NEUROMUSCULAR FATIGUE DEVELOPMENT WITH OBESITY

by

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To my husband Hafez
For being a constant source of love, motivation and unwavering support over the years,

& To my parents, Shahnaz & Amirhossein
Who put their faith on me and encouraged me to pursue a doctorate.

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Abstract

Over two-thirds of the U. S. population are either obese or overweight. The increasing prevalence of obesity among adults and its association with an increased risk of injuries has raised concerns in the occupational safety and health community. Physiological and neuromuscular changes with obesity may lead to a faster onset of muscle fatigue, which can moderate the risk of injuries. It is essential to determine obesity-related differences in fatigue development to understand the impact of obesity on the performance of occupational activities and the subsequent risk of injury. Understanding the influence of obesity on muscle functional capacity is an area that has begun to receive attention from the ergonomics and occupational safety research communities, as well as in clinical and rehabilitation settings, due to the increased prevalence of obesity and the adverse health outcomes observed. The majority of the work done in this area so far has not considered the underlying mechanisms that could be contributing to observed performance and productivity impairments with obesity. Identification of risk factors and understanding the mechanisms of fatigue can help to design some preventive strategies. This dissertation aims to identify obesity-related differences in maximum muscle capacity and fatigue mechanisms, quantifying the role of central and peripheral fatigue on task performance during submaximal exertions, and provide reliable strength estimates for practical use.

Chapter 1

1. Introduction

One demographic change in the general population has been the increasing proportion of obese ($30 \leq$ body mass index (BMI) kg/m^2) and overweight ($25 \leq$ BMI < 30 kg/m^2) individuals (Ogden et al., 2015). This along with the changes in modern workplaces toward more automated static tasks with small range of motions (Deeb & Drury, 1992) necessitate considering obesity as a risk factor in assessing muscle functional capacity (Sangachin & Cavuoto, 2016[b]). For static exertions, modeling endurance time based on relative loads has been of great interest to quantify localized muscle fatigue, which can cause musculoskeletal injuries (Chaffin, 1973). Physiological and neuromuscular changes with obesity suggest an altered fatigue development, both centrally and peripherally, which can affect force-endurance relationship.

Current force-endurance empirical models have not been tested with reliable statistical power in a large sample size. Theoretical models, on the other hand, have limited applicability because of the added complexity to explain the variability observed in the experimental fatigue data. Moreover, they have not been validated reliably or with a sample of subjects considering obesity to represent the current U.S. workforce. Therefore, the efficacy of the existing force-endurance models to account for the changing workforce is questioned in Chapter 2. For this purpose, the subject-specific fatigue rates for three tasks of hand grip exertion, shoulder flexion and trunk extension were calculated based on the popular theoretical model of Ma et al. (2009). Fatigue rates were then compared against the results of the experimental models from Ma et al. (2013) and Frey Law & Avin (2010) to evaluate the predictability of the current joint-specific models. Finally, updated exponential and power models were determined and compared from our large stratified sample representing the current demographic trends.

Obesity-related reduction in fatigue resistance ability during an endurance task might happen at the muscle (peripheral) or central nervous system (CNS) (central fatigue) levels. Signal generation and propagation impairment (Zory et al., 2005), incomplete motor unit activation or recruitment (Strojnik & Komi, 1998), lack of motivation or pain tolerance (Hill, 1926) are referred to as the central fatigue. Peripheral fatigue, on the other hand, occurs as a result of changes at the muscle level including fat-free cross-sectional area (Powell et al., 1984), muscle contractile properties and intramuscular oxidative metabolism (Baker et al., 1993; Zory et al., 2005), or impaired excitability or excitation-contraction coupling (Kent-Braun et al., 1994).

Determination of muscle fatigue mechanism differences with obesity, in terms of central versus peripheral fatigue, during sustained isometric endurance tasks is addressed in Chapters 3 and 4. In the former, an upper extremity muscle (middle deltoid) was targeted due to its frequent use during activities of the daily living and increased rates of injuries and pain complaints (Rechardt et al., 2010; Miranda et al., 2001; Østbye et al., 2007). In the latter, repeatability of the obesity impairment findings of Chapter 3 is tested for the lower extremity tibialis anterior muscle. Weaker ankle dorsiflexion muscle functional capacity is a risk factor in balance recovery and forward-directed falls (Fukagawa et al., 1995) and was suggested as a potential reason for reduced balance stability with obesity (Colné et al., 2008).

In addition to the endurance, strength is another common measure of muscle functional capacity, which is being used in design of tasks, tools and workplaces and for finding ergonomically safe limits. Localized muscle fatigue models have been frequently criticized for inaccuracy to predict endurance time for lower force intensities. For example, it was shown that Rohmert's curve (1960) overestimated the endurance time for force levels lower than 15-20% MVC (Sjogaard et al., 1986; Nag, 1991; Rose et al., 1992). The overestimation of endurance time could occur due to inaccurate measurement of maximum voluntary contraction (MVC) and therefore, underestimation of the target loads as a percentage MVC for the sustained contractions. Therefore, reliable peripheral fatigue assessment depends on true measurement of the force generating capacity (Vøllestad, 1997).

In occupational settings where voluntary tasks are expected, it is crucial to reliably estimate the muscle capacity in order to find the practical interventions to reduce work-related musculoskeletal disorders (WMSDs) for each group of population. Muscle strength measurement, however, is challenging due to motivation and pain tolerance issues, even in the presence of strong encouragement and visual feedback (Rashedi & Nussbaum, 2015[a]) or inhibitory factors related to the central nervous system (Gandevia, 1995; Vøllestad, 1997). In addition to within-subject variability of performance, including participants in a wider BMI range increases between-subject variability. Absolute and relative reliability of the strength measures in this study is discussed in Chapter 5. Having a reasonably large number of subjects and trials (i.e., repeated and replicated measures) in our experiment in addition to considering various sources of errors such as raters and subjects in all BMI-defined categories increase the reliability of our findings. For practical purposes, increased reliability helps the interpretability, decision-makings, and true estimation of the strength.

The summary of the findings from Chapter 2-5 is summarized in Chapter 6. An overall summary of the results and limitations of this work are provided in the final chapter. Future research direction suggestions are provided to help researchers continue and supplement this line of study.

Chapter 2

2. Testing the efficacy of existing force-endurance models to account for the changing workforce

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2.1 Abstract

This study evaluated whether the existing force-endurance relationship models are predictive of endurance time for overweight and obese individuals, and if not, provide revised models that can be applied for ergonomics practice. Data was collected from 141 participants (49 normal weight, 50 overweight, 42 obese) who each performed isometric endurance tasks of hand grip, shoulder flexion, and trunk extension at four levels of relative workload. Subject-specific fatigue rates and a general model of the force-endurance relationship were determined and compared to two fatigue models from the literature. There was a lack of fit between previous models and the current data for the grip (ICC = 0.8), with a shift toward lower endurance times for the new data. Application of the revised models can facilitate improved workplace design and job evaluation to accommodate the capacities of the current workforce.

2.2 Introduction

Over two-thirds (68.6%) of the U.S. population is either obese ($30 \leq$ body mass index (BMI) kg/m^2) or overweight ($25 \leq$ BMI < 30 kg/m^2) (Ogden et al., 2015). The consistently increasing prevalence of obesity and its association with increased risk of work-related musculoskeletal disorders (WMSDs) and injuries (Matter et al., 2007) have become areas of concern. WMSDs of the upper extremity (mainly shoulder and hand) and trunk are the most common, with 346,170 and 269,290 incidences, respectively, requiring days away from work in 2014 (BLS, 2015). The higher rates of WMSDs reported associated with obesity (Miranda et al., 2001; Østbye et al., 2007), particularly during prolonged submaximal exertions, might originate from associated physiological and neuromuscular changes. These changes include a higher proportion of fast-twitch, fatigable muscle fibers (Saltin et al., 1977; Wade et al., 1990), vascular occlusion (Kern et al., 1999; Newcomer et al., 2001), reduced neuromuscular activation with fatigue (Blimkie et al., 1990; Pajoutan et al., 2016[b]), and reduced oxidative enzyme activity (Goodpaster et al., 1997; Simoneau et al., 1995), all of which suggest altered physical fatigue development with obesity. On the other hand, an adaptive weight bearing training effect with obesity has been postulated, especially for the trunk and lower extremity postural muscles, which may enhance fatigue resistance ability (Lafortuna et al., 2005).

The highlighted demographic changes toward more obese individuals, who may be more prone to fatigue, along with industrial automation with higher proportion of static tasks with small range of motions in modern workplaces (Deeb & Drury, 1992), necessitates updated practical ergonomic guidelines to prevent fatigue as a risk factor of WMSDs (Ding et al., 2000) during sustained static tasks. In the literature and in ergonomics practice, localized muscle fatigue (LMF) development has been modeled by the intensity-maximum endurance time (MET) relationship, dating back over 50 years to generalized muscle fatigue models by Rohmert (1960) and Monod & Scherrer (1965). Subsequently, researchers have focused on modeling joint specific LMFs on frequently used joints such as the elbow, shoulder, hip, and knee, when the inaccuracy of using a generalized model for all muscle groups was reported due to a posture- and muscle-dependent relationship between endurance and relative loads (Rohmert et al., 1986). The force intensity (f_{MVC}) in this relationship is typically defined relative to maximum isometric contraction (MVC) of a joint or a muscle group.

A lack of generalizability to conditions beyond those tested in addition to either small sample size or very low statistical power has limited the applicability of the empirical models. While the coefficient of determination (R^2) values reported from these models indicate good fits with the data, these may be the result of overfitting due to the small samples. A well-structured summary of these models is provided by El Ahrache et al. (2006). They summarized and categorized the empirical models into general, upper limb, and back/hip models to provide the most commonly used percentiles (i.e., 5^{th}, 10^{th} and 15^{th}) of the MET for ergonomic applications. A larger meta-analysis of 194 papers on the intensity-static MET relationships was conducted by Frey Law and Avin (2010) and identified a significant joint dependency of the relationship leading to the development of best-fit power and exponential curves for each joint. This joint dependency is hypothesized to result from differences in muscle fiber type composition by joint (Brouillette et al., 2012). Despite the importance, any inter-individual variability in muscle fiber type distribution that could affect intensity-MET relationship has been disregarded in these empirical LMF models.

To account for the limitations associated with experimental models, theoretical models were proposed based on the theories of muscle activation and fiber type composition. However, most theoretical models are complex and therefore, not occupationally relevant. Moreover, their validation lacks reliable experimental power or large sample size. Liu et al. (2002) proposed a three compartment model based on three states of activated, fatigued and inactivated motor units (MUs). Constant fatigue, recovery, and brain effort rates for the three states were assumed. Also, a constant maximum brain effort during the course of exertion was assumed, which could only be valid during the short maximum exertions. Compatible with the assumptions, the model was only validated under the maximum relative load (100%MVC) and with only 10 subjects for the hand grip.

