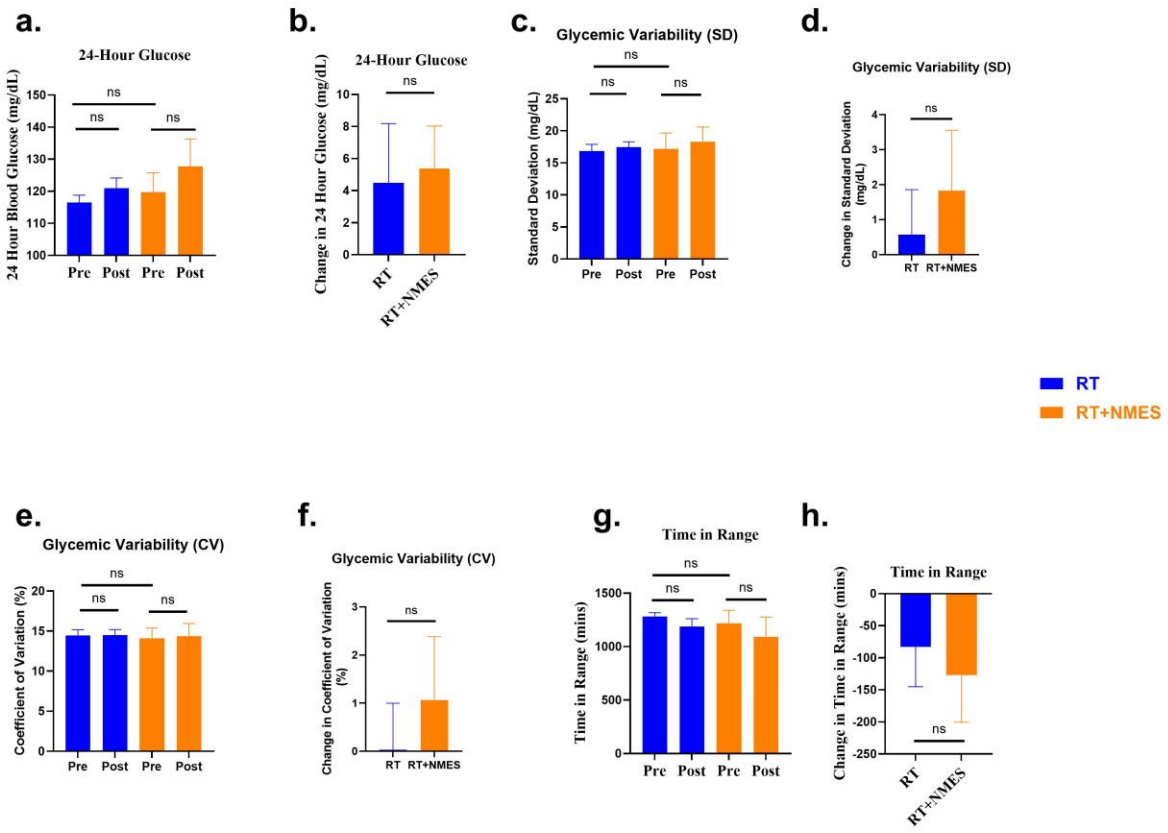

Figure 7. Glycemic control measured by continuous glucose monitoring after 8 weeks of training. Pre- and postintervention 24-hour glucose (a) and (b), glycemic variability measured by standard deviation (c) and (d), glycemic variability measured by coefficient of variation (e) and (f), and time in range (g) and (h). *p<0.05. Data are presented as mean ± SEM. Abbreviations- ns- not significant; SD- standard deviation; CV- coefficient of variation; mg- milligrams; dL- deciliter; mins- minutes; pre- preintervention; post- postintervention; RT- resistance training; RT+NMES- superimposed NMES on resistance training.

INCREASED RESTING ENERGY EXPENDITURE FOLLOWING 8 WEEKS OF RESISTANCE TRAINING WITH NO CHANGE IN SUBSTRATE UTILIZATION

Following 8 weeks ot training, there was no significant change in substrate utilization in either group (**Figure 8a and 8b**). There was a significant increase in resting energy expenditure in the resistance training group (**Figure 8c** and **8d**).

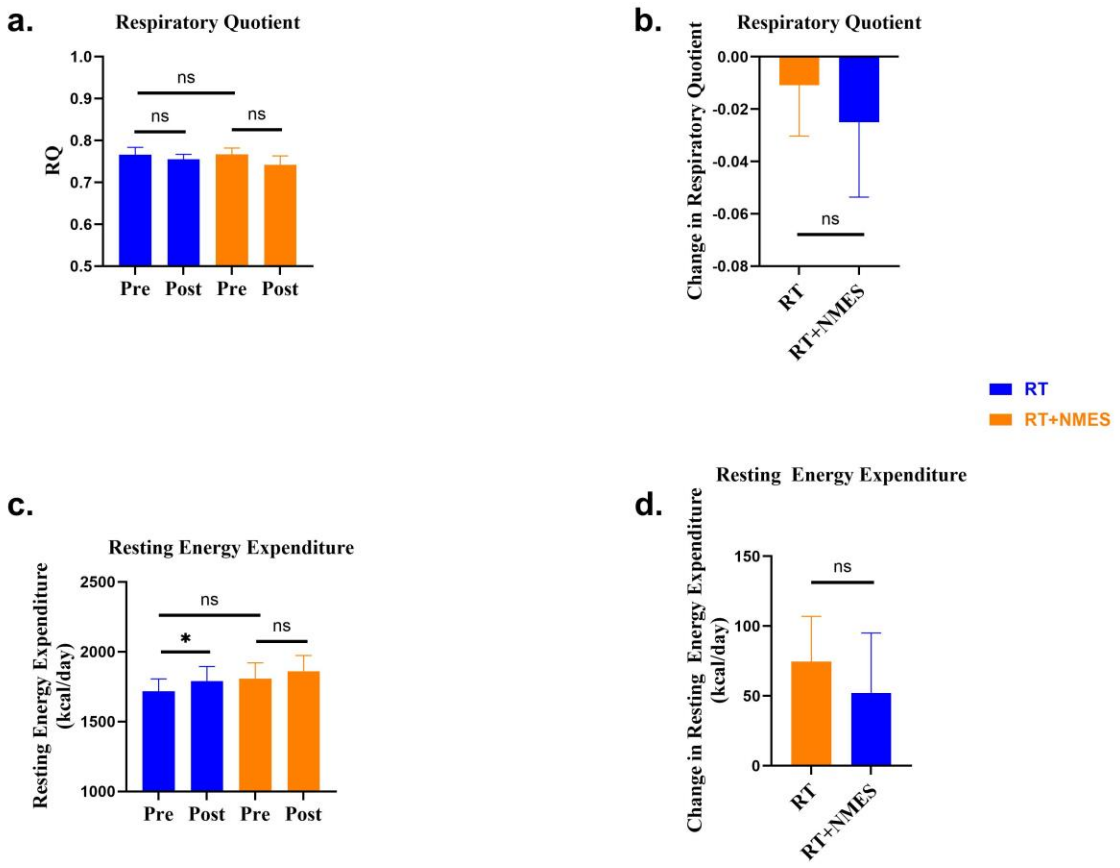

Figure 8. Substrate utilization and resting energy expenditure after 8 weeks of training. Pre- and postintervention substrate utilization (a) and (b) and resting energy expenditure (c) and (d) *p<0.05. Data are presented as mean ± SEM. Abbreviations- RQ- respiratory quotient; kcal- kilocalories; ns- not significant; pre- preintervention; post- postintervention; RT- resistance training; RT+NMES- superimposed NMES on resistance training.

BOTH GROUPS SIMILARLY INCREASED LOWER BODY STRENGTH FOLLOWING 8 WEEKS OF TRAINING

Lower body strength measured by 1 repetition maximum leg extension was similar between both groups at baseline (**Table 4)**. Following 8 weeks of resistance training with and without superimposing NMES, both groups significantly increased lower body strength in absolute measures (**Fig 9a**) with no significant difference in the degree of change between groups (**Figure 9b**).

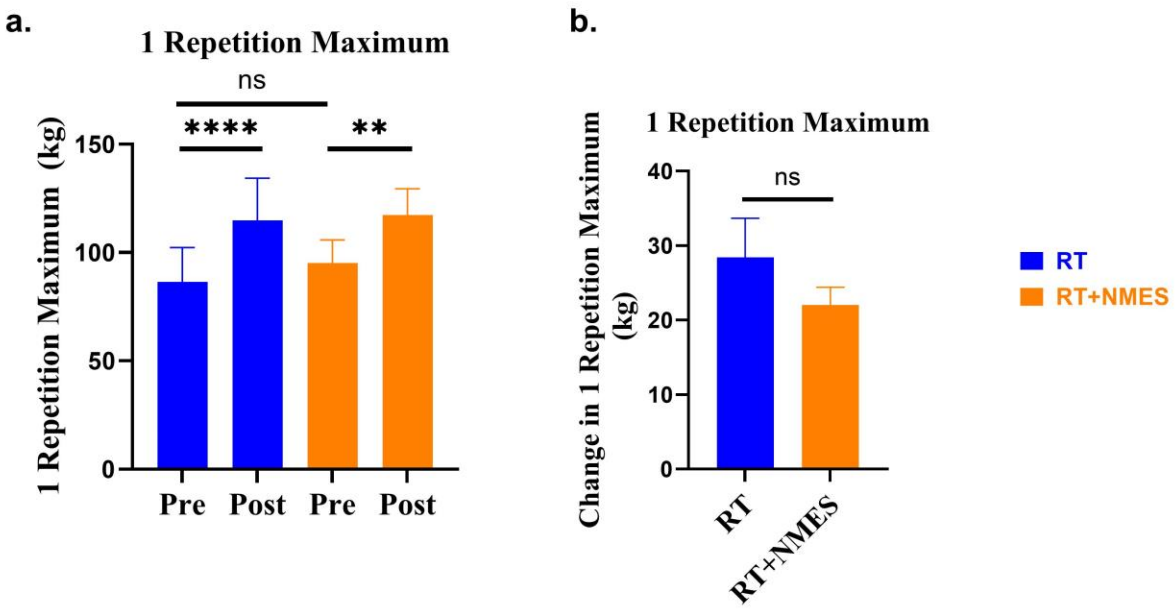

Figure 9. Lower body strength after 8 weeks of training. Pre- and postintervention lower body strength measured by 1 repetition maximum leg extension (a) and (b).**p<0.01, , ****p<0.0001. Data are presented as mean ± SEM. Abbreviations- kg- kilograms; ns- not significant; RT- resistance training; RT+NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

When normalized for bodyweight, total fat free mass, and leg fat free mass, there was a significant increase in lower body strength for both groups compared to pre-training (**Table 4**). There were no significant difference in grip strength at baseline or pre- to post-training in either group (**Figure 10a and 10b**)

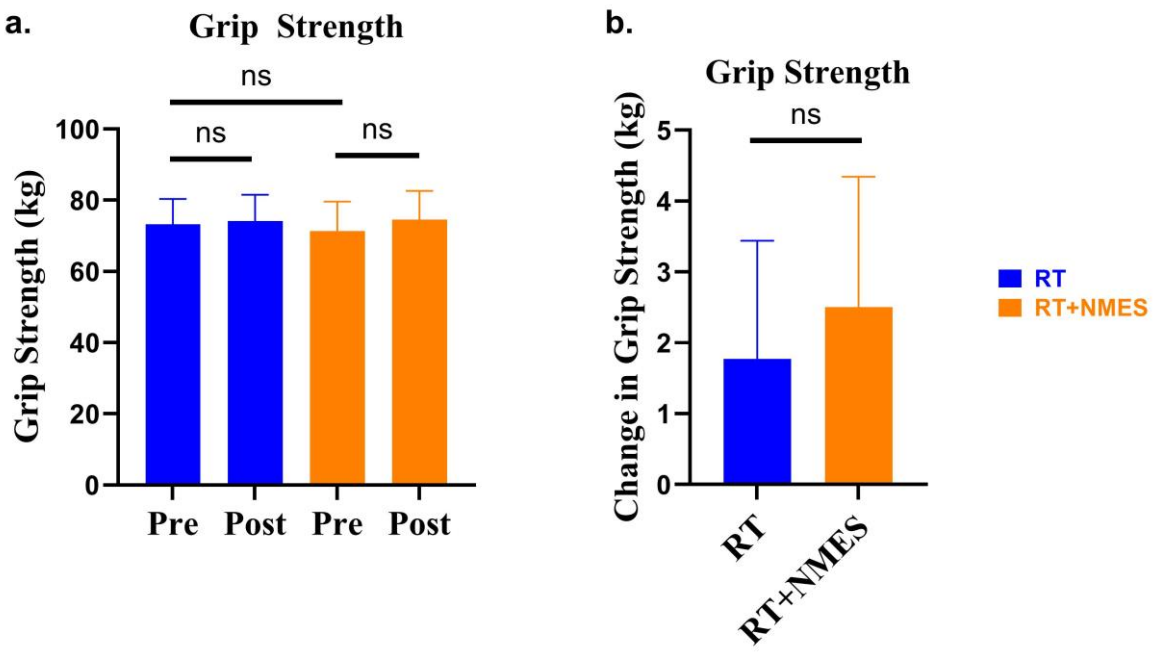

Figure 10. Grip strength after 8 weeks of training. Pre- and postintervention grip strength measured by handheld dynamometer (a) and (b)*p<0.05. Data are presented as mean ± SEM. Abbreviations- kg- kilograms; ns- not significant; RT- resistance training; RT +NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

The results for aerobic capacity demonstrated a significant increase in the superimposed NMES on resistance training group compared to pre-training, while the resistance training group did not show a significant difference (**Figure 11a)**. Superimposed NMES on resistance training also resulted in a greater degree of change in aerobic capacity compared to resistance training (**Figure 11b**).

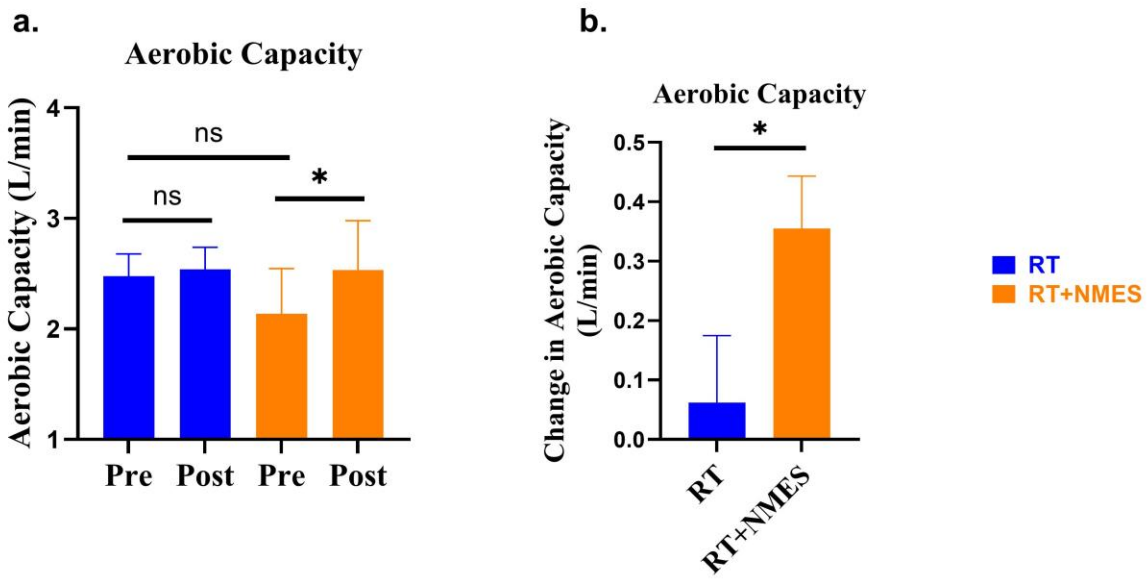

Figure 11. Aerobic capacity after 8 weeks of training. Pre- and postintervention aerobic capacity (a) and (b).*p<0.05. Data are presented as mean ± SEM. Abbreviations- L- liters; min- minute; ns- not significant; RT- resistance training; RT +NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

BOTH GROUPS SIMILARLY IMPROVED BODY COMPOSITION FOLLOWING 8 WEEKS OF TRAINING

Fat free mass showed significant increases in the resistance training group but not the superimposed group in both total fat free mass (**Figure 12a**) and leg fat free mass (**Figure 12e.**). However, when comparing delta values, there was no significant difference between groups for either total fat free mass (**Figure 12b**) or leg fat free mass (**Figure 12f**). Total fat mass (**Figure 12c and d**) and leg fat mass (**Figure 12g and h**) had no significant changes.

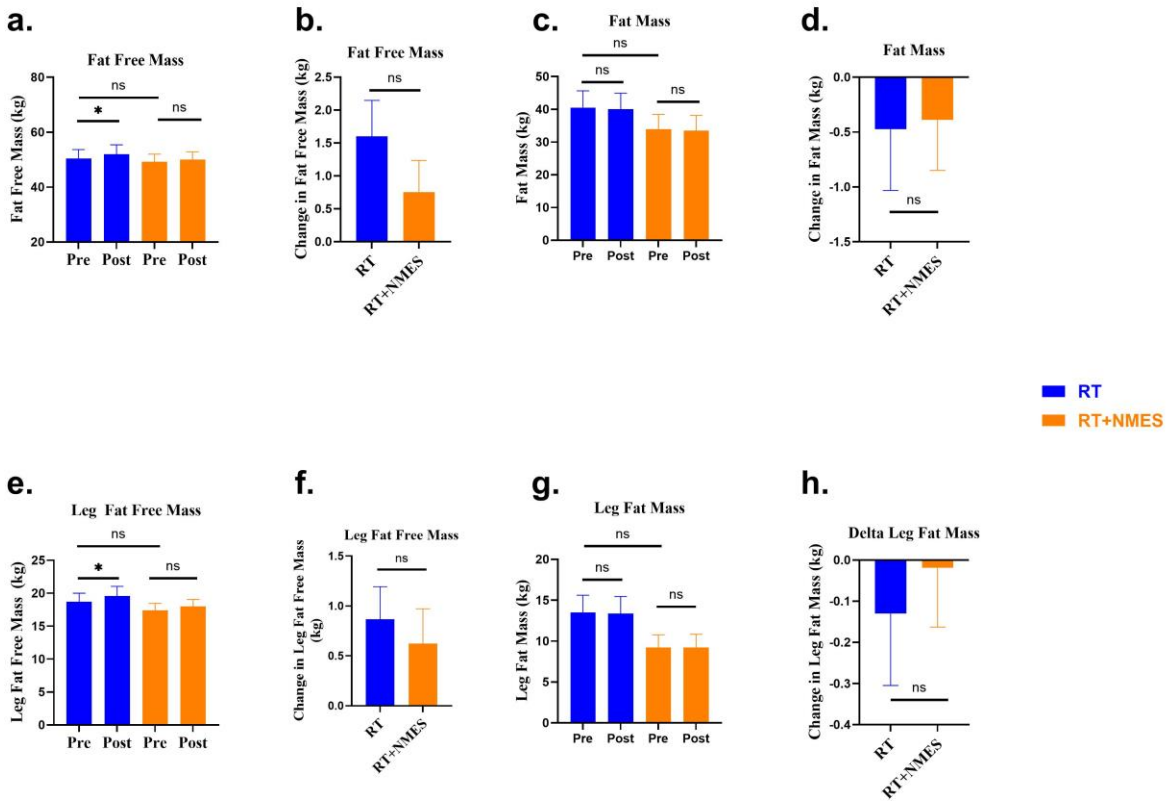

Figure 12. Muscle and fat mass after 8 weeks of training. Pre- and postintervention fat free mass (a) and (b), fat mass (c) and (d), leg fat free mass (e) and (f), and leg fat mass (g) and (h). *p<0.05. Data are presented as mean ± SEM. Abbreviations- kg- kilograms; ns- not significant; RT- resistance training; RT +NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

Total body fat percentage showed a decrease in the superimposed NMES on resistance training group with a trend for a decrease in the resistance training group (**Figure 13a and 13b).** Leg fat percentage decreased significantly in both groups with no difference between groups (**Figure 13c and 13d).** Gynoid fat percentage also decreased significantly in both groups with no difference between groups (**Figure 13g and 13h**) while android fat percentage showed no significant change (**Figure 13e and 13f**).

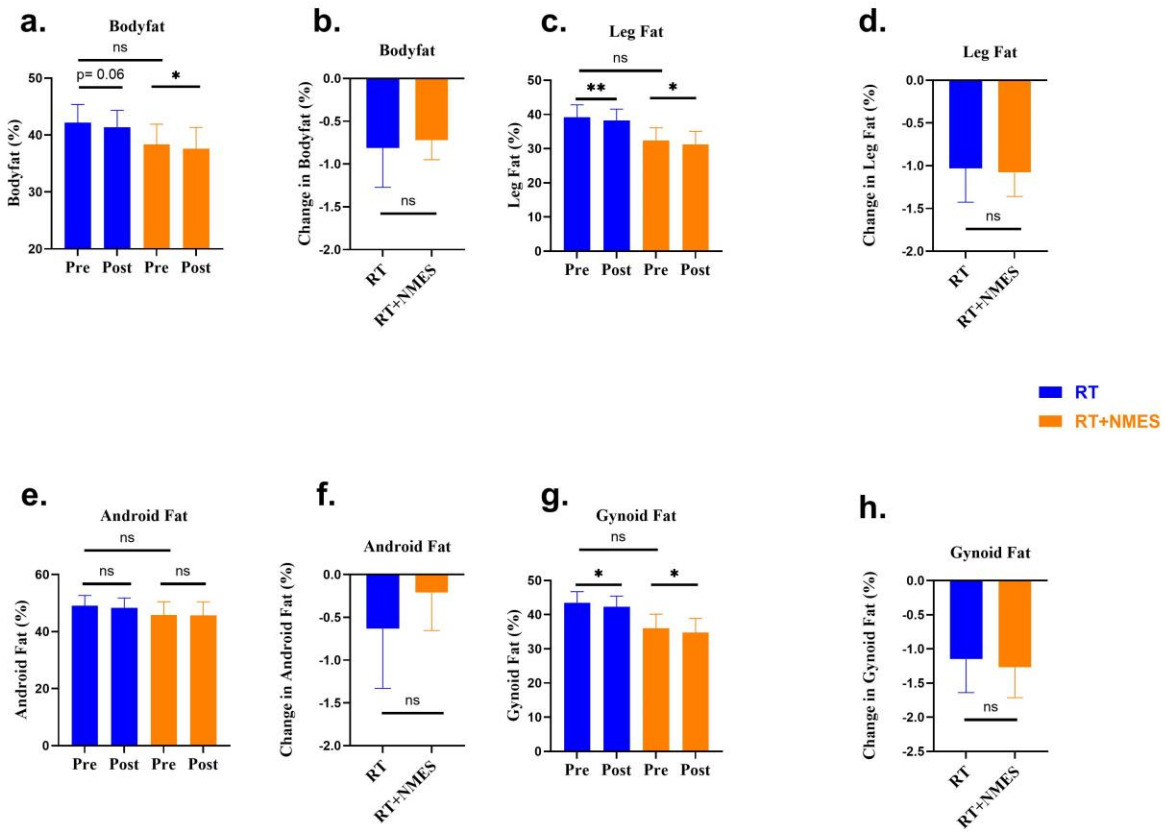

Figure 13. Regional fat percentage following 8 weeks of training. Pre- and postintervention bodyfat percentage expressed as total body fat (a) and (b), leg fat (c) and (d), android fat (e) and (f), and gynoid fat (g) and (h). *p<0.05, **p<0.01. Data are presented as mean ± SEM. Abbreviations- ns- not significant; RT- resistance training; RT +NMES- superimposed NMES on resistance training; pre- preintervention; post- postintervention.

Circumference measurements showed that both groups similarly decreased waist circumference while hip circumference and the waist to hip ratio remained unchanged (**Table 4**). Thigh circumference decreased in the resistance training group while the superimposed NMES on resistance training group had no change. Similarly, bodyweight and BMI were also unchanged in either group (**Table 4)**.

DISCUSSION

The purpose of this study was to determine if there was an additive effect in superimposing neuromuscular electrical stimulation on resistance training for glycemic control, resting energy expenditure, substrate utilization, muscle mass and muscular strength in a population that was untrained with overweight to obesity. Our data indicates that eight weeks of superimposed NMES on resistance training led to greater improvements in insulin sensitivity, as measured by HOMA-IR, QUICKI-IS, fasting and 120-minute blood glucose, than conventional resistance training. Despite these improvements in insulin sensitivity, resting energy expenditure only increased in the resistance training group with no change in substrate utilization in either group. There were also similar improvements in body composition and muscular strength for both groups. To our knowledge this is the first comprehensive, longitudinal study comparing superimposed NMES on resistance training to conventional resistance training for glycemic control, substrate utilization and resting energy expenditure.

While resistance training and NMES have been shown to improve glycemic control through a variety of assessment techniques including OGTT, HOMA-IR, fasting glucose and insulin levels, to our knowledge, only one study has compared the acute effects of superimposed NMES on resistance exercise to resistance exercise (Holzer et al., 2021). In this study they found that following a 20-minute bout of superimposed NMES on resistance, resistance, or aerobic exercise, postprandial glucose responses, glucose AUC curves, and glucose excursions were similar in all conditions. While there were comparable results for superimposed NMES on resistance and conventional resistance exercise in an acute setting, the current study found that following 8 weeks of superimposed NMES on resistance training, there were greater improvements in insulin sensitivity compared to a resistance training group. This current study is of clinical significance, demonstrating improved insulin sensitivity after 8 weeks of superimposed NMES on resistance training in a population that is at-risk, with overweight to obesity, and predominantly Hispanic.

While there are no previous studies that investigated superimposed NMES on resistance training, previous longitudinal studies utilizing resistance training and NMES independently, have demonstrated improvements in glycemic control and insulin sensitivity (Bacchi et al., 2013; DeFronzo & Beckles, 1979; Eikenberg et al., 2016; Galvan et al., 2022; Jiahao et al., 2021; Vivodtzev et al., 2013). When examining resistance training, following 12 weeks of resistance training, while fasting glucose was unchanged, 120-minute glucose during an OGTT was significantly reduced (Eikenberg et al., 2016). Our findings are in line with this as fasting glucose remained unchanged in both groups, but 120-minute blood glucose did show a trend for decreasing in the superimposed group. Similarly, in a meta-analysis, it was found that resistance training decreased insulin resistance measured by HOMA-IR in healthy older adults without T2D after an intervention of 12 or more weeks (Jiahao et al., 2021), while interventions less than 12 weeks showed no change. While our study population was primarily young adults, it was in line with this finding as HOMA-IR decreased in the superimposed NMES on resistance training group. Contrary to the 12 or more weeks where decreased HOMA-IR was seen (Jiahao et al., 2021), our study had similar results in 8 weeks. Like resistance training, NMES has been shown to decrease HOMA-IR compared to baseline following 6 weeks of NMES (Vivodtzev et al., 2013). In patients with T2D, after 10 weeks of NMES, fasting glucose and HbA1C also decreased (van Buuren et al., 2015). In the current study, while there were no significant changes in fasting blood glucose in either group, when degree of change in fasting glucose was compared, our study shows a trend for greater decreased fasting glucose in the superimposed NMES on resistance training group. Lastly, a previous meta-analysis has demonstrated that NMES is effective in improving glycemic control in a variety of measures including fasting glucose, OGTT and HOMA-IR (Sanchez et al., 2023). In totality, our results are similar as demonstrated by the trends in lowering fasting glucose and 120-minute blood glucose and significant reduction in HOMA-IR and QUICKI-IS favoring the superimposed group.