Later on, Xia & Frey Law (2008[a]) added a time varying function, rather than a constant brain intensity, as a submaximal exertion controller, with joint-specific optimal fatigue and recovery rates included in a subsequent revision (Xia & Frey Law, 2008[b]). For dynamic tasks, Ma et al. (2009) proposed an alternative model that begins to account for some individual differences by modelling MET as a function of external load relative to muscle capacity at a given time. The model was validated based on a set of experimental tests and against the static models provided in previous reviews (El Ahrache, 2006; Ma et al., 2009; Ma et al., 2012; Ma et al., 2013). Although a relatively good match was found in most cases, larger differences between models were observed for the back/hip experimental models. The deviations decreased by adjusting the fatigue rate (k) for each muscle group (i.e., shoulder, elbow, back/hip). Despite this improvement, models of the back/hip still deviated largely from the theoretical results. The remaining variability was mainly attributed to individual factors in addition to experimental methods.

Knowing the importance of individual factors, Ma et al. (2013) designed an experiment to compare the degree of the compatibility of the Ma et al. (2009) model to newly collected experimental data and to investigate inter-individual variability of fatigue rate. Results from a drilling task designed to fatigue the shoulder were reasonably fit to the theoretical model for 87% of the subjects. A high positive correlation between moment arm and fatigue rate was found indicating a significant difference between the fatigue rates of the two groups of participants, the 10 with the highest moment arm and the 10 with the lowest. This significant difference was attributed to the different muscle fiber type distribution for each group. They did not find a significant correlation between BMI and fatigue rate, however their sample was limited to normal weight and a few overweight participants.

To date, authors have added more complexity to the theoretical models to account for the variability observed in the experimental fatigue data. However, these models have only been validated with samples that did not include individuals who are obese, and thus are not representative of the current U.S. workforce demographics of over two-thirds overweight and obese.

Based on the differences in fatigability for endurance tasks that has been observed with obesity (Cavuoto & Nussbaum, 2013[a]; Mehta & Cavuoto, 2015; Mehta et al., under review), it is important that the theoretical models are re-evaluated. Therefore, one objective of the current study was to compare fatigue rates based on a sample of individuals with a range of BMIs. To achieve this objective, first, the subject-specific fatigue rates were determined and compared to the experimental results from Ma et al. (2013; Ma model). Second, the collected data was also tested against the empirical models from Frey Law & Avin (2010; FLA model) to assess the predictive ability of the models. Finally, a revised model of the force-MET relationship for hand grip, should flexion, and trunk extension was determined from a large sample representative of the proportions of normal weight, overweight and obese individuals in the general population. Since ergonomics in practice is dependent on designing to accommodate the largest segment of the population feasible, and specific models by personal characteristics is impractical, this study focused on developing models based on being representative of the current demographic trends rather than specific models based on obesity level.

2.3 Materials and methods

The data used for this paper originated from a study conducted by Mehta et al. (under review) on the effects of obesity on endurance time. This paper focuses on the development of endurance models, and a comparison to previously published models, to account for the range of BMI levels and representative proportions of obesity that are present in the U.S. workforce. For a more detailed explanation of the other aspects of the study procedure see Mehta et al. (under review).

2.3.1 Subjects and Ethical Approval

Following the approval of the standard study protocol by the Institutional Review Boards of University at Buffalo, Buffalo, NY and Texas A&M University, College Station, TX, a total of 142 healthy adults (141 of which were used due to missing demographic data from one participant) with a mean (standard deviation) age of 32.1 (9.2) were recruited between both sites. The sample consisted of 70 females and 71 males, with 34.7% non-obese, 35.5% overweight, and 29.8% obese. These proportions are consistent with the U.S. adult population breakdown (Ogden et al., 2015). Detailed demographic and anthropometric information is provided in Table 2.1. All participants provided signed informed consent to participate and completed demographic, health history, and physical activity questionnaires prior to the experiment. Only healthy individuals who did not perform extensive physical activity, determined by self-report, were included in this experiment. An electronic impedance scale (BC-568 Inner Scan, TANITA Corporation, Tokyo, Japan) was used for measuring weight and body fat percentage (%BF).

Table 2.1 Participants' information presented as mean (SD). Those groups that do not share a letter (in the order of normal, overweight and obese) are significantly different at $p < 0.05$ based on a *t*-test with gender pooled in each group

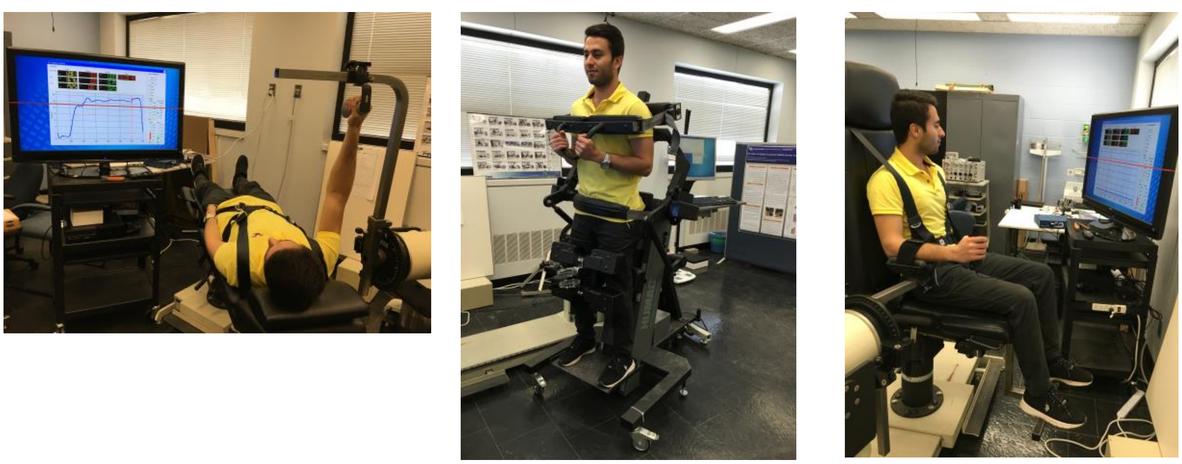
	Normal (n = 49)	**Overweight (n = 50)**	**Obese (n = 42)**
Age (yr)	31.4(8.5)	33.4(9.8)	31.4(9.4)
Body mass (kg)$^{A, B, C}$	64.8(8.4)	76.7(8.1)	100.0(15.5)
Stature (cm)	169.3(8.4)	168.2(8.4)	169.7(7.5)
BMI (kg/m^2)$^{A, B, C}$	22.6(2.1)	27.1(1.4)	34.6(3.6)
Body fat (%)$^{A, B, C}$	21.7(8.8)	29.9(7.7)	36.3(7.4)
Fat free mass (kg)$^{A, A, B}$	50.9(10.1)	54.0(10.0)	63.9(13.0)
Waist circumference (cm)$^{A, B, C}$	79.8(10.6)	90.8(7.8)	108.1(12.0)
Hip circumference (cm)$^{A, B, C}$	95.3(12.5)	103.2(7.4)	118.5(13.3)
Waist to hip ratio$^{A, B, C}$	0.84(0.06)	0.88(0.06)	0.91(0.06)

2.3.2 Experimental Setup and Protocol

Isometric endurance times for three tasks (shoulder flexion, trunk extension, and hand grip) were tested at four relative workloads (20, 40, 60, and 80% MVC). One workload for each task was tested during each session. The order of loads over the four sessions and tasks within a session were counterbalanced across subjects. Sessions were separated by at least 48 hours to minimize the effect of any residual fatigue on performance. The relative endurance targets were established based on the maximum of three consecutive MVCs completed during the first session for each task. After measurement of MVC, a sustained isometric endurance task at the assigned workload was performed. The participant was asked to exert at the target level for as long as possible, and the time at which they could no longer exert at the required level was recorded as the endurance time. Real-time visual feedback and encouragement were provided during the tests.

The shoulder flexion and trunk extension tasks were tested using an isokinetic dynamometer (Cybex Humac NORM, Ronkonkoma, NY, USA). Shoulder flexion of the right arm was tested with participants laying supine on the dynamometer chair with a seat belt around pelvis, arm flexed at 90º and elbow extended (Figure 2.1a). The dynamometer's axis of rotation and shoulder adaptor height were set with respect to the acromion process and arm length, respectively. For trunk extension, participants stood upright on the dynamometer footplate with slightly flexed (< 5°) trunk against the sacral pad (Figure 2.1b). The dynamometer's axis of rotation was aligned based on the iliac crest and L5/S1 location.

Hand grip force was tested with a hand dynamometer (SS25LA, BIOPAC Systems, Inc, Aero Camino Goleta, CA, USA) and data acquisition system (BIOPAC Systems, Inc, Aero Camino Goleta, CA, USA) with the sampling rate of 1 KHz. Participants were seated upright on the dynamometer chair with their arms at their side, resting the lower arm on a stabilizer tube, with the shoulder joint in a neutral position, and the elbow flexed at 90º (Figure 2.1c).



(a) (b) (c)

Figure 2.1 Experimental set-up: (a): shoulder flexion, (b): trunk extension, (c): hand grip

2.3.3 Statistical analysis

Statistical analyses were conducted in R (Foundation for Statistical Computing, Vienna, Austria) version 3.3.1, and SPSS version 24. Level of statistical significance was set at $\alpha = 0.05$. Relative loads of 20, 40, 60 and 80% were set according to the MVC of each individuals in the first session. In order to minimize any potential confounding based on this condition and differences in strength between days, these relative loads were recalculated based on the MVC of the corresponding session. Nonlinear model parameters were estimated using the nonlinear (weighted) least-squares method.

The fatigue rate (k) during isometric sustained endurance test was calculated for each f_{MVC}-MET combination ($N = 548$ for shoulder, 556 for grip, 501 for trunk) using the Ma et al. (2009) theoretical model presented in equation (1)

$$MET = -\ln(f_{MVC})/k\, f_{MVC} \qquad (1)$$

Fatigue rates were natural log transformed to meet the normality assumption. Homogeneity of variance, and independency of residual errors were verified by Leven's and Durbin-Watson tests, respectively, and by visual inspection of the transferred fatigue rates.

2.4 Model Comparison and Results

In order to compare the fatigue rates to the results from Ma et al. (2013), f_{MVC}-MET was modeled using equation (1) for each individual with their four data points as the inputs for curve fitting. Those individuals with missing data for any of the four points (either MVC or MET) and those with extreme values (i.e., where f_{MVC} exceeded 100% at any time or where the function could not be fit with the experimental data) were excluded from the analysis. A comparison of the model parameters and R^2 values with the Ma model are reported in Table 2.2. As Ma et al. (2013) only provided results for a shoulder task, comparison can only be made for this task. For the shoulder task, a higher fatigue rate with a greater variability was observed in the current sample.

Table 2.2 *k* (min^{-1}) are presented as mean (SD) and [min, max].