Studies investigating glycemic control using continuous glucose monitoring are much more limited. There are no longitudinal studies measuring glycemic control with CGMs,

however, acute effects of both resistance exercise and NMES have been investigated. When examining resistance exercise, in a population with type 1 diabetes, following a bout of aerobic, resistance, or combined exercise, resistance and combined exercise groups reduced 24-hour glucose, while combined exercise decreased glucose variability (glucose standard deviation and coefficient of variation) (Minnock et al., 2020). Similarly, in a population with impaired glucose tolerance, taking insulin, or glucose lowering medications, average glucose and hyperglycemia prevalence was reduced in the 24 hours following a bout of resistance exercise (Van Dijk et al., 2012). When examining NMES, in a population with T2D, following a 60-minute bout of NMES, when tracked for 6 hours, blood glucose decreased at 2, 3, and 4 hours post stimulation with no change in glucose variability (coefficient of variation, standard deviation, mean amplitude of glycemic excursions) (Macedo et al., 2024). As mentioned previously, there are no longitudinal studies investigating glycemic control using CGMs following RT or NMES. Our results did not find any significant differences in the CGM parameters following 8 weeks of either superimposed or resistance training. Previously, both RT and NMES have been shown to improve glycemic control (Bacchi et al., 2013; Bajpeyi et al., 2020; DeFronzo & Beckles, 1979; Dunstan et al., 2002; Eikenberg et al., 2016; Galvan et al., 2022; Reid et al., 2010; Sigal et al., 2007). A potential explanation for the lack of changes could be the small sample size. While 24 total participants were included in this study, not all participants had CGM data as a total of 17 were included in the analyses with only 7 of those being in the superimposed group. This could be due to participants either discarding the CGM themselves or the CGMs being misplaced before data was extracted. Another limitation of our study was that participants were not supervised while they consumed a standard diet when the CGM data were collected. While we provided the meals for 3 days pre and postintervention, often participants were unsupervised and ate outside of the lab setting. A checklist was also provided to indicate what time participants ate each meal and whether they finished each meal. It may have been possible that they ate extra food or simply did not follow the diet as instructed. While no significant changes were found using CGMs, this is the first study performed to compare the longitudinal effects of

superimposed NMES on resistance training on glycemic control in comparison to a resistance training group.

In contrast to the improvement in insulin sensitivity for the superimposed NMES on RT group, changes in resting energy expenditure favored the resistance training group. Following eight weeks of resistance training, we found increased resting energy expenditure with no change in substrate utilization. To our knowledge, there are no studies that compared superimposed NMES on resistance training to resistance training for either variable. Longitudinal studies investigating substrate utilization and energy expenditure with NMES are also limited and to our knowledge, few studies have investigated this (Galvan et al., 2022; Gorgey et al., 2021; Kemmler et al., 2010). Following 4 weeks of NMES performed 3 time per week, there was no changes found for substrate utilization or resting energy expenditure (Galvan et al., 2022). When performed for a longer period of 12 weeks, there were also no changes in substrate utilization or energy expenditure (Gorgey et al., 2021). However, resting metabolic rate which is synonymous with resting energy expenditure was maintained while a control group showed a decrease following 16 weeks of whole body NMES (Kemmler et al., 2010). While no significant increase in resting energy expenditure or improvements in substrate utilization have been found, longitudinal studies using NMES are still limited.

In contrast to research utilizing NMES on substrate utilization and energy expenditure, the evidence surrounding resistance training on these measurements is more established. Following 16 weeks of whole-body resistance training, there were increases in resting energy expenditure and diet induced thermogenesis with a decrease in RQ found, indicating improved substrate utilization (Treuth et al., 1995). After a period of 6 months of whole-body resistance training, increases in both resting and 24-hour energy expenditure were found (Kirk et al., 2009; Lemmer et al., 2001). Similarly, when performed for a longer period of 9 months, increased fat oxidation and mitochondrial content have also been found (Sparks et al., 2013). Our study found increased resting energy expenditure in the resistance training group with no significant changes in substrate utilization for either group. The lack of significant change in the superimposed

NMES on resistance training group may be explained by the small sample size as there were only 10 participants with pre- and postintervention data. The increase in resting energy expenditure for the RT group is significant however, as resting energy expenditure accounts for 60-70% of total energy expenditure per day (Lam & Ravussin, 2016; Poehlman, 1989). Increasing resting energy expenditure may reduce T2D risk as obesity, characterized by chronic energy imbalance with caloric intake exceeding energy expenditure (Lam & Ravussin, 2016), is the leading risk factor for T2D (Barnes, 2011).

In conjunction with energy expenditure, body composition is typically measured (Cunningham, 1991). In contrast to resting energy expenditure, our study found improvements in body composition in both the superimposed NMES on resistance and resistance training groups using DEXA and anthropometric measurements. Previous studies have found significantly greater improvement in body composition/muscle mass following superimposed NMES on resistance training using ultrasound (Benavent-Caballer et al., 2014; Evangelista et al., 2019). To our knowledge, no previous study comparing superimposed NMES on RT to resistance training determined body composition/muscle mass via DEXA scan. When examining body fat percentage values, the superimposed NMES on resistance training group significantly decreased total bodyfat percentage while the resistance training group had a trend for reducing bodyfat percentage. Both groups similarly decreased leg fat and gynoid fat percentages with no significant changes in android fat percentage. Our results are in line with previous findings as when used separately, both resistance training and NMES have been shown to decrease bodyfat using a DEXA scan (Li et al., 2018; Lopez et al., 2022; Miyamoto et al., 2018). Despite there being similar increases in quadricep muscle strength, there was only a significant increase in both fat free mass and leg fat free mass in the resistance training group. As previously mentioned, our lab conducted a meta-analysis comparing the effects of superimposed training to conventional resistance training for the improvement of muscle mass and muscular strength. While there was a significantly greater increase found for both variables in favor of superimposed training, a sensitivity analysis revealed that very high frequency (≥ 85 Hz) NMES

may be necessary to facilitate these greater increases. Our NMES protocol was set to a frequency of 50 Hz, so it is possible that the frequency was not high enough to lead to additive effects. Also, in the studies showing significant differences in muscle mass in the superimposed group, one study had an active population (Evangelista et al., 2019) while the other did not indicate and/or measure physical activity levels (Benavent-Caballer et al., 2014). The included population of our study was sedentary, with no differences in physical activity levels between groups. It has been shown that active populations are able to handle higher intensities of NMES (Gondin et al., 2011), and have a higher pain tolerance (Årnes et al., 2023; Naugle & Riley, 2014; Skogberg et al., 2022). Given the NMES intensity for our study was set to maximum tolerable intensity, pain tolerance may have limited the intensity of NMES participants could use. Lastly, while the DEXA scan can differentiate the body into different sections (arms, legs, trunk, etc.), it is not able to measure muscle groups individually. Given we only applied NMES to the quadricep muscles, it may be possible that differences could be found using other measurement methods such as ultrasound or magnetic resonance imaging that are able to measure muscle groups individually.

In contrast to our findings for muscle mass, we found increased aerobic capacity in the superimposed NMES on resistance training group while there was no significant difference for the resistance training group. In previous research, NMES has been shown to increase aerobic capacity when done at lower frequencies in both sedentary and active populations (Banerjee et al., 2005; Crognale et al., 2009). It has also been shown that stimulating lower body musculature is sufficient in increasing aerobic capacity (Gorgey et al., 2015; Griffin et al., 2009). A potential explanation could be histochemical changes in the stimulated muscles as NMES has been shown to increase capillary bed density, mitochondrial concentrations, oxidative enzymes and shift in muscle fiber type (Deley et al., 2005; Dobsák et al., 2006; Nuhr et al., 2004; Sheffler & Chae, 2007). Also, given the NMES protocol had the stimulation on for 10 seconds and off for 30 seconds throughout the training sessions and may be on during sets and between sets, there may have also been less rest time like aerobic training, leading to the increased aerobic capacity.

LIMITATIONS

There were limitations to be noted in this study. First this pilot study is limited by low sample size. It remains to be seen if there would be greater differences between groups with a larger sample size. Also, not all the included participants had full data due to either data not being measured/recorded, data not being saved and therefore lost, or data being misplaced. This further exacerbated the small sample size. Second, for the standard diet, while we provided all food to participants, they did not always eat in the laboratory. A large portion of participants were students, however, many worked outside of campus and were not able to come to the lab to eat each meal. Despite the lack of supervision, they were also provided with a checklist to indicate what time they ate each meal and whether they ate the entire amount. Due to this, we were under the assumption that they were only eating the standard diet on the days provided but there is no way to truly know whether they did or not. This could have played a factor in the glycemic control and substrate utilization results. However, most previous studies have investigated only one aspect of glycemic control. The strength of our study is that it comprehensively assessed glycemic control and insulin sensitivity through OGTT, CGM, and blood draws . Also, while one study has compared superimposed NMES on resistance exercise to resistance exercise for glycemic control, it was done in an acute setting and no studies have investigated substrate utilization or energy expenditure. Our study is the first to compare the longitudinal effects of superimposed NMES on resistance compared to resistance training for glycemic control, substrate utilization, and energy expenditure.

CONCLUSION

Our study found there was significantly greater improvements in insulin sensitivity following 8 weeks of superimposed NMES on resistance training compared to resistance training. Body composition demonstrated similar improvements while energy expenditure increased in the resistance training group and substrate utilization had no changes in either group. The potential impact of the study is that an at-risk population could improve their body composition and insulin sensitivity to reduce the risk of developing T2D in the future. Future directions may include a study of greater sample size, longer duration of intervention, and/or having a supervised diet potentially during the entire intervention.

REFERENCES

Abe, T., Dehoyos, D. V., Pollock, M. L., & Garzarella, L. (2000). Time course for strength and muscle thickness changes following upper and lower body resistance training in men and women. *European Journal of Applied Physiology and Occupational Physiology*, *81*(3), 0174. https://doi.org/10.1007/s004210050027

Abulhasan, J. F., Rumble, Y. L. D., Morgan, E. R., Slatter, W. H., & Grey, M. J. (2016). Peripheral Electrical and Magnetic Stimulation to Augment Resistance Training. *Journal of Functional Morphology and Kinesiology*, *1*(3), 328-342. https://doi.org/https://doi.org/10.3390/jfmk1030328

Agarwal, S. K. (2012). Cardiovascular benefits of exercise. *International Journal of General Medicine*, *5*(null), 541-545. https://doi.org/10.2147/IJGM.S30113

Aguiar, S. S., Sousa, C. V., Simões, H. G., Neves, R. V. P., Costa, F., de Souza, C. R., de Moraes, M. R., Prestes, J., Sales, M. M., Haro, A. S., Willardson, J. M., & Rosa, T. d.-S. (2018). Acute metabolic responses following different resistance exercise protocols. *Applied Physiology, Nutrition, and Metabolism*, *43*(8), 838-843. https://doi.org/https://doi.org/10.1139/apnm-2017-0771

Alkhayl, F. F. A., Ismail, A. D., Celis-Morales, C., Wilson, J., Radjenovic, A., Johnston, L., Welsh, P., Sattar, N., Gill, J. M. R., Preston, T., & Gray, S. R. (2022). Muscle protein synthesis and muscle/metabolic responses to resistance exercise training in South Asian and White European men. *Scientific Reports*, *12*(1). https://doi.org/10.1038/s41598-022-06446-7

Andersen, L. L., Saervoll, C. A., Mortensen, O. S., Poulsen, O. M., Hannerz, H., & Zebis, M. K. (2011). Effectiveness of small daily amounts of progressive resistance training for frequent neck/shoulder pain: randomised controlled trial. *Pain*, *152*(2), 440-446. https://doi.org/10.1016/j.pain.2010.11.016

Anderson, T., & Kearney, J. T. (1982). Effects of Three Resistance Training Programs on Muscular Strength And Absolute and Relative Endurance. *Research Quarterly for Exercise and Sport*, *53*(1), 1-7. https://doi.org/10.1080/02701367.1982.10605218

Årnes, A. P., Nielsen, C. S., Stubhaug, A., Fjeld, M. K., Johansen, A., Morseth, B., Strand, B. H., Wilsgaard, T., & Steingrímsdóttir, Ó. A. (2023). Longitudinal relationships between habitual physical activity and pain tolerance in the general population. *PLoS One*, *18*(5), e0285041. https://doi.org/10.1371/journal.pone.0285041