	Ma model	**New model**		
	Shoulder	Shoulder	Trunk	Grip
k (min^{-1})	1.02 (0.49) [0.37, 2.29]	1.76 (0.88) [0.49, 4.96]	0.61 (0.64) [0.08, 4.50]	1.95 (0.86) [0.65, 6.92]
R^2	0.87 (0.14) [0.23, 0.99]	0.90 (0.14) [0.20, 1]	0.82 (0.23) [0.07, 1]	0.81 (0.18) [0.05, 1]
Participants	40	119 [35 Ob, 42 Ov , 42 N]	61 [15 Ob, 25 Ov, 21 N]	122 [35 Ob, 42 Ov, 45 N]

The f_{MVC}-MET relationship for the full sample was also modeled in power and exponential function formats. These new models for grip, shoulder, and trunk were compared to the corresponding FLA models of the grip, shoulder and trunk. The model parameters and comparison measures are presented in Table 2.3. One-way-random ICC_1 was used to compare the models. For the shoulder and trunk-related tasks, a good agreement ($ICC_1 > 0.9$) was observed between the models. RMS and average deviations were also calculated. For the grip task, the FLA model overestimated endurance times. Coefficient of determination was calculated to measure the goodness of fit for the new model. Higher coefficients of determination were observed for the exponential functions compared to the power functions (plotted in Figure 2.2).

Table 2.3 Power and exponential model fits and comparisons

	FLA model		New model			Model Comparison		
	b_0	b_1	b_0	b_1	Adj-R^2	Average deviations (s)	RMS(s)	ICC_1
$MET = b_0*exp^{(fMVC*b1)}$								
Shoulder	685.46	-4.97	541.71	-4.27	0.68	0.95	12.86	0.99
Trunk	1165.09	-4.51	1240.05	-3.35	0.33	-98.34	111.59	0.90
Grip	808.15	-4.01	420.37	-3.67	0.71	67.18	89.95	0.80
Power: $MET = b_0*(fMVC)^{b1}$								
Shoulder	14.86	-1.83	13.91	-1.87	0.67	1.36	1.65	1
Trunk	22.69	-2.27	70.51	-1.46	0.32	-14.45	174.86	0.93
Grip	33.55	-1.61	18.21	-1.57	0.69	89.97	126.37	0.77

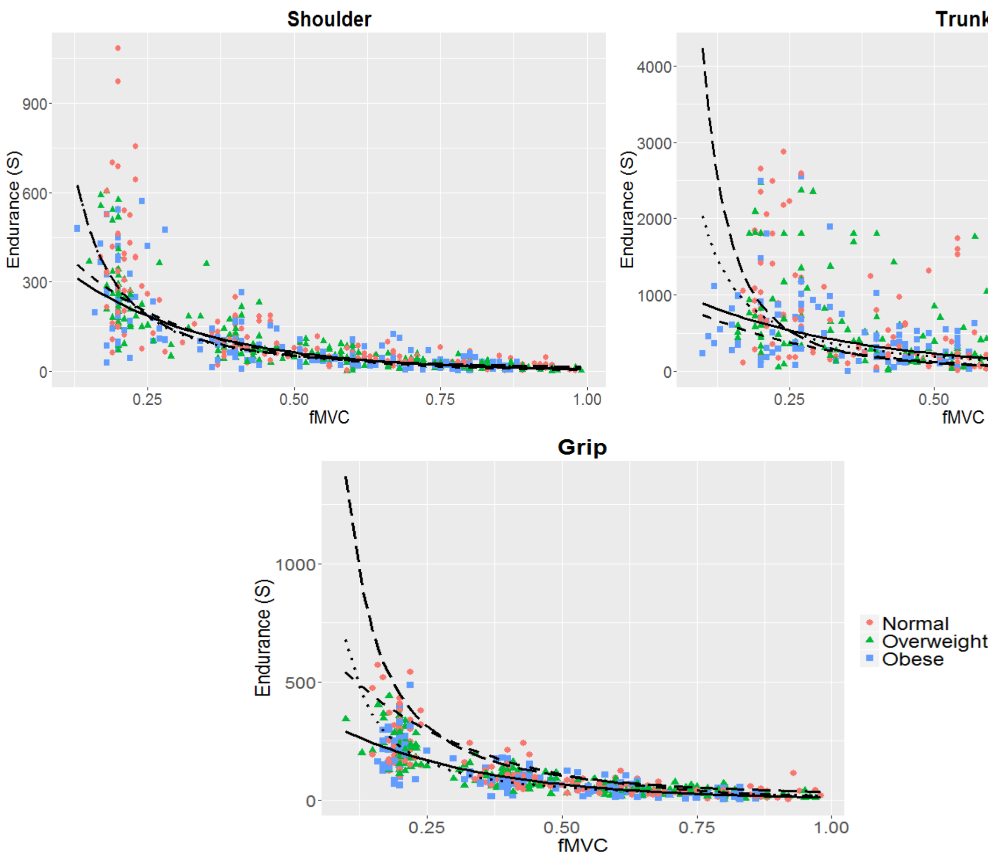


Figure 2.2 Models of fMVC-Endurance. Solid line: new model, exponential function; Dashed line: FLA model, exponential function; Dotted line: new model, power function; Long dashed: FLA model, power function.

2.5 Discussion

Compared to the experimental results of Ma et al. (2013), using the same theoretical model, a 42% faster fatigue rate was observed for the current sample during a shoulder task, indicating that the current theoretical model may not be a good predictor of static endurance time. Even general fatigue prediction models, based on previous experimental models, overestimated grip endurance time when obesity effect was not considered in the analysis. The results of this study support the hypothesis that the current models are not predictive of endurance time with obesity. Revised force-endurance exponential models were provided based on the current proportional sample including obese, overweight, and normal weight subjects, which can allow for more accurate predictions of upper extremity and trunk endurance time.

Previously, there was an attempt to show the effect of personal factors on localized fatigue models. Based on the idea that fatigue rate depends on muscle fiber type distribution, Zhang et al. (2014) designed a pushing experiment including 77 workers (38 males and 39 females) to assess the Ma et al. (2009) model for gender differences and to compare the results with static experimental model outputs for the shoulder muscle. Results indicated a higher fatigue resistance ability of females compared to male workers corresponding to a greater force decline. This was predicted due to a relatively lower cross-sectional area of fast-twitch muscle fibers for females. The effect of BMI on the fatigue rate was also tested and no significant effect was found, keeping gender as the only significant personal factor in this experiment. However, their sample only included normal weight and overweight subjects.

To our knowledge, this is the first study of localized fatigue modeling considering obesity. In this case, the log-linear relationship better represented the joint-specific nonlinear decay in the new proposed model (higher R^2) compared to the power function. The power function overestimated endurance time especially for $f_{MVC} < 0.25$ (Figure 2.2). The observed R^2 values in this study, especially for the trunk extension task, were relatively low due to a large and heterogeneous sample of subjects which includes ranges of BMI from 18 to 47.5 kg/m^2 with potentially different muscle functional capacity. Previous experimental models with high reported goodness-of-fit had either very small or homogeneous samples. Trunk extension endurance had the greatest variability compared to the shoulder flexion and hand grip tasks. Similarly, a higher variability for back/hip models observed compared to shoulder and elbow models has been reported previously (Ma et al., 2009). This has been attributed to the higher complexity of the musculoskeletal structure and muscle contributions at the back/hip (Ma et al., 2009). Also, back/hip was found to be the most fatigue-resistant body part in this study compared to the shoulder and hand grip. A similar pattern was reported previously for empirical models that found the trunk as the joint with the second longest endurance following only the ankle (Frey Law & Avin, 2010).

Previous models of handgrip failed to accurately predict endurance time in this study. On average, the model overestimated endurance by ~67 seconds with the summary of the previous grip models suggesting a reduced grip endurance in accordance to a shift toward higher obese individuals in the general population. In the literature, a 32% shorter isometric handgrip endurance was reported with obesity (Mehta & Cavuoto, 2015). Likewise, a negative effect of BMI on sustained hand grip endurance time was observed in another study (Eksioglu, 2011). The reduced hand grip endurance in the general population is critical in ergonomic practice where muscle fatigue is estimated based on the existing models to design work-rest schedules in order to prevent or minimize fatigue related injuries.

While this study presents a comparison to two of the main occupationally-relevant localized fatigue models, it is important to acknowledge that other models have been proposed in the literature and are not considered in this analysis (Rashedi & Nussbaum, 2015[a]). These particular models were selected based on their common application and based on the results of a recent analysis by Rashedi & Nussbaum (2015[b]). In addition, the findings of this paper are limited to endurance during static exertions with a sample of young to middle-aged, healthy individuals who were only recreationally active. Endurance time has been shown to be affected by age, strength, and health status, and the effects of these conditions are not captured in the current sample. Future work is needed to explore the effects of other individual factors and the interaction with obesity level.

2.6 Conclusions

This was the first empirical fatigue modeling study to include a large sample with a distribution of normal weight, overweight, and obese individuals in proportion with the general population. Significantly higher fatigue rates with obesity were found for the shoulder flexion and hand grip tasks. For the former task, there was a 42% higher fatigue rate compared to previous experimental results, indicating the importance of considering obesity in fatigue modeling for the shoulder. For the latter task, a lack of fit of the previous models with the current data was observed. In general, there was a shift of the predictive model toward lower endurance times. This paper presents new force-MET models based on the empirical data for estimation of endurance time for ergonomic application.

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Chapter 3

3. Central and Peripheral Fatigue Development in the Shoulder Muscle with Obesity during an Isometric Endurance Task

Submitted for publication in *European Journal of Applied Physiology*

3.1 Abstract

The current trend of increasing obesity prevalence and the accompanying increase in musculoskeletal injuries, especially at the shoulder, is concerning. Physiological and neuromuscular changes with obesity suggest an altered fatigue mechanism and development, which could lead to higher injury rates. The goals of this study were to investigate the effect of obesity on central vs. peripheral fatigue as well as on the physical signs of fatigue on the middle deltoid muscle. For this purpose, 22 non-obese (18 < body mass index (BMI) < 25 kg/m^2) and 17 obese (30 < BMI < 40 kg/m^2) individuals aged 18-32 years old completed superimposed maximum voluntary isometric contractions of shoulder abduction before and after a sustained isometric fatiguing task at either 30% or 60% of the muscle capacity. Results indicated an altered fatigue mechanism toward a higher contribution of central fatigue with obesity. A greater reduction of voluntary activation of motor units (p = 0.001) with fatigue was observed for individuals who are obese.

3.2 Introduction

The growing prevalence of obesity worldwide (13% of the population; Obesity and overweight 2015) and in the USA (37.7% in 2014, Ogden et al., 2015) has resulted in negative consequences of increased risk of work-related musculoskeletal disorders (WMSDs) (Han et al., 1997), lost workdays, and related economic burden (Hertz et al. 2004). Among WMSDs, injuries of the upper extremities had the highest incidence rate (32%), most frequently occurring at the hand (12.7%) and shoulder joint (8.2%) (Bureau of Labor Statistics, 2015). With increasing BMI, the chances of neck/shoulder injury claims increase (Østbye et al., 2007) to the extent that workers with shoulder pain are twice as likely to have a BMI ≥ 29 kg/m2 (Miranda et al., 2001). Shoulder pain in the deltoid region complaints during active resistive tests, including shoulder abduction, were associated with increased BMI and abdominal obesity (Rechardt et al., 2010).

For individuals who are obese there was a longer arm movement time to complete rapid tasks (Berrigan et al., 2006) and a farther reach from the work area due to an increased abdominal circumference (Gilleard & Smith, 2007; Hamilton et al., 2013). This, along with reduced blood flow and oxygen supplies to the muscle as a result of decreased capillary density (Kern et al., 1999; Newcomer et al., 2001), and a higher proportion of fast-twitch type II fatigable muscle fibers and the accumulation of fat tissues throughout the muscle without muscle contractile support (Saltin et al., 1977; Wade et al., 1990) may lead to a greater fatigue development. In agreement with this, shorter endurance times and higher rates of strength loss with obesity have been observed during shoulder flexion tasks (Cavuoto & Nussbaum 2013[a]; 2014).

Fatigue interferes with force generation (Helbostad et al., 2010) and muscle motor control capabilities, increases the likelihood of WMSD development (Rempel et al., 1992; Takala, 2002), and decreases neural drive to the motor units (Hakkinen, 1995). Muscle fatigue might occur at the muscle (peripheral) or central nervous system (CNS) (central fatigue) levels. Understanding the obesity-related differences of central versus peripheral fatigue requires an examination of the force production pathway both at the neuromuscular junction and at the muscle level.

At neuromuscular junction, central fatigue can occur as a reduction in voluntary activation of motor neurons due to neural drive deficiency, signal propagation impairment, incomplete motor unit activation (Strojnik & Komi 1998), and lack of motivation or pain tolerance (Hill, 1926). An increased chance of signal propagation failure for type II muscle fibers (Boerio et al., 2005) and a higher perceived postural stress reported with increased BMI (Park et al., 2009) may imply a greater contribution of central fatigue for individuals who are obese. Supporting this theory, reduced central activation and neuromuscular control of the lower extremities were previously diagnosed with obesity by means of superimposing electrical stimulation (ES) signals (Blimkie et al., 1990; Maffiuletti et al., 2007; Pajoutan et al., 2016[b]). The altered fatigue development with obesity of the lower extremities may be due to the added weight training effect (Lafortuna et al., 2005). Further examinations of central fatigue with obesity in the upper extremities and, of particular interest in this study, on the middle deltoid muscle are necessary.

Peripheral fatigue, on the other hand, is a decline in the force generating capacity as a function of differences at the muscle level resulting from fat-free cross-sectional area (Powell et al., 1984), muscle contractile properties and intramuscular oxidative metabolism (Baker et al., 1993; Zory et al., 2005), or impaired excitability or excitation-contraction coupling (Kent-Braun et al., 1994). Peripheral fatigue was previously quantified by measuring the twitch response of an inactivated muscle to a single stimulus (Ng et al., 2004). Reduction in the muscle twitch amplitude following a fatigue protocol was used as an indication of peripheral fatigue (McKenzie et al., 1992). Physiological changes with obesity necessitate further research on the possible altered role of peripheral fatigue with obesity.

It remains unknown whether fatigue resistance of the deltoid muscle with obesity would be affected at the muscle- or neural-level. Therefore, the main objective of this study was to quantify obesity-related differences in the muscle fatigue mechanism in terms of central versus peripheral fatigue for the commonly used middle deltoid muscle. It was hypothesized that ES would determine an altered contribution of central and peripheral fatigue with obesity. A reduced muscle activation after fatigue was anticipated for individuals who are obese. As a secondary objective, the effect of obesity on general fatigue manifestation during the endurance task was studied. A reduced muscle functional capacity with obesity was hypothesized.

3.3 Materials and Methods

3.3.1 Participants

Thirty-nine young healthy individuals aged 18-32 years volunteered from the university and local communities to form two groups of twenty-two non-obese ($18 < BMI < 25$ kg/m^2) and seventeen obese ($30 < BMI < 40$ kg/m^2) participants. The non-obese group consisted of eleven males and eleven females and the obese group included eleven males and six females. Detailed anthropometric and demographic information is provided in Table 3.1. The experiment was approved by the University at Buffalo Institutional Review Board and all participants provided written informed consent. To qualify for the experiment, subjects were required to have no history of physical disorders at the shoulder joint. In addition, participants who had extensive physical activities like heavy lifting, digging, aerobics or fast bicycling for more than 3 hours per week were excluded from this experiment. Weight and body fat percentage (%BF) were measured using an electronic impedance scale (BC-568 Inner Scan, TANITA Corporation, Tokyo, Japan).

Table 3.1 Participants' information presented as mean (SD). * indicates a significant difference at $p < 0.05$ based on a t-test

	Normal (n = 22)	Obese (n = 17)
Age (yr)*	21.5 (2.3)	23.2 (3.5)
Body mass (kg)*	63.1 (9.4)	98.0 (10.4)
Stature (cm)*	168.3 (8.46)	173.1 (8.65)
BMI (kg/m^2)*	22.2 (2.0)	32.7 (2.6)
Body fat (%)*	21.8 (7.3)	35.2 (6.8)
Fat free mass (kg)*	49.7 (10.3)	63.8 (11.4)
Waist circumference (cm)*	76.5 (5.8)	102.8 (8.6)
Hip circumference (cm)*	82.2 (5.8)	108.6 (8.3)
Waist to hip ratio*	0.93 (0.02)	0.95 (0.02)

3.3.2 Experimental Design

Subjects sat upright in an isokinetic dynamometer (Cybex Humac NORM, Ronkonkoma, NY, USA) chair with torso strapped to the chair by shoulder and seat stabilizer belts. Their right shoulder was abducted at 60º, elbow flexed at 90º and hand faced downward in a neutral position with their feet in a footrest with knees flexed at 90º. This position of the arm falls within the middle of the range of motion of the shoulder abduction, as the prime recruiter of the middle deltoid (Gorelick & Brown, 2007), and is commonly used during activities of daily living. Pilot testing confirmed the suitability of this testing position in terms of maximum output while isolating middle deltoid as much as possible. The shoulder angle was confirmed with a goniometer. All participants completed the task with their right arm. A padded shoulder adaptor was attached ~10 cm down from the acromion process and firmly secured to detect even small movements but not too tight to occlude blood circulation. This attachment supported the weight of the upper arm. Visual feedback was provided on a monitor in front of the subject. Figure 3.1 illustrates the experimental setup schematically.

Two 3.2 cm diameter round surface ES electrodes were placed ~2.5 cm apart (Baker & Parker, 1986) longitudinally on the motor points of the middle deltoid. The cathode was placed above the anode for more effective results (Nalty & Sabbahi, 2001). When needed, electrodes were trimmed to fit in the middle deltoid of each subject. An electromyography (EMG) mini sensor (Trigno

Wireless, Delsys Systems, MA) was attached in between the ES electrodes on the middle deltoid muscle belly (Hermens et al., 2000) to collect EMG signals at a collection frequency of 2048 Hz. The skin was shaved and cleaned prior to electrode placement. ES signals were set as single 70 ms supramaximal voltage electrical signal delivered by a stimulus isolation unit and constant current unit connected in series (Grass Instruments S88 stimulator, SIU5 stimulus isolation unit, and CCU1 constant current unit, Natus Neurology, West Warwick, RI). For each individual, signal intensity and optimal location of the ES electrodes were examined by tracking the changes in EMG M-wave amplitude until it reached its maximum. This method has been used extensively in the literature to account for inter-individual variability of the motor point locations and pain thresholds (i.e., Minetto et al., 2013; Neyroud et al., 2013; Okuma et al., 2013; Zory et al., 2005). Maximal tolerable current was found individually by progressively increasing the intensity by 10 mA, with a limit of 50 mA, until the M-wave amplitudes plateaued. A custom LabView program (version 13.0.0) was coded to drive the stimulator, alarm the participants to start and stop each subtask, and log the torque data for further analyses. Torque data were acquired at 1024 Hz rate and low-pass filtered using a fourth order Butterworth filter with a 4 Hz cutoff frequency.

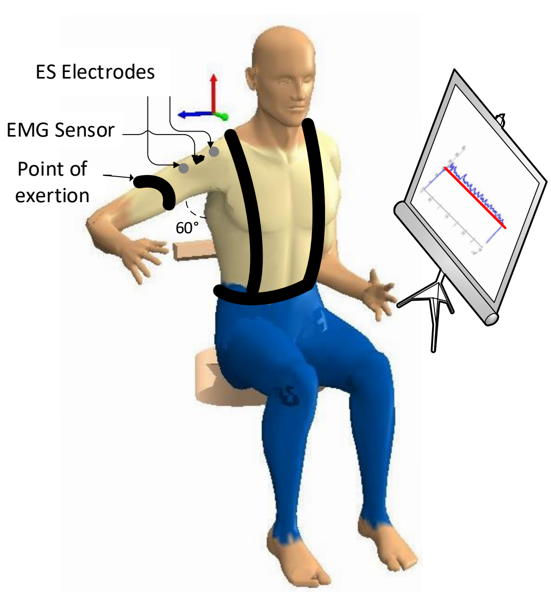

Figure 3.1 Experimental set-up simulated in 3DSSPP

After a short warm up of repeated shoulder abduction and adduction, the experiment started with an ES delivered at muscle rest (ES_0) while participants were instructed to sit relaxed and keep their arm in the described posture without exerting any force. After a 10 second rest, they performed three consecutive isometric maximum voluntary contractions (MVCs) of the shoulder abduction, each one 5 seconds long separated by 2 minutes rest. ES was superimposed on the third second of each MVC, when the torque output had plateaued. Excluding the first second of each MVC to disregard any initial sudden movements, the maximum torque of the three repetitions determined the muscle capacity of each participant, hereafter called the pre-MVC. Following one minute of rest after the last MVC, another ES was delivered at muscle rest (ES_1).

Four minutes later, a sustained isometric endurance task until exhaustion was conducted at either 30% or 60% of the pre-MVC, with each relative target torque (TT) performed during one session. Sessions were separated by at least two days and task order was counterbalanced to minimize any residual effects of fatigue. The TTs were set relative to pre-MVCs to minimize the potential confounding effect of supporting a heavier arm in obese individuals, in order to find any physiological differences with obesity. For the endurance task, participants were instructed to ramp up their torque after an alarm and maintain it right above the TT until exhaustion. To attain the target, analog and digital visual feedback in real-time was provided. The endurance task was terminated when the mean torque dropped below 10% of the TT for at least one second. After a short stop (200 ms) post endurance termination, an ES was superimposed on another 5 sec MVC (post-MVC). The 200 ms was considered to standardize the stop time between terminating the endurance task and quickly starting the post-MVC for all participants. After five seconds, participants received the last ES potentiated at muscle rest (ES_2). Figure 3.2 shows the experimental protocol.