Babatunde, O. O., Jordan, J. L., Van der Windt, D. A., Hill, J. C., Foster, N. E., & Protheroe, J. (2017). Effective treatment options for musculoskeletal pain in primary care: A systematic overview of current evidence. *PLoS One*, *12*(6), e0178621. https://doi.org/10.1371/journal.pone.0178621

Bacchi, E., Negri, C., Targher, G., Faccioli, N., Lanza, M., Zoppini, G., Zanolin, E., Schena, F., Bonora, E., & Moghetti, P. (2013). Both resistance training and aerobic training reduce hepatic fat content in type 2 diabetic subjects with nonalcoholic fatty liver disease (the RAED2 randomized trial). *Hepatology*, *58*(4), 1287-1295. https://doi.org/10.1002/hep.26393

Bacchi, E., Negri, C., Zanolin, M. E., Milanese, C., Faccioli, N., Trombetta, M., Zoppini, G., Cevese, A., Bonadonna, R. C., Schena, F., Bonora, E., Lanza, M., & Moghetti, P. (2012). Metabolic Effects of Aerobic Training and Resistance Training in Type 2 Diabetic Subjects: A randomized controlled trial (the RAED2 study). *Diabetes Care*, *35*(4), 676-682. https://doi.org/https://doi.org/10.2337/dc11-1655

Bajpeyi, S., Galvan, M., Sanchez, M. J., Boyle, J. B., Min, K., Agullo, F. J., & Covington, J. D. (2020). 846-P: Improvement in Glucose Metabolism with Four Weeks of Neuromuscular Electrical Stimulation in Sedentary Adults. *Diabetes*, *69*(Supplement_1). https://doi.org/10.2337/db20-846-P

Bamman, M. M., Hill, V. J., Adams, G. R., Haddad, F., Wetzstein, C. J., Gower, B. A., Ahmed, A., & Hunter, G. R. (2003). Gender differences in resistance-training-induced myofiber hypertrophy among older adults. *J Gerontol A Biol Sci Med Sci*, *58*(2), 108-116. https://doi.org/10.1093/gerona/58.2.b108

Banerjee, P., Caulfield, B., Crowe, L., & Clark, A. (2005). Prolonged electrical muscle stimulation exercise improves strength and aerobic capacity in healthy sedentary adults. *Journal of Applied Physiology*, *99*(6), 2307-2311. https://doi.org/10.1152/japplphysiol.00891.2004

Barnes, A. S. (2011). The epidemic of obesity and diabetes: trends and treatments. *The Texas Heart Institute Journal*, *38*(2), 142-144.

Battelino, T., Danne, T., Bergenstal, R. M., Amiel, S. A., Beck, R., Biester, T., Bosi, E., Buckingham, B. A., Cefalu, W. T., Close, K. L., Cobelli, C., Dassau, E., Devries, J. H., Donaghue, K. C., Dovc, K., Doyle, F. J., Garg, S., Grunberger, G., Heller, S.,…Phillip, M. (2019). Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. *Diabetes Care*, *42*(8), 1593-1603. https://doi.org/10.2337/dci19-0028

Beck, B. R., Daly, R. M., Singh, M. A. F., & Taaffe, D. R. (2017). Exercise and Sports Science Australia (ESSA) position statement on exercise prescription for the prevention and management of osteoporosis. *Journal of Science and Medicine in Sport*, *20*(5), 438-445. https://doi.org/10.1016/j.jsams.2016.10.001

Benavent-Caballer, V., Rosado-Calatayud, P., Segura-Orti, E., Amer-Cuenca, J. J., & Lison, J. (2014). Effects of three different low-intensity exercise interventions on physical performance, muscle CSA and activities of daily living: A randomized controlled trial. *Experimental Gerontology*, *58*, 159-165. https://doi.org/https://doi.org/10.1016/j.exger.2014.08.004

Bergenstal, R. M., Beck, R. W., Close, K. L., Grunberger, G., Sacks, D. B., Kowalski, A., Brown, A. S., Heinemann, L., Aleppo, G., Ryan, D. B., Riddlesworth, T. D., & Cefalu, W. T. (2018). Glucose Management Indicator (GMI): A New Term for Estimating A1C From Continuous Glucose Monitoring. *Diabetes Care*, *41*(11), 2275-2280. https://doi.org/10.2337/dc18-1581

Boluyt, M. O., Zheng, J. S., Younes, A., Long, X., O'Neill, L., Silverman, H., Lakatta, E. G., & Crow, M. T. (1997). Rapamycin inhibits alpha 1-adrenergic receptor-stimulated cardiac myocyte hypertrophy but not activation of hypertrophy-associated genes. Evidence for involvement of p70 S6 kinase. *Circulation Research*, *81*(2), 176-186. https://doi.org/10.1161/01.res.81.2.176

Boone, C. H., Stout, J. R., Beyer, K. S., Fukuda, D. H., & Hoffman, J. R. (2015). Muscle strength and hypertrophy occur independently of protein supplementation during short-term resistance training in untrained men. *Applied Physiology, Nutrition, and Metabolism*, *40*(8), 797-802. https://doi.org/10.1139/apnm-2015-0027 %M 26154345

Borghouts, L. B., Wagenmakers, A. J., Goyens, P. L., & Keizer, H. A. (2002). Substrate utilization in non-obese Type II diabetic patients at rest and during exercise. *Clinical Science (London)*, *103*(6), 559-566. https://doi.org/10.1042/cs1030559

Botter, A., Oprandi, G., Lanfranco, F., Allasia, S., Maffiuletti, N. A., & Minetto, M. A. (2011). Atlas of the muscle motor points for the lower limb: implications for electrical stimulation procedures and electrode positioning. *European Journal of Applied Physiology*, *111*(10), 2461-2471. https://doi.org/10.1007/s00421-011-2093-y

Brellenthin, A. G., Lanningham-Foster, L. M., Kohut, M. L., Li, Y., Church, T. S., Blair, S. N., & Lee, D.-c. (2019). Comparison of the Cardiovascular Benefits of Resistance, Aerobic, and Combined Exercise (CardioRACE): Rationale, design, and methods. *American Heart Journal*, *217*, 101-111. https://doi.org/https://doi.org/10.1016/j.ahj.2019.08.008

Brooks, N., Layne, J. E., Gordon, P. L., Roubenoff, R., Nelson, M. E., & Castaneda-Sceppa, C. (2007). Strength training improves muscle quality and insulin sensitivity in Hispanic older adults with type 2 diabetes. *International Journal of Medical Sciences*, 19-27. https://doi.org/10.7150/ijms.4.19

Campbell, W. W., Crim, M. C., Young, V. R., & Evans, W. J. (1994). Increased energy requirements and changes in body composition with resistance training in older adults. *Am J Clin Nutr*, *60*(2), 167-175. https://doi.org/10.1093/ajcn/60.2.167

Candow, D. G., & Burke, D. G. (2007). Effect of Short-Term Equal-Volume Resistance Training with Different Workout Frequency on Muscle Mass and Strength in Untrained Men and Women. *The Journal of Strength and Conditioning Research*, *21*(1), 204-207. https://doi.org/https://doi.org/10.1519/00124278-200702000-00037

Cauza, E., Hanusch-Enserer, U., Strasser, B., Ludvik, B., Metz-Schimmerl, S., Pacini, G., Wagner, O., Georg, P., Prager, R., Kostner, K., Dunky, A., & Haber, P. (2005). The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Arch Phys Med Rehabil*, *86*(8), 1527-1533. https://doi.org/10.1016/j.apmr.2005.01.007

CDC. (2019). *Nutrition, Physical Activity, and Obesity: Data, Trends and Maps*. Centers For Disease Control and Prevention. https://www.cdc.gov/nccdphp/dnpao/data-trends-maps/index.html .

CDC. (2022a). *Adult Physical Inactivity Prevalence Maps by Race/Ethnicity*. Center for Disease Control and Prevention. Retrieved September 22, 2023 from https://www.cdc.gov/physicalactivity/data/inactivity-prevalence-maps/index.html

CDC. (2022b). *Defining Adult Overweight & Obesity*. Center for Disease Control and Prevention. Retrieved March 15, 2023 from https://www.cdc.gov/obesity/basics/adult-defining.html#:~:text=If%20your%20BMI%20is%2018.5,falls%20within%20the%20obesity%20range.

CDC. (2022c). *Diabetes Fast Facts*. Center for Disease Control and Prevention. Retrieved March 15, 2023 from https://www.cdc.gov/diabetes/basics/quick-facts.html

Census. (2020). *Quick Facts El Paso County, Texas*. United States Census Bureau. Retrieved March 15, 2023 from https://www.census.gov/quickfacts/fact/table/elpasocountytexas/PST045221#PST045221

Chen, Y.-C., Davies, R. G., Hengist, A., Carroll, H. A., Perkin, O. J., Betts, J. A., & Thompson, D. (2022). Effects of neuromuscular electrical stimulation on energy expenditure and postprandial metabolism in healthy men. *Applied Physiology, Nutrition, and Metabolism*, *47*(1), 27-33. https://doi.org/10.1139/apnm-2021-0361

Chilibeck, P. D., Calder, A. W., Sale, D. G., & Webber, C. E. (1997). A comparison of strength and muscle mass increases during resistance training in young women. *European Journal of Applied Physiology*, *77*(1-2), 170-175. https://doi.org/10.1007/s004210050316

Crognale, D., Crowe, L., Devito, G., Minogue, C., & Caulfield, B. (2009, 2009-09-01). Neuromuscular electrical stimulation training enhances maximal aerobic capacity in healthy physically active adults. 2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society,

Croymans, D. M., Paparisto, E., Lee, M. M., Brandt, N., Le, B. K., Lohan, D., Lee, C. C., & Roberts, C. K. (2013). Resistance training improves indices of muscle insulin sensitivity and β-cell function in overweight/obese, sedentary young men. *Journal of Applied Physiology*. https://doi.org/https://doi.org/10.1152/japplphysiol.00485.2013

Csapo, R., & Alegre, L. M. (2016). Effects of resistance training with moderate vs heavy loads on muscle mass and strength in the elderly: A meta-analysis. *Scandinavian Journal of Medicine & Science in Sports*, *26*(9), 995-1006. https://doi.org/10.1111/sms.12536

Cunningham, J. J. (1991). Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. *The American Journal of Clinical Nutrition*, *54*(6), 963-969. https://doi.org/https://doi.org/10.1093/ajcn/54.6.963

Dal Corso, S., Napolis, L., Malaguti, C., Gimenez, A. C., Albuquerque, A., Nogueira, C. R., De Fuccio, M. B., Pereria, R. D. B., Bulle, A., McFarlane, N., Nery, L. E., & Neder, J. A. (2007). Skeletal muscle structure and function in response to electrical stimulation in moderately impaired COPD patients. *Respiratory Medicine*, *101*(6), 1236-1243. https://doi.org/https://doi.org/10.1016/j.rmed.2006.10.023

Damas, F., Libardi, C. A., & Ugrinowitsch, C. (2018). The development of skeletal muscle hypertrophy through resistance training: the role of muscle damage and muscle protein synthesis. *European Journal of Applied Physiology*, *118*(3), 485-500. https://doi.org/10.1007/s00421-017-3792-9

De Freitas, G. R., Szpoganicz, C., & Ilha, J. (2018). Does Neuromuscular Electrical Stimulation Therapy Increase Voluntary Muscle Strength After Spinal Cord Injury? A Systematic Review. *Topics in Spinal Cord Injury Rehabilitation*, *24*(1), 6-17. https://doi.org/10.1310/sci16-00048

de Oliveira Melo, M., Aragão, F. A., & Vaz, M. A. (2013). Neuromuscular electrical stimulation for muscle strengthening in elderly with knee osteoarthritis - a systematic review. *Complement Ther Clin Pract*, *19*(1), 27-31. https://doi.org/10.1016/j.ctcp.2012.09.002

Deepshikha Sharma, S. S., Jaspal Singh. (2010). Effect of electrical stimulation on blood glucose level and lipid profile of sedentary type 2 diabetic patients. *International Journal of Diabetes in Developing Countries*, *30*(4). https://doi.org/10.4103/0973-3930.70859

Defreitas, J. M., Beck, T. W., Stock, M. S., Dillon, M. A., & Kasishke, P. R. (2011). An examination of the time course of training-induced skeletal muscle hypertrophy. *European Journal of Applied Physiology*, *111*(11), 2785-2790. https://doi.org/10.1007/s00421-011-1905-4

DeFronzo, R. A., & Beckles, A. D. (1979). Glucose intolerance following chronic metabolic acidosis in man. *American Journal of Physiology-Endocrinology and Metabolism*, *236*(4), E328. https://doi.org/10.1152/ajpendo.1979.236.4.E328

Dehail, P., Duclos, C., & Barat, M. M. (2008). Electrical Stimulation and Muscle Strengthening. *Annales De Réadaptation Et De Médecine Physique*, *51*(6), 441-451. https://doi.org/https://doi.org/10.1016/j.annrmp.2008.05.001

Deley, G., Kervio, G., Verges, B., Hannequin, A., Petitdant, M.-F., Salmi-Belmihoub, S., Grassi, B., & Casillas, J.-M. (2005). Comparison of low-frequency electrical myostimulation and conventional aerobic exercise training in patients with chronic heart failure. *European*

Journal of Cardiovascular Prevention & Rehabilitation, *12*(3), 226-233. https://doi.org/10.1097/01.hjr.0000166455.23346.a5

Di Filippo, E. S., Mancinelli, R., Marrone, M., Doria, C., Verratti, V., Toniolo, L., Dantas, J. L., Fulle, S., & Pietrangelo, T. (2017). Neuromuscular electrical stimulation improves skeletal muscle regeneration through satellite cell fusion with myofibers in healthy elderly subjects. *Journal of Applied Physiology*, *123*(3), 501-512. https://doi.org/10.1152/japplphysiol.00855.2016