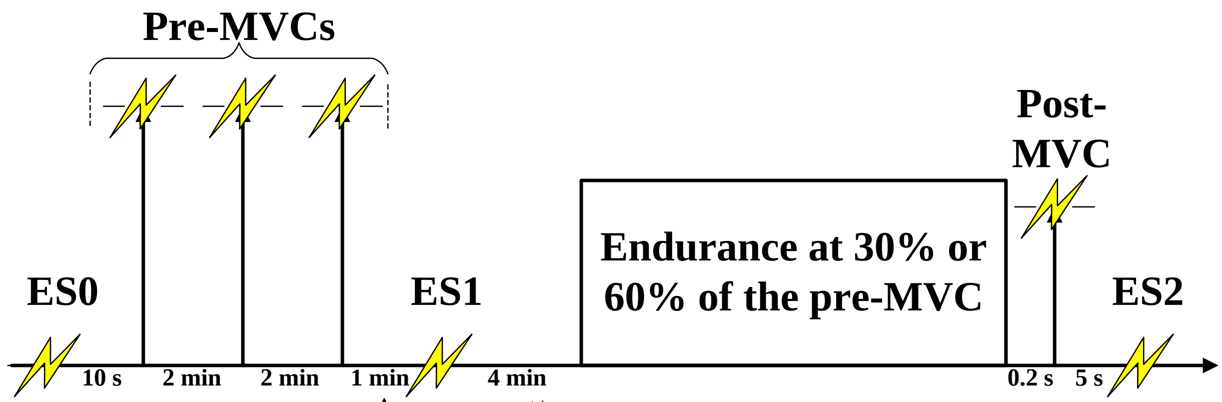

Figure 3.2 Experimental protocol (↑: exertions; : ES)

3.3.3 Assessments

Investigating the effect of BMI-defined obesity on the fatigue mechanism was the primary goal of this study. For that purpose, a measure of central activation ratio (CAR) was used, as calculated by equation (1), to quantify central fatigue by considering the increment in the torque output by superimposing ES (superimposed twitch) relative to its corresponding MVC. Prior to the fatiguing task, %CAR was averaged over the three pre-MVCs and called pre-CAR. The superimposed ES over the post-MVC determined the post-CAR value after the fatiguing task. The change in %CAR from pre- to post-fatigue has been a common measure in many studies to compare central fatigue (i.e., Kent-Braun & Le Blanc, 1996; Kent-Braun, 1999; Kent-Braun et al., 2002; Ng et al., 2004). Percent CAR (%CAR) shows the percent of unfatigued motor units activated voluntarily during maximum contractions. Thus, central fatigue was quantified as a fatigue-induced reduction in activation capability from pre- to post-endurance task (pre- minus post-CAR) (Kent-Braun, 1999).

$$\%CAR = MVC/(MVC+Superimposed\ twitch)\times 100 \qquad (1)$$

Peripheral fatigue, on the other hand, was quantified by considering the stimulations of the muscle at rest (i.e., ES_1 and ES_2). At muscle rest, the effect of voluntary activation would be eliminated to measure the un-fatigued motor units available to be activated by the ES (Neyroud et al., 2013). ES_0 was applied only to ensure that all subjects had the same level of muscle fatigue when participating in this experiment. Peripheral fatigue was quantified as a decrease of muscle twitch amplitude from pre- to post-task relative to the pre-task stimulation ((ES_1 - ES_2)/ ES_1).

In a few cases, relatively small increases of the motor unit activation after the fatiguing task result from the effect of synergistic muscles or a lack of maximum effort during the pre-activations. To minimize the likelihood of these errors, these small changes were disregarded resulting in equal pre- and post-twitch amplitudes or zero fatigue quantification.

In addition to the mechanism of fatigue, the physical manifestation of fatigue development was evaluated by endurance time, torque fluctuation, and torque loss. Torque loss was quantified as the percent of change from pre- to post-MVC relative to the pre-MVC. In addition, rate of torque loss per second over the endurance time ((pre- minus post-MVCs)/endurance) was calculated. Torque fluctuation were calculated by the coefficient of variation (CV = standard deviation/mean) for each 5 second non-overlapping window during the endurance task. The average (TF_a) and linear rate of torque fluctuation (TF_r) were then considered. To test the fatigue state of the muscle, the root-mean-square (RMS) and median-power-frequency (MPF) of the EMG power spectrum were calculated over 0.125 s windows with 0.0625 s overlaps during the endurance effort. Built-in noise reduction and filters from Delsys EMGWorks Acquisition software Version 4.1.1 were used to process the EMG data in real-time. The slopes of the linear regression for RMS and MPF were calculated and used for EMG temporal behavior. The joint changes in the EMG measures were used to indicate the muscle fatigue- versus force-induced states (Luttman et al., 2000). Based on this analysis, four states of recovery, force increasing, force decreasing and fatigue can be recognized with considering the slopes of RMS and MPF changes simultaneously.

Finally, relative target loads (i. e., 30% or 60%MVC) were converted to the absolute target loads (in Nm) that each participant exerted at in each session. The effect of absolute TT on the endurance time was then modeled. After testing linear, logarithmic, polynomial, power, and hyperbolic curves, the best fit curve (the highest R2) was achieved by a negative exponential curve in the form of $Endurance\ time = ae^{-b \times TT}$, where a is the endurance time at zero TT, and b is the exponential decay rate. Independent samples t-tests were performed to compare model parameters between the obese and non-obese groups.

3.3.4 Statistical Analysis

After extracting all dependent variables, separate analyses of covariance (ANCOVA) were conducted to assess differences between the obese and non-obese groups controlling for age and gender. All three assumptions of normality, homogeneity of variance, and independency of residual errors were checked by using Shapiro-Wilk test, Leven's and Durbin-Watson tests, respectively, and by visual inspections. For the pre- and post-MVC and TF_a data, natural log transformation was used to meet the assumptions. Also, square root transformation and Box-cox transformation with $\lambda = 3$ were used for endurance time, and post-CAR, respectively. Non-parametric Mann-Whitney tests were applied for torque loss, rate of torque loss, TF_r, RMS, MPF, central and peripheral fatigue, where data transformation could not validate the assumptions. Wherever relevant, statistical analyses were controlled for the stimulation intensity and dominant hand effect. All statistical analyses were performed in SPSS Version 22 (IBM Corporation) with the level of significant set at $\alpha = 0.05$.

3.4 Results

Obese individuals tolerated a higher ($p = 0.001$) current intensity with an average (SD) of 36.3 (10.35) mA compared to 29.75 (7.05) mA for the non-obese group. For the dependent measures, means, standard deviations (SD) are summarized in Table 3.2 for each load and obesity group. Also, p-values of the statistical analyses between the obese and non-obese groups are reported in Table 3.2.

3.4.1 Central vs. Peripheral Fatigue with Obesity

A comparable muscle twitch was observed at the beginning of the experiment with an average (SD) ES_0 of 0.65 (0.79) Nm for the non-obese and 0.63 (0.66) Nm for the obese group. On average, obese individuals had a higher pre-CAR compared to the non-obese individuals (88.3% compared to 85.1%, respectively). However, the post-fatigue activation ability of the obese group decreased ~11.7% versus an ~3.5% reduction for the non-obese group resulted in the post-CAR values of 76.6% and 81.6%, respectively. Results show a significant between group difference in the pre-CAR ($p = 0.018$) and a trend toward significant difference in the post-CAR ($p = 0.068$). A higher central fatigue ($p = 0.001$) for individuals who are obese compared to non-obese individuals was observed. Contrary to the effect of obesity on central fatigue, a trend toward reduced peripheral fatigue ($p = 0.06$) was observed for the obese group compared to the non-obese group by calculating the percent change from ES_1 and ES_2 before and after the endurance task relative to the ES_1 (24.0 (26.5) % for non-obese vs. 15.4 (27.8) for obese). Obese subjects had on average 8.6% less decrease on the relative number of available motor units when getting fatigued. A significantly higher positive trend of RMS change ($p = 0.019$) with obesity was observed. The slope of MPF was comparable and negative for both groups.

3.4.2 Physical Fatigue Manifestations with Obesity

Comparable pre- and post-MVC, endurance time, and torque loss were found between the obese and non-obese groups. However, normalizing the torque loss to the endurance time, to calculate the torque loss rate per second, resulted in a tendency toward a significant effect of obesity ($p = 0.081$). Obese individuals had on average a 14% higher rate of torque loss per second compared to non-obese subjects.

The relationship between endurance time and absolute TT was assessed after converting the relative to absolute TT for each subject. The best fit curve is shown in Figure 3.3 with $R^2 = 0.48$ and 0.32 for the non-obese and obese groups, respectively. Two independent samples t-tests indicated significant differences of model parameters a ($p < 0.001$) and b ($p = 0.009$) between the two groups. Endurance time estimation at very low TT (asymptotic to zero) indicated that the tolerance of the obese individuals is ~19% of the tolerance of the non-obese individuals. However, exponential decay rate for the obese individuals is ~12% of the decay rate for the non-obese group when moving toward higher loads.

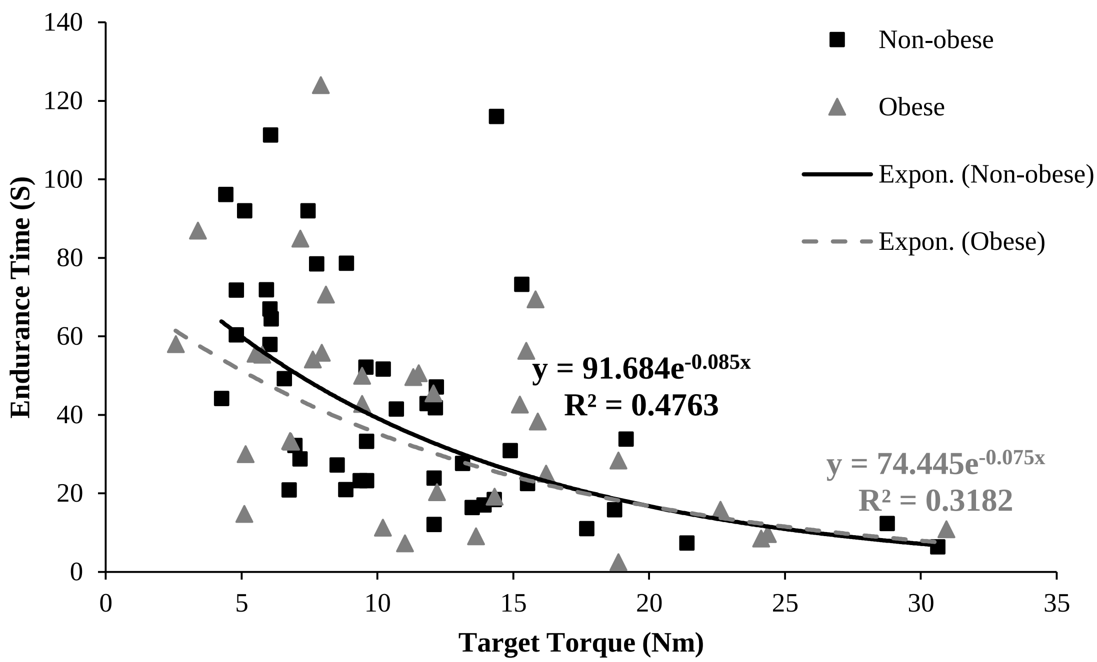

Figure 3.3 Endurance (s) and absolute target load (Nm) relationship

Table 3.2 Results are presented as mean(SD). Significant p-values are bolded and marked with *

Measures	**Normal**		**Obese**		***p***
	30%	**60%**	**30%**	**60%**	
Pre-MVC (Nm)	24.8(9.3)	25.7(9.6)	28.0(13.4)	30.7(13.8)	.955
Endurance (s)	64.6(26.9)	24.6(12.8)	56.3(25.6)	24.2(18.2)	.266
Post-MVC (Nm)	17.3(6.9)	20.5(9.8)	17.7(9.2)	24.8(12.7)	.483
Pre-CAR (%)	85.0(6.2)	85.1(6.6)	86.4(5.2)	90.3(5.3)	**.018***
Post-CAR (%)	80.3(12.1)	82.9(9.9)	73.2(15.6)	79.9(9.0)	.068
Central fatigue (%)	7.2(9.6)	4.3(5.4)	14.2(12.8)	11.3(8.4)	**.001***
Peripheral fatigue (%)	26.6(29.0)	21.4(24.0)	17.7(30.2)	13.2(25.8)	.061
RMS Slope($\times 10^{-6}$)	-.58(1.2)	-.74(9.7)	.23(.68)	2.18(6.4)	**.019***
MPF Slope	-.48(.37)	-.91(.78)	-.58(.31)	-.75(1.72)	.496
TF_r (1/s)	.03(.04)	.08(.10)	.04(.07)	.08(.09)	.232
TF_a (Nm)	.17(.02)	.15(.07)	.17(.05)	.15(.05)	.911
Torque loss (% Pre-MVC)	29.8(17.4)	20.4(16.2)	38.0(18.1)	19.8(16.5)	.304
Torque loss rate (Nm/s)	.14(.12)	.29(.32)	.21(.16)	.49(.91)	.081

3.5 Discussion

The increased central fatigue with obesity found in this experiment supported the first hypothesis. The second hypothesis was partially supported by the results. Obesity-related impairment of the middle deltoid muscle capacity was evident only in a trend toward a higher rate of torque loss.