Dobsák, P., Nováková, M., Fiser, B., Siegelová, J., Balcárková, P., Spinarová, L., Vítovec, J., Minami, N., Nagasaka, M., Kohzuki, M., Yambe, T., Imachi, K., Nitta, S., Eicher, J. C., & Wolf, J. E. (2006). Electrical stimulation of skeletal muscles. An alternative to aerobic exercise training in patients with chronic heart failure? *Int Heart J*, *47*(3), 441-453. https://doi.org/10.1536/ihj.47.441

Dörmann, U., Wirtz, N., Micke, F., Morat, M., Kleinöder, H., & Donath, L. (2019). The Effects of Superimposed Whole-Body Electromyostimulation During Short-Term Strength Training on Physical Fitness in Physically Active Females: A Randomized Controlled Trial. *Frontiers in Physiology*, *10*. https://doi.org/10.3389/fphys.2019.00728

Dunstan, D. W., Daly, R. M., Owen, N., Jolley, D., De Courten, M., Shaw, J., & Zimmet, P. (2002). High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care*, *25*(10), 1729-1736. https://doi.org/10.2337/diacare.25.10.1729

Eikenberg, J. D., Savla, J., Marinik, E. L., Davy, K. P., Pownall, J., Baugh, M. E., Flack, K. D., Boshra, S., Winett, R. A., & Davy, B. M. (2016). Prediabetes Phenotype Influences Improvements in Glucose Homeostasis with Resistance Training. *PLoS One*, *11*(2), e0148009. https://doi.org/10.1371/journal.pone.0148009

Esteve, V., Carneiro, J., Moreno, F., Fulquet, M., Garriga, S., Pou, M., Duarte, V., Saurina, A., Tapia, I., & Ramírez de Arellano, M. (2017). The effect of neuromuscular electrical stimulation on muscle strength, functional capacity and body composition in haemodialysis patients. *Nefrologia*, *37*(1), 68-77. https://doi.org/10.1016/j.nefro.2016.05.010 (Efecto de la electroestimulación neuromuscular sobre la fuerza muscular, capacidad funcional y composición corporal en los pacientes en hemodiálisis.)

Evangelista, A. L., Teixeira, C. V., Barros, B. M., de Azevedo, J. B., Paunksnis, M. R., R., d. S. C., Wadhi, T., Rica, R. L., Braz, T. V., & Bocalini, D. S. (2019). Does whole-body electrical muscle stimulation combined with strength training promote morphofunctional alterations? *Clinics (Sao Paolo)*, *74*(1334). https://doi.org/https://doi.org/10.6061/clinics/2019/e1334

Evans, P. L., McMillin, S. L., Weyrauch, L. A., & Witczak, C. A. (2019). Regulation of Skeletal Muscle Glucose Transport and Glucose Metabolism by Exercise Training. *Nutrients*, *11*(10). https://doi.org/10.3390/nu11102432

Eves, N. D., & Plotnikoff, R. C. (2006). Resistance Training and Type 2 Diabetes: Considerations for implementation at the population level. *Diabetes Care*, *29*(8), 1933-1941. https://doi.org/https://doi.org/10.2337/dc05-1981

Farinatti, P., Castinheiras Neto, A. G., & Amorim, P. R. (2016). Oxygen Consumption and Substrate Utilization During and After Resistance Exercises Performed with Different Muscle Mass. *Int J Exerc Sci*, *9*(1), 77-88.

Feng, Y. Z., Nikolić, N., Bakke, S. S., Kase, E. T., Guderud, K., Hjelmesæth, J., Aas, V., Rustan, A. C., & Thoresen, G. H. (2015). Myotubes from lean and severely obese subjects with

and without type 2 diabetes respond differently to an in vitro model of exercise. *Am J Physiol Cell Physiol*, *308*(7), C548-556. https://doi.org/10.1152/ajpcell.00314.2014

Fiatarone, M. A., Marks, E. C., Ryan, N. D., Meredith, C. N., Lipsitz, L. A., & Evans, W. J. (1990). High-intensity strength training in nonagenarians. Effects on skeletal muscle. *JAMA*, *263*(22), 3029-3034.

Fischer, A., Spiegl, M., Altmann, K., Winkler, A., Salamon, A., Themessl-Huber, M., Mouhieddine, M., Strasser, E. M., Schiferer, A., Paternostro-Sluga, T., & Hiesmayr, M. (2016). Muscle mass, strength and functional outcomes in critically ill patients after cardiothoracic surgery: does neuromuscular electrical stimulation help? The Catastim 2 randomized controlled trial. *Critical Care*, *20*(1). https://doi.org/10.1186/s13054-016-1199-3

Flack, K. D., Johnson, L., & Roemmich, J. N. (2017). Aerobic and resistance exercise reinforcement and discomfort tolerance predict meeting activity guidelines. *Physiology and Behavior*, *170*, 32-36. https://doi.org/https://doi.org/10.1016/j.physbeh.2016.11.032

Flegal, K. M., Kit, B. K., Orpana, H., & Graubard, B. I. (2013). Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories. *JAMA*, *309*(1), 71. https://doi.org/10.1001/jama.2012.113905

Frank, P., Andersson, E., Pontén, M., Ekblom, B., Ekblom, M., & Sahlin, K. (2016). Strength training improves muscle aerobic capacity and glucose tolerance in elderly. *Scand J Med Sci Sports*, *26*(7), 764-773. https://doi.org/10.1111/sms.12537

Freedson, P., Bowles, H. R., Troiano, R., & Haskell, W. (2012). Assessment of physical activity using wearable monitors: recommendations for monitor calibration and use in the field. *Med Sci Sports Exerc*, *44*(1 Suppl 1), S1-4. https://doi.org/10.1249/MSS.0b013e3182399b7e

Galgani, J. E., Moro, C., & Ravussin, E. (2008). Metabolic flexibility and insulin resistance. *American Journal of Physiology-Endocrinology and Metabolism*, *295*(5), E1009-E1017. https://doi.org/10.1152/ajpendo.90558.2008

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences*, *21*(17), 6275. https://doi.org/10.3390/ijms21176275

Galvan, M. J., Sanchez, M. J., McAinch, A. J., Covington, J. D., Boyle, J. B., & Bajpeyi, S. (2022). Four weeks of electrical stimulation improves glucose tolerance in a sedentary overweight or obese Hispanic population. *Endocrine Connections*, *11*(2). https://doi.org/https://doi.org/10.1530/EC-21-0533

Gayoso-Diz, P., Otero-González, A., Rodriguez-Alvarez, M. X., Gude, F., García, F., De Francisco, A., & Quintela, A. G. (2013). Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: effect of gender and age: EPIRCE cross-sectional study. *BMC Endocrine Disorders*, *13*(1), 47. https://doi.org/10.1186/1472-6823-13-47

Gobbo, M., Maffiuletti, N. A., Orizio, C., & Minetto, M. A. (2014). Muscle motor point identification is essential for optimizing neuromuscular electrical stimulation use. *Journal of NeuroEngineering and Rehabilitation*, *11*(1), 17. https://doi.org/10.1186/1743-0003-11-17

Gondin, J., Brocca, L., Bellinzona, E., D'Antona, G., Maffiuletti, N. A., Miotti, D., Pellegrino, M. A., & Bottinelli, R. (2011). Neuromuscular electrical stimulation training induces atypical

adaptations of the human skeletal muscle phenotype: a functional and proteomic analysis. *Journal of Applied Physiology*, *110*(2), 433-450. https://doi.org/https://doi.org/10.1152/japplphysiol.00914.2010

Gonzalez, A. M., Hoffman, J. R., Stout, J. R., Fukuda, D. H., & Willoughby, D. S. (2016). Intramuscular Anabolic Signaling and Endocrine Response Following Resistance Exercise: Implications for Muscle Hypertrophy. *Sports Medicine*, *46*(5), 671-685. https://doi.org/10.1007/s40279-015-0450-4

Gordon, B. R., McDowell, C. P., Hallgren, M., Meyer, J. D., Lyons, M., & Herring, M. P. (2018). Association of Efficacy of Resistance Exercise Training With Depressive Symptoms: Meta-analysis and Meta-regression Analysis of Randomized Clinical Trials. *JAMA Psychiatry*, *75*(6), 566-576. https://doi.org/10.1001/jamapsychiatry.2018.0572

Gorgey, A. S., Dolbow, D. R., Dolbow, J. D., Khalil, R. K., & Gater, D. R. (2015). The effects of electrical stimulation on body composition and metabolic profile after spinal cord injury--Part II. *J Spinal Cord Med*, *38*(1), 23-37. https://doi.org/10.1179/2045772314y.0000000244

Gorgey, A. S., Lai, R. E., Khalil, R. E., Rivers, J., Cardozo, C., Chen, Q., & Lesnefsky, E. J. (2021). Neuromuscular electrical stimulation resistance training enhances oxygen uptake and ventilatory efficiency independent of mitochondrial complexes after spinal cord injury: a randomized clinical trial. *Journal of Applied Physiology*, *131*(1), 265-276. https://doi.org/10.1152/japplphysiol.01029.2020

Griffin, L., Decker, M. J., Hwang, J. Y., Wang, B., Kitchen, K., Ding, Z., & Ivy, J. L. (2009). Functional electrical stimulation cycling improves body composition, metabolic and neural factors in persons with spinal cord injury. *J Electromyogr Kinesiol*, *19*(4), 614-622. https://doi.org/10.1016/j.jelekin.2008.03.002

Groennebaek, T., & Vissing, K. (2017). Impact of Resistance Training on Skeletal Muscle Mitochondrial Biogenesis, Content, and Function. *Front Physiol*, *8*, 713. https://doi.org/10.3389/fphys.2017.00713

Grosset, J. F., Crowe, L., De Vito, G., O'Shea, D., & Caulfield, B. (2013). Comparative effect of a 1 h session of electrical muscle stimulation and walking activity on energy expenditure and substrate oxidation in obese subjects. *Appl Physiol Nutr Metab*, *38*(1), 57-65. https://doi.org/10.1139/apnm-2011-0367

Hackney, K. J., Engels, H.-J., & Gretebeck, R. J. (2008). Resting Energy Expenditure and Delayed-Onset Muscle Soreness After Full-Body Resistance Training With an Eccentric Concentration. *The Journal of Strength & Conditioning Research*, *22*(5), 1602-1609. https://doi.org/10.1519/JSC.0b013e31818222c5

Haddock, B. L., & Wilkin, L. D. (2006). Resistance Training Volume and Post Exercise Energy Expenditure. *International Journal of Sports Medicine*, *27*(2), 143-148. https://doi.org/10.1055/s-2005-865601

Haff, G. G., & Triplett, T. N. (2021). *Essentials of Strength Training and Conditioning* (4th ed.). Human Kinetics.

Häkkinen, K., Kraemer, W. J., Newton, R. U., & Alen, M. (2001). Changes in electromyographic activity, muscle fibre and force production characteristics during heavy resistance/power strength training in middle-aged and older men and women. *Acta Physiol Scand*, *171*(1), 51-62. https://doi.org/10.1046/j.1365-201X.2001.00781.x

Hamada, T., Hayashi, T., Kimura, T., Nakao, K., & Moritani, T. (2004). Electrical stimulation of human lower extremities enhances energy consumption, carbohydrate oxidation, and

whole body glucose uptake. *J Appl Physiol (1985)*, *96*(3), 911-916. https://doi.org/10.1152/japplphysiol.00664.2003

Hamada, T., Sasaki, H., Hayashi, T., Moritani, T., & Nakao, K. (2003). Enhancement of whole body glucose uptake during and after human skeletal muscle low-frequency electrical stimulation. *Journal of Applied Physiology*, *94*(6), 2107-2112. https://doi.org/https://doi.org/10.1152/japplphysiol.00486.2002

Happ, K. A., & Behringer, M. (2021). Neuromuscular Electrical Stimulation Training vs Conventional Strength Training A Systematic Review and Meta-Analysis of the Effect of Strength Development. *The Journal of Strength and Conditioning Research*. https://doi.org/10.1519/JSC.0000000000004119

Heden, T., Lox, C., Rose, P., Reid, S., & Kirk, E. P. (2011). One-set resistance training elevates energy expenditure for 72 h similar to three sets. *European Journal of Applied Physiology*, *111*(3), 477-484. https://doi.org/10.1007/s00421-010-1666-5

Henneman, E., Somien, G., & Carpenter, D. O. (1965). Functional Significance of Cell Size in Spinal Motoneurons. *Journal of Neurophysiology*, *28*(3), 560-580. https://doi.org/https://doi.org/10.1152/jn.1965.28.3.560

HHS. (2021). *Diabetes and Hispanic Americans*. U.S. Department of Health and Human Services. https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=63

HHS. (2022). *Causes of Obesity*. U.S. Department of Health and Human Services. https://www.cdc.gov/obesity/basics/causes.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fobesity%2Fadult%2Fcauses.html

Higgins, J. P. T., Altman, D. G., Gotzche, P. C., Juni, P., Moher, D., Oxman, A. D., Savocic, J., Schulz, K. F., Weeks, L., & Stern, J. A. C. (2011). The Cochrane Collaboration's Tool For Assessing Bias In Randomized Trials. *BMJ*, *343*. https://doi.org/https://doi.org/10.1136/bmj.d5928