3.5.1 Central vs. Peripheral Fatigue with Obesity

The joint analysis of EMG measures (Luttmann et al., 2000), the positive trend of RMS and negative trend of MPF change, indicate a fatigued state for the obese individuals. In contrast, the negative trends of RMS and MPF change indicate a force decreasing state for the non-obese group, which suggests that they stopped the endurance task prior to a fatigued state. The fatigue state of the middle deltoid of the obese individuals was diagnosed as the result of central rather than peripheral fatigue in this study. This was found from a greater reduction from pre- to post- CAR, which indicated a greater reduction in the ability of the obese group to voluntarily activate their available motor units once they fatigued. Similarly, reduced motor unit activation with obesity was reported for knee extensor (Blimkie et al., 1990; Maffiuletti et al., 2007) and ankle dorsiflexor (Pajoutan et al., 2016 [b]) muscles suggesting a greater role of central fatigue with obesity for the lower extremities. Central fatigue impairment with obesity reported for the lower extremities was verified for the middle deltoid muscle in this study.

Quantification of the role of central fatigue in torque loss provides a useful metric for between-group comparison. Previously, 16% central fatigue, calculated as a CAR drop from 0.94 to 0.78, during a fatiguing task of ankle dorsiflexor resulted in a 78% torque loss for normal weight participants (Kent-Braun, 1999). Therefore, a 20% contribution of central fatigue in the muscle fatigue development was estimated. In this study, the ~12% CAR reduction caused an ~29% torque loss, leading to an estimation of ~42% contribution of central fatigue for the obese individuals. For the non-obese group, only ~14% (~3.5% central fatigue of the ~25% torque loss) of the muscle fatigue was due to central fatigue. An ~3 times greater contribution of central fatigue for the obese individuals compared to non-obese individuals could be a concern especially during longer exertions, where a higher contribution of central fatigue has been suggested (Baker et al., 1993).

Contrary to having a higher central fatigue impairment, obese individuals had a trend toward a lower peripheral fatigue compared to their non-obese counterparts. Keeping the ES intensity constant, a greater decrease in the ES amplitude from pre- to post-task relative to pre- task was observed for the non-obese group. Central fatigue impairment might cause a faster task termination for the obese individuals before they reach to a comparable peripheral fatigue. A comparable peripheral fatigue would be expected for the obese group if central fatigue did not hinder the task continuation.

3.5.2 Physical Fatigue Manifestations with Obesity

An equivalent endurance time at both 30% and 60% MVC was observed between obese and non-obese groups, which is consistent with comparable times to task failure at relative TTs reported for the quadriceps muscle (Minetto et al., 2013; Paolillo et al., 2012). However, when considering absolute targets that participants tolerated, a shorter endurance time of obese individuals compared to non-obese individuals was more evident for lower absolute TT (i.e., less than 15 Nm; Figure 2.3), where type I muscle fibers are mainly engaged in the force retention. This is consistent with a reduced isometric shoulder muscle endurance at a low absolute TT (9 Nm) reported by Cavuoto & Nussbaum (2013[a]). They also found a greater shoulder muscle torque loss, which suggested an obesity-related impairment of shoulder muscle functional capacity at low loads. At high absolute TTs or short endurance times, any obesity-related differences might not have a chance to manifest.

Impaired middle deltoid muscle capacity was not evident in the torque loss and torque fluctuation or its rate of change over the endurance trial at either low or high relative TT for young healthy subjects. Similar results were reported with an isometric ankle dorsiflexion endurance task at 60% MVC (Pajoutan & Shortz, 2014) and shoulder (Cavuoto & Nussbaum, 2013[a]; 2013[b]) flexion tasks were observed previously. Likewise, upper extremity neuromuscular control between non-obese and obese groups at relative TT of 15% and 40% MVC found to be comparable in another study (Hue et al., 2008).

3.5.3 Limitations

Due to some limitations, the results of this study should be interpreted with caution. First, the BMI and age recruitment criteria in this study were limited to Class I and Π obesity (30 < BMI < 40 kg/m^2) and younger adults, respectively. Extremely obese individuals (BMI > 40 kg/m^2) were excluded from this study since they only consist ~6% of the population (Flegal et al., 2010). Second, there are some limitations associated with using ES to quantify central and peripheral fatigue. Detecting small twitches with regards to the background noises of maximal exertions was challenging. To minimize errors, a higher resolution (1024 Hz data collection frequency), averaging technique over pre-MVCs, and a custom-written Matlab code and visual inspection were used to identify and confirm the twitches, however this might have introduced some error in the results. Surface ES might not have activated those motor units deep in the muscle (Hultman et al., 1983). Even after identifying central fatigue with obesity using ES, the underlying reasons of this impairment, including impaired signal generation or propagation, incomplete motor unit activation or recruitment, or lack of motivation, are not known. Further investigations on the possible reasons for central fatigue impairment with obesity are needed to supplement this research. Third, the effect of possible excitation of antagonist muscles was neglected. To minimize this effect, participants were firmly secured in a fixed posture to isolate the middle deltoid in shoulder abduction. Lastly, the comparisons in this study were based on relative TTs, whereas, in most settings absolute loads are required regardless of individuals' capacities. It is unclear whether the same results would have been observed under the same absolute TT for both groups.

3.6 Conclusion

Overall, the results of this study suggest that a meaningful difference of physical fatigue manifestations of the middle deltoid muscle is unlikely unless at extreme levels of obesity or when interacting with the effects of aging. However, a greater contribution of central fatigue was observed with obesity during the sustained endurance tasks. This suggests that the faster fatigue development with obesity observed in many other studies likely originated in the central elements rather than the peripheral factors for young healthy obese individuals. The current signs of central fatigue could lead to impaired motor performance, especially for extremely obese or older obese individuals.

3.7 Acknowledgements

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Chapter 4

4. The Effect of Obesity on Central Activation Failure during Ankle Fatigue: A Pilot Investigation

Pajoutan M., Mehta R. K., Cavuoto L. A. (2016[b]). The effect of obesity on central activation failure during ankle fatigue: a pilot investigation. *Fatigue: Biomedicine, Health & Behavior*. *4*(2), 115-126.doi: 10.1080/21641846.2016.1175178.

4.1 Abstract

In a forward-directed oscillation, Individuals who are obese may be at higher risk of falls due to weaker ankle dorsiflexor muscles as the prime controllers of the balance recovery. Muscle recovery may be negatively affected by fatigue at either the central (activation) and/or peripheral (contraction) levels. Additional body weight support, as required with obesity, may increase lower extremity muscle fatigue development. The objective of this pilot study was to quantify the relationship among BMI and fatigue symptoms measured as endurance time, torque loss, and central activation failure for the tibialis anterior. Twenty-two young males (mean body mass index (BMI) = 27.0 kg/m^2 (range: 20.5-36.7 kg/m^2) completed maximum voluntary isometric contractions (MVICs) of the ankle dorsiflexors before (pre-MVIC) and after (post-MVIC) a sustained isometric fatiguing task at 60% of their strength. Electrical stimulation was superimposed during each MVIC to identify central activation failure. Pre-fatigue central activation was equivalent across participants. However, BMI and pre-MVIC explained 59% of the variation in central activation failure after the fatiguing task as well as 29% of the variation in endurance time. In fact, a significant effect of obesity on central activation failure was observed with fatigue. Finally, 43% of the torque loss following fatigue variation was explained only with pre-MVIC. The findings of this

pilot investigation indicate that endurance and central activation after fatigue may be impaired with increased BMI. This finding may aid in the evaluation of falls mechanisms and the development of falls prevention strategies.

Keywords: tibialis anterior; endurance; electrical stimulation; central activation ratio

4.2 Introduction

The prevalence of body mass index (BMI)-defined overweight and obesity (BMI $\geq$ 25 kg/m^2) in the US had increased to an epidemic level of ~69% in 2012 (Flegal et al., 2010). This growing trend has raised concerns about the consequences of obesity, including the implications for injury risk (Finkelstein et al., 2007; Kouvonen et al., 2013). A positive correlation between obesity and an increased risk of fall-related injuries has been observed (Fjeldstad et al., 2008). Moreover, a higher proportion of falls- and overexertion-related injuries requiring medical treatment has been reported in obese individuals when compared to injury mechanisms for individuals who are not obese (Matter et al., 2007).

A decline in lower extremity strength has been identified as a risk factor for falls and a predictor of the ability to recover balance equilibrium (Fukagawa et al., 1995). Of the lower extremity muscles, ankle dorsiflexor muscle strength is a primary predictor of balance recovery, gait speed, and occurrence of forward-directed falls (Fukagawa et al., 1995). Ankle muscle weakness, especially the dorsiflexor muscles, has also been shown to be a significant risk factor of falls for older adults (Whipple et al., 1987). When controlling for body mass and height, Grabiner et al. (2005) found a significant effect of isokinetic ankle dorsiflexor strength on forward fall resistance capability, based on maximum forward lean angle. With obesity, impaired balance recovery from a forward leaning position with an initial angular velocity was observed (Matrangola & Madigan, 2011). Weaker ankle muscle strength was suggested as a potential reason for reduced balance stability with obesity (Colné et al., 2008). Individuals who are obese also alter their walking gait pattern to include significantly higher ankle dorsiflexion and lower ankle plantarflexion angles (Spyropoulos et al., 1991). Therefore, additional demand is placed on the ankle dorsiflexor muscles, requiring additional strength and fatigue resistance for balance and mobility (Corbeil et al., 2001).

Muscle fatigue can increase postural sway and increase the ability of the muscle to generate force, interfering with balance control (Helbostad et al., 2010). The measured reduction in fatigue resistance of the lower limbs with obesity, as observed by Maffiuletti et al. (2007) could compromise balance control and lead to an increased risk of falls. The added body mass associated with obesity increases muscular load, which may result in decreased endurance and faster fatigue initiation. Moreover, individuals who are obese tend to complete tasks more slowly and over a longer time, which may result in prolonged muscle loading (Tetteh et al., 2009).

Obesity-related impairment of fatigue resistance during an endurance task could happen at the central (activation) and/or peripheral (contraction) levels. In this study, central activation failure with fatigue, equivalently referred to as central fatigue, was examined. Impaired central activation through the nervous system (Zory et al., 2005) and impaired or incomplete motor neuron activations (Strojnik & Komi, 1998) or lack of motivation to generate sufficient signals are all related to central fatigue. Failure to fully recruit motor neurons of the lower extremity was reported with obesity, implying impaired neuromuscular control in the absence of fatigue (Blimkie et al., 1990) which may facilitate central fatigue. Neuromuscular propagation failure is more evident for type II muscle fibers (Boerio et al., 2005) and obesity is associated with a higher proportion of type II muscle fibers (Wade et al., 1990).

Experimentally, obese individuals demonstrated greater voluntary fatigue development than non-obese during knee extensions. Maffiuletti et al. (2007) identified this finding as a central rather than a peripheral fatigue impairment with obesity, based on an electrically stimulated isokinetic fatigue protocol. Additionally, higher perceived postural stress reported with increased BMI (Park et al., 2009) could exacerbate the negative affect of central elements on muscle capacity and fatigue resistance. Deeper understanding of the severity effect of central fatigue with increasing BMI in lower extremity muscles is needed to provide insight for determining intervention and prevention strategies.

Fatigue negatively affects neural drive to motor units (Hakkinen, 1995). Task parameters such as high frequency and intensity may change the fatigue mechanism by reducing central nervous system (CNS) capacity (Gandevia, 2001). In addition, lack of motivation and low pain tolerance may lead to an earlier termination of the fatiguing task (Hill, 1926). In occupational settings where voluntary tasks are expected, it is crucial to measure the true capacity of the muscle in order to identify the practical interventions that reduce work-related musculoskeletal disorders for each group in the population.

True measurement of muscle capacity, however, is challenging because voluntary force generation is confounded by lack of motivation, pain tolerance threshold, and inhibitory factors related to the CNS (Gandevia et al., 1995). Even strong encouragement to maximum voluntary exertion and visual feedback might not be sufficient to eliminate the central limitations. Thus, superimposed electrical stimulation (ES) has been applied to measure maximum evocable strength and to understand activation failure (Bigland-Ritchie et al., 1995). Superimposed ES usually increases the force output because either all motor units may not be completely recruited or motor units are voluntarily activated below the maximum brain effort (Belanger & McComas, 1981). An increase in the superimposed twitch after the fatiguing task is a sign of central fatigue (Kent-Braun, 1999).

To our knowledge, no studies have addressed the effect of central fatigue development of the tibialis anterior (TA) muscle with increasing BMI. The role of the ankle dorsiflexor muscles in stability control and balance recovery supports a need for additional research. The overall goal of this study was to quantify the relationship between BMI, as the main obesity indicator, and fatigue symptoms measured as endurance time, torque loss, and central activation failure for the TA. It was hypothesized that adults with higher BMI would demonstrate impaired endurance and neuromuscular activation.

4.3 Method

4.3.1 Participants

Twenty-two healthy males, including seven normal weight, eight overweight, and seven obese subjects, mean age of 25.1 ± 4 years with BMIs ranging from 20.5 to 36.7 kg/m^2 (mean (SD) = 27.0(4.6) kg/m^2) and body fat percentage ranging from 10% to 36% (mean (SD) = 23.2(6.6)%) participated in this study (more details in Table 4.1). The study procedures were approved by the University at Buffalo Institutional Review Board and all participants provided their informed consent at the start of the study. At the beginning of the experimental session, anthropometric measurements including body mass, height, body fat percentage, and waist and hip circumference were taken. Body fat percentage was assessed by using an electronic impedance scale (BC-568 Inner Scan, TANITA Corporation, Tokyo, Japan). Individuals with self-reported extensive physical activities were excluded from the experiment.

Table 4.1 Participant Anthropometric Measurements

Measure	Mean (Standard Deviation)	Range
Age (yr)	25.1 (4.0)	18-33
Body Mass (kg)	84.8 (14.9)	63.7-109.0
Stature (m)	1.77 (0.06)	1.67-1.89
Body Mass Index (BMI; kg/m^2)	27.0 (4.6)	20.5-36.7
Waist Circumference (cm)	98.7 (11.3)	81.0-117.0
Hip Circumference (cm)	111.6 (9.5)	97.0-138.0
Body Fat (%)	23.2 (6.6)	10.0-36.0

4.3.2 Procedure

Right ankle dorsiflexor muscle strength and endurance were tested using an isokinetic dynamometer (Cybex Humac NORM, Ronkonkoma, NY, USA). After a short warm up of repeated ankle plantar- and dorsiflexion exercises, participants were asked to lay supine on the dynamometer chair with their right thigh strapped to a thigh pad and right foot fixed to a footplate. The dynamometer center of rotation was aligned to the participant's ankle with the right knee flexed at 90° and the ankle at 110° (with neutral being 90°). The experimental protocol consisted of three pre-task maximum voluntary isometric contractions (pre-MVICs), a sustained isometric endurance task with a workload level of 60% MVIC, and a post-endurance MVIC. ES was applied during each of the MVICs. The experimental protocol is shown graphically in Figure 4.1.

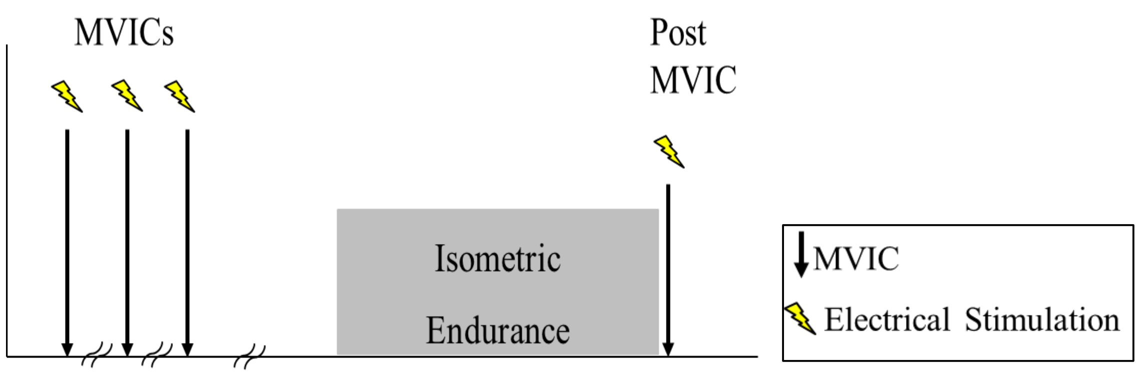

Figure 4.1. Experimental protocol

Prior to the MVICs, the optimal level of ES was determined. A superimposed 250 μs, 50 Hz bipolar ES train at supramaximal voltage (Grass Instruments S88 stimulator, SIU5 stimulus isolation unit, and CCU1 constant current unit, Natus Neurology, West Warwick, RI) was delivered to the TA through two 5 × 5 cm electrodes placed 1 cm apart over the muscle belly, with the cathode ~3 cm below the fibular head. This positioning has been reported to yield the most efficient activation of the superficial motor points in the TA, which consists of 75% type I muscle fibers (Gregory et al., 2001; Jakobsson et al., 1988) located in superficial regions (Henriksson-Larsen et al., 1983), with minimum current, discomfort, and co-activation of other muscles for torque levels greater than 60% of MVIC (Okuma et al., 2013). The size of the electrodes was modified, if needed, to fit in each individual's TA muscle. The torque developed by the voluntary exertion and superimposed ES was measured with a custom-written LabView program.

Observation of the generated torque was supplemented with surface electromyography (EMG) analysis. A mini-head surface EMG electrode (Trigno Wireless, Delsys Systems, MA) was placed between the ES electrodes along the ankle dorsiflexor muscle. The skin over the TA was shaved and cleaned prior to placement of the surface electrode. The electrode was placed at the center of the muscle parallel with the muscle fiber orientation. The EMG signals were collected at a rate of 2048 Hz.

At muscle rest, EMG M-waves were used to find the optimum placement of the ES electrodes and current in order to account for inter-individual variability. Monitoring the Mwaves progression of motor unit recruitment to reach to the max has been widely used in the literature to control the stimulation intensity and electrode positioning (Zory et al., 2005; Belanger & McComas, 1981; Okuma et al., 2013; Behm et al., 1996; Galea, 2001; Minetto et al., 2013; Neyroud et al., 2013). For each participant, the ES current was increased gradually by 10 mA increments, within tolerance range, until the TA M-wave amplitudes were plateaued. The optimum stimulation intensity was then increased by 20%, with a limit of 50 mA, in order to counterbalance for limiting factors including pain and electrode displacement relative to motor points during the MVICs (Neyroud et al., 2013).

After finding the optimum ES current, the experiment began with three MVICs, lasting 5 s each with 2 min rests in between, with superimposed ES delivered to the ankle dorsiflexor muscle at the third second of each contraction. During the contraction, participants were instructed to ramp up to their maximum torque during the first second and then hold that level for the remainder of the contraction. The largest of at least three MVICs was used to determine the voluntary strength for each participant. Participants were asked to generate additional MVICs, if needed, until the final three were within 20% of each other.

After 10 min of rest, a submaximal isometric fatiguing exercise at 60% of MVIC was performed. This level was selected to activate both slow and fast twitch muscle fibers and to represent a large perturbation that may happen in occupational settings or fall recovery conditions. Participants were instructed to ramp up their torque after hearing a beep and keep their torque level at 60% of MVIC until voluntary exhaustion. Real-time digital and analog visual feedback was provided to help track the target torque level. Failure to maintain the torque at or above the target level, a drop in the mean generated torque >10% below the target for 1 s without re-attaining it, terminated the endurance task. At the endurance limit, a post-fatigue MVIC with superimposed ES was completed.

Superimposed ES is applied during maximal voluntary exertions (Merton, 1954) to show the inability to fully activate motor units despite the maximal effort to activate them. Otherwise, it would be unclear whether the increase in the force by the ES (twitch amplitude) is due to the inability to activate the motor units or deliberately neglected activation of motor units during submaximal exertions. In a previous study, central fatigue of the TA was measured by superimposing a train of ES during endurance task at 100% MVIC (Vie et al., 2013). Using a submaximal fatiguing task in the current protocol, the ES was superimposed right after the endurance task, during the post-MVC to avoid any confusion in the interpretation of the results.