Hioki, M., Kanehira, N., Koike, T., Saito, A., Takahashi, H., Shimaoka, K., Sakakibara, H., Oshida, Y., & Akima, H. (2021). Effect of electromyostimulation on intramyocellular lipids of the vastus lateralis in older adults: a randomized controlled trial. *BMC Musculoskelet Disord*, *22*(1), 569. https://doi.org/10.1186/s12891-021-04456-6

Holzer, R., Schulte-Körne, B., Seidler, J., Predel, H.-G., & Brinkmann, C. (2021). Effects of Acute Resistance Exercise with and without Whole-Body Electromyostimulation and Endurance Exercise on the Postprandial Glucose Regulation in Patients with Type 2 Diabetes Mellitus: A Randomized Crossover Study. *Nutrients*, *13*(12), 4322. https://doi.org/10.3390/nu13124322

Hoshiai, M., Ochiai, K., Tamura, Y., Tsurumi, T., Terashima, M., Tamiya, H., Maeno, E., Mizuguchi, S., Tomoe, T., Kawabe, A., Uema, A., Ueno, A., Sugiyama, T., Horie, Y., Sugimura, H., Koike, R., & Yasu, T. (2021). Effects of whole-body neuromuscular electrical stimulation device on hemodynamics, arrhythmia, and sublingual microcirculation. *Heart Vessels*, *36*(6), 844-852. https://doi.org/10.1007/s00380-020-01755-1

Howell, C. R., Juarez, L., Agne, A. A., Nassel, A. F., Scarinci, I. C., Ayala, G. X., & Cherrington, A. L. (2022). Assessing Hispanic/Latino and Non-Hispanic White Social Determinants of Obesity Among a Community Sample of Residents in the Rural Southeast US. *Journal of Immigrant and Minority Health*, *24*(6), 1469-1479. https://doi.org/10.1007/s10903-022-01334-8

Ibañez, J., Izquierdo, M., Argüelles, I., Forga, L., Larrión, J. L., García-Unciti, M., Idoate, F., & Gorostiaga, E. M. (2005). Twice-weekly progressive resistance training decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. *Diabetes Care*, *28*(3), 662-667. https://doi.org/10.2337/diacare.28.3.662

Ishii, T., Yamakita, T., Sato, T., Tanaka, S., & Fujii, S. (1998). Resistance Training Improves Insulin Sensitivity in NIDDM Subjects Without Altering Maximal Oxygen Uptake. *Diabetes Care*, *21*(8), 1353-1355. https://doi.org/10.2337/diacare.21.8.1353

Jackson, J. K., Shepherd, T. R., & Kell, R. T. (2011). The Influence of Periodized Resistance Training on Recreationally Active Males with Chronic Nonspecific Low Back Pain. *The Journal of Strength & Conditioning Research*, *25*(1), 242-251. https://doi.org/10.1519/JSC.0b013e3181b2c83d

Jamurtas, A. Z., Koutedakis, Y., Paschalis, V., Tofas, T., Yfanti, C., Tsiokanos, A., Koukoulis, G., Kouretas, D., & Loupos, D. (2004). The effects of a single bout of exercise on resting energy expenditure and respiratory exchange ratio. *Eur J Appl Physiol*, *92*(4-5), 393-398. https://doi.org/10.1007/s00421-004-1156-8

Jekauc, D. (2015). Enjoyment during Exercise Mediates the Effects of an Intervention on Exercise Adherence. *Psychology*, *06*(01), 48-54. https://doi.org/10.4236/psych.2015.61005

Jeon, J., Weiss, C., Steadward, R., Ryan, E., Burnham, R., Bell, G., Chilibeck, P., & Wheeler, G. (2002). Improved glucose tolerance and insulin sensitivity after electrical stimulation-assisted cycling in people with spinal cord injury. *Spinal Cord*, *40*(3), 110-117. https://doi.org/10.1038/sj.sc.3101260

Jiahao, L., Jiajin, L., & Yifan, L. (2021). Effects of resistance training on insulin sensitivity in the elderly: A meta-analysis of randomized controlled trials. *J Exerc Sci Fit*, *19*(4), 241-251. https://doi.org/10.1016/j.jesf.2021.08.002

Johnson, M. J., Lortie, G., Simoneau, J.-A., & Boulay, M. R. (2003). Glycogen Depletion of Human Skeletal Muscle Fibers in Response to High-Frequency Electrical Stimulation. *Canadian Journal of Applied Physiology*, *28*(3), 424-433. https://doi.org/10.1139/h03-031 %M 12955869

Jordy, A. B., & Kiens, B. (2014). Regulation of exercise-induced lipid metabolism in skeletal muscle. *Experimental Physiology*, *99*(12), 1586-1592. https://doi.org/10.1113/expphysiol.2014.082404

Joubert, M., Metayer, L., Prevost, G., Morera, J., Rod, A., Cailleux, A., Parienti, J.-J., & Reznik, Y. (2015). Neuromuscular electrostimulation and insulin sensitivity in patients with type 2 diabetes: the ELECTRODIAB pilot study. *Acta Diabetologica*, *52*(2), 285-291. https://doi.org/10.1007/s00592-014-0636-5

Kalapotharakos, V. I., Michalopoulou, M., Godolias, G., Tokmakidis, S. P., Malliou, P. V., & Gourgoulis, V. (2004). The effects of high- and moderate-resistance training on muscle function in the elderly. *J Aging Phys Act*, *12*(2), 131-143. https://doi.org/10.1123/japa.12.2.131

Katsuki, A., Sumida, Y., Gabazza, E. C., Murashima, S., Urakawa, H., Morioka, K., Kitagawa, N., Tanaka, T., Araki-Sasaki, R., Hori, Y., Nakatani, K., Yano, Y., & Adachi, Y. (2002). QUICKI Is Useful for Following Improvements in Insulin Sensitivity after Therapy in Patients with Type 2 Diabetes Mellitus. *The Journal of Clinical Endocrinology & Metabolism*, *87*(6), 2906-2908. https://doi.org/10.1210/jcem.87.6.8592

Kelley, D. E., Goodpaster, B., Wing, R. R., & Simoneau, J. A. (1999). Skeletal muscle fatty acid metabolism in association with insulin resistance, obesity, and weight loss. *Am J Physiol*, *277*(6), E1130-1141. https://doi.org/10.1152/ajpendo.1999.277.6.E1130

Kemmler, W., Schliffka, R., Mayhew, J. L., & von Stengel, S. (2010). Effects of whole-body electromyostimulation on resting metabolic rate, body composition, and maximum strength in postmenopausal women: the Training and ElectroStimulation Trial. *J Strength Cond Res*, *24*(7), 1880-1887. https://doi.org/10.1519/JSC.0b013e3181ddaeee

Kemmler, W., Stengel, S. V., Schwarz, J., & Mayhew, J. L. (2012). Effect of Whole-Body Electromyostimulation on Energy Expenditure During Exercise. *Journal of Strength & Conditioning Research*, *26*(1), 240-245. https://doi.org/10.1519/JSC.0b013e31821a3a11

Kim, J. K. (2009). Hyperinsulinemic–Euglycemic Clamp to Assess Insulin Sensitivity In Vivo. In *Methods in Molecular Biology* (pp. 221-238). Humana Press. https://doi.org/10.1007/978-1-59745-448-3_15

Kirk, E. P., Donnelly, J. E., Smith, B. K., Honas, J., Lecheminant, J. D., Bailey, B. W., Jacobsen, D. J., & Washburn, R. A. (2009). Minimal resistance training improves daily energy expenditure and fat oxidation. *Med Sci Sports Exerc*, *41*(5), 1122-1129. https://doi.org/10.1249/MSS.0b013e318193c64e

Kitamura, I., Takeshima, N., Tokudome, M., Yamanouchi, K., Oshida, Y., & Sato, Y. (2003). Effects of aerobic and resistance exercise training on insulin action in the elderly. *Geriatrics & Gerontology International*, *3*(1), 50-55. https://doi.org/10.1046/j.1444-1586.2003.00054.x

Koistinen, H. A., & Zierath, J. R. (2002). Regulation of glucose transport in human skeletal muscle. *Annals of Medicine*, *34*(6), 410-418. https://doi.org/10.1080/078538902321012351

Kraemer, W. J., Mazzetti, S. A., Nindl, B. C., Gotshalk, L. A., Volek, J. S., Bush, J. A., Marx, J. O., Dohl, K., Gomez, A. L., Miles, M., Fleck, S. J., Newton, R. U., & Hakkinen, K. (2001). Effect of resistance training on women's strength/power and occupational performances. *Medicine & Science in Sports & Exercise*, *33*(6), 1011-1025.

Lam, Y. Y., & Ravussin, E. (2016). Analysis of energy metabolism in humans: A review of methodologies. *Molecular Metabolism*, *5*(11), 1057-1071. https://doi.org/10.1016/j.molmet.2016.09.005

Lambernd, S., Taube, A., Schober, A., Platzbecker, B., Görgens, S. W., Schlich, R., Jeruschke, K., Weiss, J., Eckardt, K., & Eckel, J. (2012). Contractile activity of human skeletal muscle cells prevents insulin resistance by inhibiting pro-inflammatory signalling pathways. *Diabetologia*, *55*(4), 1128-1139. https://doi.org/10.1007/s00125-012-2454-z

Langeard, A., Bigot, L., Chastan, N., & Gauthier, A. (2017). Does neuromuscular electrical stimulation training of the lower limb have functional effects on the elderly?: A systematic review. *Exp Gerontol*, *91*, 88-98. https://doi.org/10.1016/j.exger.2017.02.070

Lavie, C. J., Lee, D.-c., Sui, X., Arena, R., O'Keefe, J. H., Church, T. S., Milani, R. V., & Blair, S. N. (2015). Effects of Running on Chronic Diseases and Cardiovascular and All-Cause Mortality. *Mayo Clinic Proceedings*, *90*(11), 1541-1552. https://doi.org/https://doi.org/10.1016/j.mayocp.2015.08.001

LeBouthillier, D. M., & Asmundson, G. J. G. (2017). The efficacy of aerobic exercise and resistance training as transdiagnostic interventions for anxiety-related disorders and constructs: A randomized controlled trial. *Journal of Anxiety Disorders*, *52*, 43-52. https://doi.org/https://doi.org/10.1016/j.janxdis.2017.09.005

Lemmer, J. T., Ivey, F. M., Ryan, A. S., Martel, G. F., Hurlbut, D. E., Metter, J. E., Fozard, J. L., Fleg, J. L., & Hurley, B. F. (2001). Effect of strength training on resting metabolic rate and physical activity: age and gender comparisons. *Medicine & Science in Sports & Exercise*, *33*(4), 532-541.

Li, J., Polston, K. F. L., Eraslan, M., Bickel, C. S., Windham, S. T., McLain, A. B., Oster, R. A., Bamman, M. M., & Yarar-Fisher, C. (2018). A high-protein diet or combination exercise training to improve metabolic health in individuals with long-standing spinal cord injury: a pilot randomized study. *Physiol Rep*, *6*(16), e13813. https://doi.org/10.14814/phy2.13813

Liguori, G. (2021). *ACSM's Guidelines for Exercise Testing and Prescription* (11th ed.). Wolters Kluwer.

Lin, J., Thompson, T. J., Cheng, Y. J., Zhuo, X., Zhang, P., Gregg, E., & Rolka, D. B. (2018). Projection of the future diabetes burden in the United States through 2060. *Population Health Metrics*, *16*(1). https://doi.org/10.1186/s12963-018-0166-4

Lopez, P., Taaffe, D. R., Galvão, D. A., Newton, R. U., Nonemacher, E. R., Wendt, V. M., Bassanesi, R. N., Turella, D. J. P., & Rech, A. (2022). Resistance training effectiveness on body composition and body weight outcomes in individuals with overweight and obesity across the lifespan: A systematic review and meta-analysis. *Obes Rev*, *23*(5), e13428. https://doi.org/10.1111/obr.13428

Ludwig, O., Berger, J., Schuh, T., Backfisch, M., Becker, S., & Frohlich, M. (2020). Can A Superimposed Whole-Body Electromyostimulation Intervention Enhance the Effects of a 10-Week Athletic Strength Training in Youth Elite Soccer Players? *Journal of Sports Science and Medicine*, *19*(3), 535-546.

Macedo, A. C. P., Bock, P. M., Saffi, M. A. L., Madalosso, M. M., Lago, P. D., Casali, K. R., & Schaan, B. D. (2024). Neuromuscular electrical stimulation changes glucose, but not its variability in type 2 diabetes: a randomized clinical trial. *Anais da Academia Brasileira de Ciências*, *96*(1). https://doi.org/10.1590/0001-3765202320220282

Maeda, N., Shimomura, I., Kishida, K., Nishizawa, H., Matsuda, M., Nagaretani, H., Furuyama, N., Kondo, H., Takahashi, M., Arita, Y., Komuro, R., Ouchi, N., Kihara, S., Tochino, Y., Okutomi, K., Horie, M., Takeda, S., Aoyama, T., Funahashi, T., & Matsuzawa, Y. (2002). Diet-induced insulin resistance in mice lacking adiponectin/ACRP30. *Nature Medicine*, *8*(7), 731-737. https://doi.org/10.1038/nm724

Mcclave, S., Lowen, C., Kleber, M., Mcconnell, J., Jung, L., & Goldsmith, L. (2003). Clinical use of the respiratory quotient obtained from indirect calorimetry. *Journal of Parenteral and Enteral Nutrition*, *27*(1), 21-26. https://doi.org/10.1177/014860710302700121

McGarry, J. D. (1992). What if Minkowski had been ageusic? An alternative angle on diabetes. *Science*, *258*(5083), 766-770. https://doi.org/10.1126/science.1439783

Melo, M. d. O., Aragao, F. A., & Vaz, M. A. (2012). Neuromuscular electrical stimulation for muscle strengthening in elderly with knee osteoarthritis – A systematic review. *Complementary Therapies in Clinical Practice*, *19*(1), 27-31. https://doi.org/https://doi.org/10.1016/j.ctcp.2012.09.002

Merz, K. E., & Thurmond, D. C. (2020). Role of Skeletal Muscle in Insulin Resistance and Glucose Uptake. *Comprehensive Physiology*, 785-809. https://doi.org/10.1002/cphy.c190029

Mettler, J. A., Magee, D. M., & Doucet, B. M. (2018). High-Frequency Neuromuscular Electrical Stimulation Increases Anabolic Signaling. *Med Sci Sports Exerc*, *50*(8), 1540-1548. https://doi.org/10.1249/mss.0000000000001610

Micke, F., Kleinoeder, H., Dormann, U., Wirtz, N., & Donath, L. (2018). Effects of an Eight-Week Superimposed Submaximal Dynamic Whole-Body Electromyostimulation Training on Strength and Power Parameters of the Leg Muscles: A Randomized Controlled Intervention Study. *Frontiers in Physiology*, *9*. https://doi.org/https://doi.org/10.3389/fphys.2018.01719

Mifflin, M. D., St Jeor, S. T., Hill, L. A., Scott, B. J., Daugherty, S. A., & Koh, Y. O. (1990). A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr*, *51*(2), 241-247. https://doi.org/10.1093/ajcn/51.2.241

Miller, J. P., Pratley, R. E., Goldberg, A. P., Gordon, P., Rubin, M., Treuth, M. S., Ryan, A. S., & Hurley, B. F. (1994). Strength training increases insulin action in healthy 50- to 65-yr-old men. *Journal of Applied Physiology*, *77*(3), 1122-1127. https://doi.org/10.1152/jappl.1994.77.3.1122

Minnock, D., Annibalini, G., Le Roux, C. W., Contarelli, S., Krause, M., Saltarelli, R., Valli, G., Stocchi, V., Barbieri, E., & De Vito, G. (2020). Effects of acute aerobic, resistance and combined exercises on 24-h glucose variability and skeletal muscle signalling responses in type 1 diabetics. *European Journal of Applied Physiology*, *120*(12), 2677-2691. https://doi.org/10.1007/s00421-020-04491-6

Misra, A., Alappan, N. K., Vikram, N. K., Goel, K., Gupta, N., Mittal, K., Bhatt, S., & Luthra, K. (2008). Effect of Supervised Progressive Resistance-Exercise Training Protocol on Insulin Sensitivity, Glycemia, Lipids, and Body Composition in Asian Indians With Type 2 Diabetes. *Diabetes Care*, *31*(7), 1282-1287. https://doi.org/10.2337/dc07-2316

Miyamoto, T., Iwakura, T., Matsuoka, N., Iwamoto, M., Takenaka, M., Akamatsu, Y., & Moritani, T. (2018). Impact of prolonged neuromuscular electrical stimulation on metabolic profile and cognition-related blood parameters in type 2 diabetes: A randomized controlled cross-over trial. *Diabetes Research and Clinical Practice*, *142*, 37-45. https://doi.org/10.1016/j.diabres.2018.05.032

Mizgier, M. L., Casas, M., Contreras-Ferrat, A., Llanos, P., & Galgani, J. E. (2014). Potential role of skeletal muscle glucose metabolism on the regulation of insulin secretion. *Obesity Reviews*, *15*(7), 587-597. https://doi.org/10.1111/obr.12166

Morton, R. W., Murphy, K. T., Mckellar, S. R., Schoenfeld, B. J., Henselmans, M., Helms, E., Aragon, A. A., Devries, M. C., Banfield, L., Krieger, J. W., & Phillips, S. M. (2018). A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. *British Journal of Sports Medicine*, *52*(6), 376-384. https://doi.org/10.1136/bjsports-2017-097608

Müller, M. J., Geisler, C., Hübers, M., Pourhassan, M., Braun, W., & Bosy-Westphal, A. (2018). Normalizing resting energy expenditure across the life course in humans: challenges and hopes. *Eur J Clin Nutr*, *72*(5), 628-637. https://doi.org/10.1038/s41430-018-0151-9

Murach, K. A., Fry, C. S., Dupont-Versteegden, E. E., Mccarthy, J. J., & Peterson, C. A. (2021). Fusion and beyond: Satellite cell contributions to loading-induced skeletal muscle adaptation. *The FASEB Journal*, *35*(10). https://doi.org/10.1096/fj.202101096r

Naugle, K. M., & Riley, J. L. r. (2014). Self-reported Physical Activity Predicts Pain Inhibitory and Facilitatory Function. *Medicine & Science in Sports & Exercise*, *46*(3), 622-629. https://doi.org/10.1249/MSS.0b013e3182a69cf1

Nesher, R., Karl, I. E., & Kipnis, D. M. (1985). Dissociation of effects of insulin and contraction on glucose transport in rat epitrochlearis muscle. *Am J Physiol*, *249*(3 Pt 1), C226-232. https://doi.org/10.1152/ajpcell.1985.249.3.C226

NIH. (2020). *Diabetes Statistics*. National Institute of Health. Retrieved March 15, 2023 from https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics#:~:text=Total%3A%20An%20estimated%2034.2%20million,percent%20of%20the%20U.S.%20population).

Nikolić, N., Görgens, S. W., Thoresen, G. H., Aas, V., Eckel, J., & Eckardt, K. (2017). Electrical pulse stimulation of cultured skeletal muscle cells as a model for in vitro exercise - possibilities and limitations. *Acta Physiol (Oxf)*, *220*(3), 310-331. https://doi.org/10.1111/apha.12830

Nuhr, M. J., Pette, D., Berger, R., Quittan, M., Crevenna, R., Huelsman, M., Wiesinger, G. F., Moser, P., Fialka-Moser, V., & Pacher, R. (2004). Beneficial effects of chronic low-frequency stimulation of thigh muscles in patients with advanced chronic heart failure. *Eur Heart J*, *25*(2), 136-143. https://doi.org/10.1016/j.ehj.2003.09.027

Paoli, A., Moro, T., Marcolin, G., Neri, M., Bianco, A., Palma, A., & Grimaldi, K. (2012). High-Intensity Interval Resistance Training (HIRT) influences resting energy expenditure and respiratory ratio in non-dieting individuals. *Journal of Translational Medicine*, *10*(1), 237. https://doi.org/10.1186/1479-5876-10-237

Patel, H., Kerndt, C. C., & Bhardwaj, A. (2023). *Physiology, Respiratory Quotient*. StatPearls Publishing, Treasure Island (FL). http://europepmc.org/abstract/MED/30285389

Phillips, S. M., & Winett, R. A. (2010). Uncomplicated resistance training and health-related outcomes: evidence for a public health mandate. *Curr Sports Med Rep*, *9*(4), 208-213. https://doi.org/10.1249/JSR.0b013e3181e7da73

Ploug, T., Galbo, H., Vinten, J., Jørgensen, M., & Richter, E. A. (1987). Kinetics of glucose transport in rat muscle: effects of insulin and contractions. *Am J Physiol*, *253*(1 Pt 1), E12-20. https://doi.org/10.1152/ajpendo.1987.253.1.E12

Poehlman, E. T. (1989). A review: exercise and its influence on resting energy metabolism in man. *Med Sci Sports Exerc*, *21*(5), 515-525.

Poehlman, E. T., Denino, W. F., Beckett, T., Kinaman, K. A., Dionne, I. J., Dvorak, R., & Ades, P. A. (2002). Effects of Endurance and Resistance Training on Total Daily Energy Expenditure in Young Women: A Controlled Randomized Trial. *The Journal of Clinical Endocrinology & Metabolism*, *87*(3), 1004-1009. https://doi.org/10.1210/jcem.87.3.8282

Poehlman, E. T., Dvorak, R. V., DeNino, W. F., Brochu, M., & Ades, P. A. (2000). Effects of Resistance Training and Endurance Training on Insulin Sensitivity in Nonobese, Young Women: A Controlled Randomized Trial1. *The Journal of Clinical Endocrinology & Metabolism*, *85*(7), 2463-2468. https://doi.org/10.1210/jcem.85.7.6692

Pratley, R., Nicklas, B., Rubin, M., Miller, J., Smith, A., Smith, M., Hurley, B., & Goldberg, A. (1994). Strength training increases resting metabolic rate and norepinephrine levels in healthy 50- to 65-yr-old men. *J Appl Physiol (1985)*, *76*(1), 133-137. https://doi.org/10.1152/jappl.1994.76.1.133

Rachdaoui, N. (2020). Insulin: The Friend and the Foe in the Development of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences*, *21*(5), 1770. https://doi.org/10.3390/ijms21051770

Rahmati, M., Gondin, J., & Malakoutinia, F. (2021). Effects of Neuromuscular Electrical Stimulation on Quadriceps Muscle Strength and Mass in Healthy Young and Older Adults: A Scoping Review. *Physical Therapy*, *101*(9). https://doi.org/10.1093/ptj/pzab144

Rasmussen, B. B., & Wolfe, R. R. (1999). Regulation of fatty acid oxidation in skeletal muscle. *Annual Review of Nutrition*, *19*(1), 463-484. https://doi.org/10.1146/annurev.nutr.19.1.463

Reid, R. D., Tulloch, H. E., Sigal, R. J., Kenny, G. P., Fortier, M., Mcdonnell, L., Wells, G. A., Boulé, N. G., Phillips, P., & Coyle, D. (2010). Effects of aerobic exercise, resistance exercise or both, on patient-reported health status and well-being in type 2 diabetes mellitus: a randomised trial. *Diabetologia*, *53*(4), 632-640. https://doi.org/10.1007/s00125-009-1631-1

Sakaguchi, K., Takeda, K., Maeda, M., Ogawa, W., Sato, T., Okada, S., Ohnishi, Y., Nakajima, H., & Kashiwagi, A. (2016). Glucose area under the curve during oral glucose tolerance test as an index of glucose intolerance. *Diabetol Int*, *7*(1), 53-58. https://doi.org/10.1007/s13340-015-0212-4

Sanchez, M. J., Mossayebi, A., Sigaroodi, S., Apaflo, J. N., Galvan, M. J., Min, K., Agullo, F. J., Wagler, A., & Bajpeyi, S. (2023). Effects of neuromuscular electrical stimulation on glycemic control: a systematic review and meta-analysis. *Front Endocrinol (Lausanne)*, *14*, 1222532. https://doi.org/10.3389/fendo.2023.1222532

Scanlon, T. C., Fragala, M. S., Stout, J. R., Emerson, N. S., Beyer, K. S., Oliveira, L. P., & Hoffman, J. R. (2014). Muscle architecture and strength: Adaptations to short-term resistance training in older adults. *Muscle & Nerve*, *49*(4), 584-592. https://doi.org/https://doi.org/10.1002/mus.23969

Schoenfeld, B. J., Ogborn, D., & Krieger, J. W. (2017). Dose-response relationship between weekly resistance training volume and increases in muscle mass: A systematic review and meta-analysis. *Journal of Sports Sciences*, *35*(11), 1073-1082. https://doi.org/https://doi.org/10.1080/02640414.2016.1210197

Segers, J., Vanhorebeek, I., Langer, D., Charususin, N., Wei, W., Frickx, B., Demeyere, I., Clerckx, B., Casaer, M., Derese, I., Derde, S., Pauwels, L., Van Den Berghe, G., Hermans, G., & Gosselink, R. (2021). Early neuromuscular electrical stimulation reduces the loss of muscle mass in critically ill patients – A within subject randomized controlled trial. *Journal of Critical Care*, *62*, 65-71. https://doi.org/10.1016/j.jcrc.2020.11.018

Sheffler, L. R., & Chae, J. (2007). Neuromuscular electrical stimulation in neurorehabilitation. *Muscle & Nerve*, *35*(5), 562-590. https://doi.org/10.1002/mus.20758

Shen, S.-W., Reaven, G. M., & Farquhar, J. W. (1970). Comparison of impedance to insulin-mediated glucose uptake in normal subjects and in subjects with latent diabetes. *Journal of Clinical Investigation*, *49*(12), 2151-2160. https://doi.org/10.1172/jci106433

Sigal, R. J., Kenny, G. P., Boule, N. G., Wells, G. A., Prud'homme, D., Fortier, M., Reid, R. D., Tulloch, H. E., Coyle, D., Philips, P., Jennings, A., & Jaffey, J. (2007). Effects of Aerobic Training, Resistance Training, or Both on Glycemic Control in Type 2 Diabetes. *Annals of Internal Medicine*, *147*(6), 357-369. https://doi.org/10.7326/0003-4819-147-6-200709180-00005 %m 17876019

Silveira, A. P. S., Bentes, C. M., Costa, P. B., Simão, R., Silva, F. C., Silva, R. P., & Novaes, J. S. (2014). Acute Effects of Different Intensities of Resistance Training on Glycemic Fluctuations in Patients With Type 1 Diabetes Mellitus. *Research in Sports Medicine*, *22*(1), 75-87. https://doi.org/10.1080/15438627.2013.852096

Silverthorn DU, O. W., Garrison CW, Silverthorn AC, & Johnson BR. (2020). *Human Physiology: An Integrated Approach* (8th ed.). Pearson.

Skogberg, O., Karlsson, L., Börsbo, B., Arendt-Nielsen, L., Graven-Nielsen, T., Gerdle, B., Bäckryd, E., & Lemming, D. (2022). Pain Tolerance in Chronic Pain Patients Seems to be More Associated with Physical Activity than with Depression and Anxiety. *Journal of Rehabilitation Medicine*, *54*, jrm00286. https://doi.org/10.2340/jrm.v54.241

Sparks, L. M., Johannsen, N. M., Church, T. S., Earnest, C. P., Moonen-Kornips, E., Moro, C., Hesselink, M. K., Smith, S. R., & Schrauwen, P. (2013). Nine months of combined training improves ex vivo skeletal muscle metabolism in individuals with type 2 diabetes. *J Clin Endocrinol Metab*, *98*(4), 1694-1702. https://doi.org/10.1210/jc.2012-3874

Stevens-Lapsley, J. E., Balter, J. E., Wolfe, P., Eckhoff, D. G., & Kohrt, W. M. (2012). Early Neuromuscular Electrical Stimulation to Improve Quadriceps Muscle Strength After Total Knee Arthroplasty: A Randomized Controlled Trial. *Physical Therapy*, *92*(2), 210-226. https://doi.org/10.2522/ptj.20110124

Stump, C. S., Henriksen, E. J., Wei, Y., & Sowers, J. R. (2006). The metabolic syndrome: Role of skeletal muscle metabolism. *Annals of Medicine*, *38*(6), 389-402. https://doi.org/https://doi.org/10.1080/07853890600888413

Swain, D. P., & Franklin, B. A. (2006). Comparison of Cardioprotective Benefits of Vigorous Versus Moderate Intensity Aerobic Exercise. *The American Journal of Cardiology*, *97*(1), 141-147. https://doi.org/https://doi.org/10.1016/j.amjcard.2005.07.130

Takala, T. O., Nuutila, P., Knuuti, J., Luotolahti, M., & Yki-Järvinen, H. (1999). Insulin action on heart and skeletal muscle glucose uptake in weight lifters and endurance athletes. *American Journal of Physiology-Endocrinology and Metabolism*, *276*(4), E706-E711. https://doi.org/https://doi.org/10.1152/ajpendo.1999.276.4.E706

Talbot, L. A., Gaines, J. M., Ling, S. M., & Metter, E. J. (2003). A home-based protocol of electrical muscle stimulation for quadriceps muscle strength in older adults with osteoarthritis of the knee. *The Journal of Rheumatology*, *30*(7), 1571-1578. https://www.jrheum.org/content/jrheum/30/7/1571.full.pdf

Tanaka, H., Monahan, K. D., & Seals, D. R. (2001). Age-predicted maximal heart rate revisited. *Journal of the American College of Cardiology*, *37*(1), 153-156. https://doi.org/https://doi.org/10.1016/S0735-1097(00)01054-8

Theurel, J., Lepers, R., Pardon, L., & Maffiuletti, N. A. (2007). Differences in cardiorespiratory and neuromuscular responses between voluntary and stimulated contractions of the quadriceps femoris muscle. *Respir Physiol Neurobiol*, *157*(2-3), 341-347. https://doi.org/10.1016/j.resp.2006.12.002

Tokudome, M., Nagasaki, M., Shimaoka, K., & Sato, Y. (2004). Effects of home-based combined resistance training and walking on metabolic profiles in elderly Japanese. *Geriatrics & Gerontology International*, *4*(3), 157-162. https://doi.org/https://doi.org/10.1111/j.1447-0594.2004.00241.x

Trappe, S., Godard, M., Gallagher, P., Carroll, C., Rowden, G., & Porter, D. (2001). Resistance training improves single muscle fiber contractile function in older women. *Am J Physiol Cell Physiol*, *281*(2), C398-406. https://doi.org/10.1152/ajpcell.2001.281.2.C398

Treuth, M. S., Hunter, G. R., Weinsier, R. L., & Kell, S. H. (1995). Energy expenditure and substrate utilization in older women after strength training: 24-h calorimeter results. *Journal of Applied Physiology*, *78*(6), 2140-2146. https://doi.org/https://doi.org/10.1152/jappl.1995.78.6.2140

Tsurumi, T., Tamura, Y., Nakatani, Y., Furuya, T., Tamiya, H., Terashima, M., Tomoe, T., Ueno, A., Shimoyama, M., & Yasu, T. (2022). Neuromuscular Electrical Stimulation during Hemodialysis Suppresses Postprandial Hyperglycemia in Patients with End-Stage Diabetic Kidney Disease: A Crossover Controlled Trial. *J Clin Med*, *11*(21). https://doi.org/10.3390/jcm11216239

TTUHSC. (2023). *Center of Emphasis in Diabetes and Metabolism*. Texas Tech University Health Sciences Center El Paso. https://elpaso.ttuhsc.edu/research/MTM/coe/diabetes-and-metabolism/default.aspx

van Buuren, F., Horstkotte, D., Mellwig, K. P., Fründ, A., Vlachojannis, M., Bogunovic, N., Dimitriadis, Z., Vortherms, J., Humphrey, R., & Niebauer, J. (2015). Electrical Myostimulation (EMS) Improves Glucose Metabolism and Oxygen Uptake in Type 2 Diabetes Mellitus Patients--Results from the EMS Study. *Diabetes Technol Ther*, *17*(6), 413-419. https://doi.org/10.1089/dia.2014.0315

Van Der Heijden, G.-J., Wang, Z. J., Chu, Z., Toffolo, G., Manesso, E., Sauer, P. J. J., & Sunehag, A. L. (2010). Strength Exercise Improves Muscle Mass and Hepatic Insulin Sensitivity in Obese Youth. *Medicine & Science in Sports & Exercise*, *42*(11), 1973-1980. https://doi.org/10.1249/mss.0b013e3181df16d9

Van Dijk, J.-W., Manders, R. J. F., Tummers, K., Bonomi, A. G., Stehouwer, C. D. A., Hartgens, F., & Van Loon, L. J. C. (2012). Both resistance- and endurance-type exercise reduce the prevalence of hyperglycaemia in individuals with impaired glucose tolerance and in insulin-treated and non-insulin-treated type 2 diabetic patients. *Diabetologia*, *55*(5), 1273-1282. https://doi.org/10.1007/s00125-011-2380-5

Vivodtzev, I., Decorte, N., Wuyam, B., Gonnet, N., Durieu, I., Levy, P., Cracowski, J.-L., & Cracowski, C. (2013). Benefits of neuromuscular electrical stimulation prior to endurance training in patients with cystic fibrosis and severe pulmonary dysfunction. *Chest*, *143*(2), 485-493. https://doi.org/10.1378/chest.12-0584

Webb, P. (1981). Energy expenditure and fat-free mass in men and women. *The American Journal of Clinical Nutrition*, *34*(9), 1816-1826. https://doi.org/https://doi.org/10.1093/ajcn/34.9.1816

Weiss, A., Glaviano, N. R., Resch, J., & Saliba, S. (2018). Reliability of a novel approach for quadriceps motor point assessment. *Muscle & Nerve*, *57*(1), E1-e7. https://doi.org/https://doi.org/10.1002/mus.25728

Williams, M. A., Haskell, W. L., Ades, P. A., Amsterdam, E. A., Bittner, V., Franklin, B. A., Gulanick, M., Laing, S. T., & Stewart, K. J. (2007). Resistance Exercise in Individuals With and Without Cardiovascular Disease: 2007 Update. *Circulation*, *116*(5), 572-584. https://doi.org/10.1161/circulationaha.107.185214

Williams, N. (2017). The Borg Rating of Perceived Exertion (RPE) scale *Occupational Medicine*, *67*(5), 404-405. https://doi.org/https://doi.org/10.1093/occmed/kqx063

Wingfield, H. L., Smith-Ryan, A. E., Melvin, M. N., Roelofs, E. J., Trexler, E. T., Hackney, A. C., Weaver, M. A., & Ryan, E. D. (2015). The acute effect of exercise modality and nutrition manipulations on post-exercise resting energy expenditure and respiratory exchange ratio in women: a randomized trial. *Sports Medicine - Open*, *1*(1). https://doi.org/10.1186/s40798-015-0010-3

Wirtz, N., Zinner, C., Doermann, U., Kleinoeder, H., & Mester, J. (2016). Effects of Loaded Squat Exercise with and without Application of Superimposed EMS on Physical Performance. *Journal of Sports Science and Medicine*, *15*(1), 26-33.

Yardley, J. E., Kenny, G. P., Perkins, B. A., Riddell, M. C., Balaa, N., Malcolm, J., Boulay, P., Khandwala, F., & Sigal, R. J. (2013). Resistance Versus Aerobic Exercise: Acute effects on glycemia in type 1 diabetes. *Diabetes Care*, *36*(3), 537-542. https://doi.org/10.2337/dc12-0963

Yki-Järvinen, H., & Koivisto, V. A. (1983). Effects of Body Composition on Insulin Sensitivity *Diabetes*, *32*(10), 965-969. https://doi.org/https://doi.org/10.2337/diab.32.10.965

Yoo, J. H., & Kim, J. H. (2020). Time in Range from Continuous Glucose Monitoring: A Novel Metric for Glycemic Control. *Diabetes & Metabolism Journal*, *44*(6), 828-839. https://doi.org/10.4093/dmj.2020.0257

APPENDIX

PHONE INTERVIEW

**Names of individuals will not be disclosed during the phone screening as informed consent has not yet been obtained. Rather, individuals will be provided with a participant number and will be identified only by this number until informed consent has been provided.*

1. Female or Male?
    a. If FEMALE, are you or is there any chance you could be pregnant? Y / N
        i. Y→ Disqualified
2. What is your age? (between 18 and 50 years)
    a. DOB(mm/dd/yyyy): __/__/____
    b. AGE (years): _____
3. How tall are you (ft/cm)? (1in= 2.54cm)
4. How much do you weigh (lbs./kg)? (2.2lbs = 1 kg)
    a. BMI (kg/m2) (between 25 and 40): $\frac{Weight\ (kg)}{(\frac{Height\ (cm)}{100})^2}$ =_____
5. What is your Race?
6. Do you exercise regularly? Y / N
    a. How often do you exercise? How many minutes per week do you spend exercising? (<150min per week of structured exercise)
    b. What type of Exercises do you perform?
    c. How likely are you to stick to coming three times a week to the exercise lab?

VERY LIKELY – MODERATLY – NOT VERY LIKELY

7. Do you have any medical conditions or illness (Evidence of Cardiovascular Disease, Diabetes, High/Low Blood Pressure, Hyperlipidemia)? Y / N
    a. If Yes list→
8. Are you currently taking any medications (Such as drugs affecting your energy metabolism and body weight; supplements)? Y / N
    a. If so, what are they for?
9. Do you use any alcohol, drug abuse, or smoking in excess?

10. Do you have any electronic implants or electrical devices (i.e. Pacemakers. metal implants) Y / N
11. Do you have any leg injuries/surgeries where you weren't allowed to use your leg for a period of time (greater than a month)?

Eligible: Yes / No

Set Up Accelerometer pick up date/time: _____

*Print Accelerometer Instructions, and give to participant with accelerometer

DAY OF ACCELEROMETER

Physical Screening (Initial Each)
_____ Height, Weight BMI _____ (>25kg/m^2)

_____ Blood Pressure (5 min. rest; 3 different trials)
Normal? Yes____ No____ Value____

_____ Resting Heart Rate
Normal? Yes____ No____ Value____

_____ Fasting Blood Glucose
Normal? Yes____ No____ Value____

_____ Lipid Panel
Normal Cholesterol? Yes____ No____ Value____
Normal HDL? Yes____ No____ Value____
Normal LDL? Yes____ No____ Value____
Normal Triglycerides Yes____ No____ Value____

Cholesterol	Normal
TCL	<200mg/dL
HDL	>60mg/dL
LDL	Optimal<100mg/dL Near Optimal 100-129 mg/dL Borderline High 130-159 mg/dL
Triglyceride	Optimal<100mg/dL Normal<150mg/dL Borderline High 150-199 mg/dL

Initials

_____ Sedentary Lifestyle Confirmed? (less than 150 minutes structured exercise per week)
_____ Study Summary reviewed
_____ Study consent reviewed with participant, signed and copy provided
_____ Age confirmed to be 18-50
_____ BMI confirmed to be 25-40
_____ Concomitant Medications taken in the last 3 months
(ask specifically: cortisone injections/medications)
Medications: _____
_____ Use of alcohol, tobacco, or recreational drug use
Drinks per week ____ Use of tobacco per week____
_____ Food allergies? Yes____ No____

PASS or FAIL:

VITA

Gabriel earned a Bachelor of Science in Kinesiology from the University of Texas at El Paso and is earning his master's degree in Kinesiology as well. During his time as a graduate student, Gabriel served as a teaching assistant for the department of Kinesiology. As a research assistant under Dr. Sudip Bajpeyi in the Metabolic, Nutrition and Exercise Research (MiNER) Laboratory Gabriel received the Spring 2022 Dodson grant. As part of the masters in Kinesiology program, he also served as the head coach of the 2023 Texas ACSM Student Bowl team representing UTEP against other universities from the state of Texas. Gabriel plans to pursue a PhD in Exercise Physiology at Texas Tech University with the goal of furthering knowledge on cardiovascular function/disease to help others improve their health and wellbeing.

Contact information: gnarvaez@miners.utep.edu

This thesis was written by Gabriel Narvaez