4.3.3 Study Measures and Statistical Analysis

Dependent variables included time to exhaustion (endurance time), torque loss after the endurance task, and central activation measure. Ankle strength was quantified as the absolute torque recorded during the pre-MVICs. Voluntary torque loss from pre- to post-MVIC and endurance were measured as the gold standard indicators of localized muscle fatigue. Torque data were sampled at 1024 Hz and low-pass filtered using a fourth order Butterworth filter with a 4 Hz cutoff frequency.

Central activation ratio (CAR) (Kent-Braun & Le Blanc, 1996) was used to quantify the torque generated by the activation of motor units by the superimposed ES. CAR was calculated using Equation (1) (Kent-Braun, 1999). In this equation, *a* is the peak voluntary force at the superimposed ES, and *b* is the voluntary torque just before the ES was applied. The difference between *a* and *b* shows the twitch amplitude as a result of superimposed ES. Prior to the endurance task, CAR was averaged over the three MVICs to calculate the overall voluntary activation percentage for each subject.

$$CAR = MVIC/(MVIC + (a\text{-}b)) \qquad (1)$$

Pre-CAR is the CAR superimposed to the pre-MVICs prior to the endurance task, and post-CAR is the CAR for the post-fatigue MVIC. A greater decline observed for MVIC compared to twitch torque indicates a failure in central activation (Kent-Braun, 1999). In other words, a further increase in the twitch torque (e.g. (a–b)) relative to the maximum force from pre-to post-MVIC is an indicator of a central fatigue.

For each dependent measure, a stepwise multiple linear regression analysis was performed with the obesity measurements (waist-to-hip ratio (WHR)), BMI and body fat percentage (%BF), and strength (pre-MVIC) as potential independent variables. Probabilities of F-statistics for a variable entry and removal were set to correspond to less than $p = .1$ and greater than $p = .15$, respectively. For each regression model, the normality assumption was checked using the Shapiro–Wilk test. Collinearity between independent variables was checked to avoid including highly correlated predictors in each linear regression. Multivariate regression analysis (linear canonical correlation analysis) was performed where there was a correlation between dependent variables, to find the omnibus linear effect of independent variables on a set of dependent variables.

In addition, repeated measure analyses of variance (ANOVA) was conducted to find any significant difference of dependent variables between normal weight, overweight, and obese groups. For multivariate regression analysis and ANOVA, assumptions of homogeneity of variance, normality, and independence of residual errors were checked. Statistical analysis was performed in SPSS Version 22 (IBM Corporation) and the level of significance was set at $\alpha = .05$ for all analyses.

4.4 Results

All regression models meet the normality assumption. Collinearity analysis revealed that WHR and BMI and %BF were highly correlated. When considering the influence of each obesity indicator in the models, a change in BMI had a greater impact on the fatigue outcome measures. Therefore, all further presentation of results is based on BMI as the indicator. Obtained data on TA pre- and post-MVIC, endurance time, torque loss, and pre- and post-CAR are presented in Table 4.2. The results of the stepwise multiple regression analyses are shown in Table 4.3. As seen in the table, 29% of the variance in endurance can be explained by BMI and pre-MVIC.

The regression coefficients indicate a negative, trending toward a significant ($p = .056$) relationship between BMI and endurance (scatterplot in Figure 4.2). Pre-MVC had a significant ($p = .046$) positive linear relationship with endurance. Pre-MVC was also a sole, highly significant ($p = .001$) linear predictor of torque loss in the best fitted model. It explained 43% of the variability observed in the torque loss variable. The higher the pre-MVC, the more reduction in the post-MVIC from pre-MVIC after the fatiguing task was observed. Torque loss and endurance were correlated significantly (Pearson correlation = 0.599, $p = .003$) and can be considered as a general sign of physical fatigue. The multivariate regression analysis showed a significant effect of pre-MVC (p = .006) on the set of these two dependent variables. None of the obesity indicators had a significant effect on the general fatigue.

Repeated measures ANOVA revealed that while all groups of participants had comparable central activation capability before the fatiguing task (pre-CAR), the obese group had a significantly (p = .01) lower post-CAR compared to non-obese and/or overweight group (s) (Figure 4.3). Stepwise regression analysis showed that both BMI and pre-MVC were significantly (p < .001 and p = .031, respectively) associated with post-CAR. BMI and pre-MVC explained 59% of the variance in post-CAR with a linear negative effect of BMI and a positive effect of MVC on post-CAR. These relationships indicate that strength and BMI are associated with endurance time and post-fatigue central activation.

Table 4.2 Strength and Fatigue Responses

Measure	Mean (Standard Deviation)	Range
Pre-MVIC (Nm)	38.8 (9.3)	21.8-57.4
Endurance (s)	52.6 (16.6)	15.0-82.3
Post-MVIC (Nm)	24.0 (7.2)	13.1-37.1
Change in MVIC (% Pre-MVIC)	61.5 (8.5)	45.1-84.2
Pre-CAR (%)	99.2 (0.66)	97.4-99.9
Post-CAR (%)	96.5 (2.86)	90.4-99.9

Table 4.3 Stepwise Regression Unstandardized Coefficients (with 95% confidence interval)

Variable	BMI	pre-MVIC	Intercept	R^2
Endurance	-1.43 (-2.89,0.04)	0.74[a] (0.016,1.46)	62.4 (16.4,108.5)	.29
Torque loss		0.34[a] (0.154,0.513)	1.836 (-5.32,8.9)	.43
Post-CAR	-0.45[a] (-0.65,-0.26)	0.106[a] (0.01,0.20)	104.67 (98.61,110.72)	.59

[a] Significant coefficients.

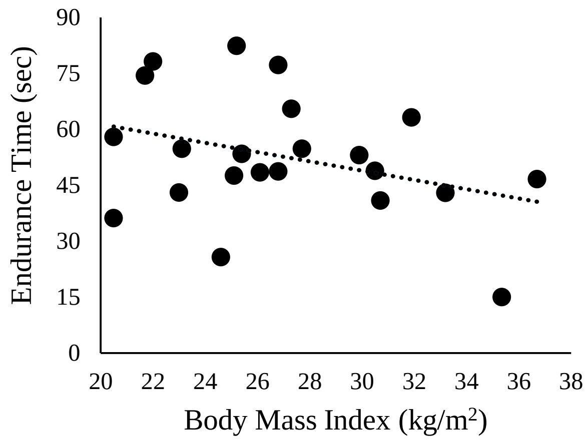

Figure 4.2 Relationships between BMI and endurance time

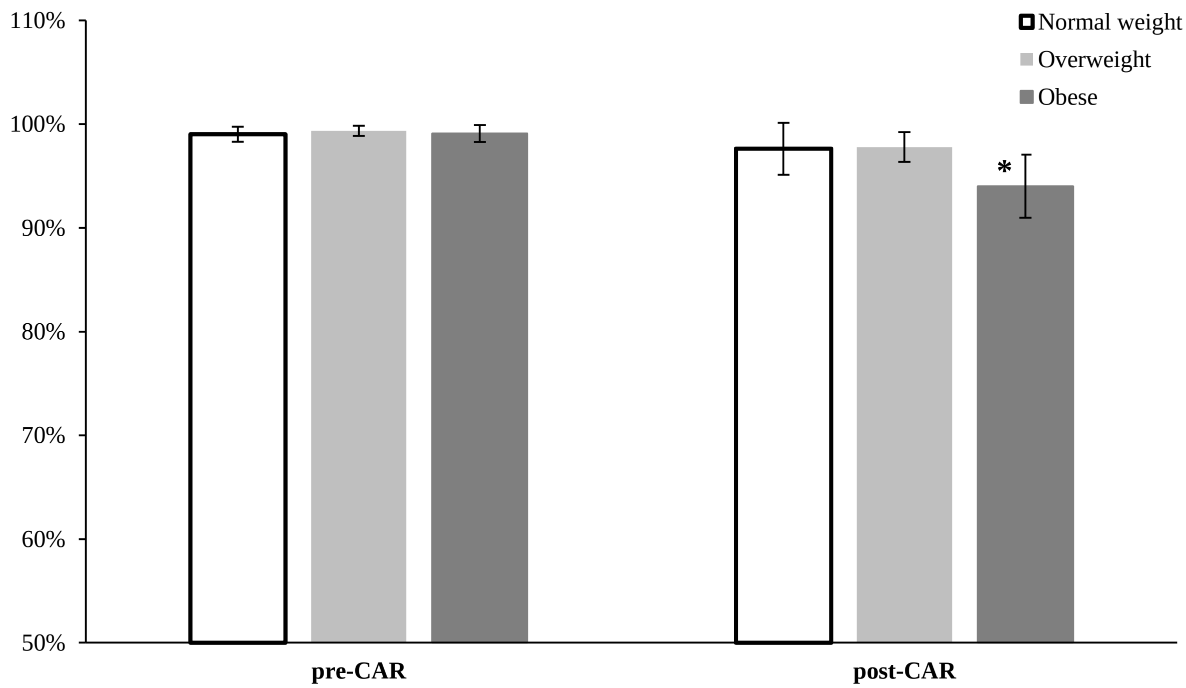

Figure 4.3 Between-group comparison of pre- and post-CAR (* indicates a significant difference)

4.5 Discussion

4.5.1 Obesity and Fatigue Development

Sustained isometric contractions to exhaustion have commonly been used to measure muscle performance and fatigue development (Ma et al., 2009). A higher proportion of fiber II muscles (Wade et al., 1990) and decreased capillary density with obesity are suggested to reduce muscle endurance (Maffiuletti et al., 2013). In this study, endurance time was lower for participants with increased BMI. While holding strength constant, each unit increase in BMI would be predicted to reduce endurance time by 1.43 s (~2% relative to the mean endurance time). Previous studies that have shown obesity-related differences in voluntary endurance time for hand grip (Mehta & Cavuoto, 2015; Mehta, 2015), shoulder flexion (Cavuoto & Nussbaum, 2013[a]), and knee extension (Garcia-Vicencio et al., 2015) tasks have also found negative effect of obesity on endurance. The regression model including pre-MVIC and BMI explained 29% of the variability in endurance time, indicating a probable influence of obesity and muscle strength together on fatigue development. This suggests that in obesity studies, individual differences in terms of physical strength should also be considered.

A significant voluntary torque loss after the fatiguing task, as another mechanical sign of muscle fatigue (Park et al., 2009), was expected with increasing obesity signs. However, all participants had comparable strength loss values at the end of the endurance trial leaving pre-MVC as the only significant predictor of the torque loss. Endurance and torque loss were highly positively correlated (p = .002) in this experiment indicating a greater torque loss for a longer endurance. On the other hand, endurance time decreased with higher BMI resulting in comparable torque loss between participants. This finding implies that, for similar protocols, considering torque loss alone as a sign of muscle fatigue might not be reliable.

The effect of obesity on fatigue progression has been studied in different protocols. A significant effect of obesity on the voluntary fatigue of the quadriceps, measured by strength loss, was previously reported in a set of 50 repetitive isokinetic (180°/s) maximum contractions (Maffiuletti et al., 2007). In contrast, Minetto et al. (2013) found equivalent time to task failure for knee extension between obese and non-obese individuals using both voluntary intermittent and stimulated isometric fatiguing protocols. Likewise, comparable fatigue resistance ability of the quadriceps muscle between obese and non-obese postmenopausal women was observed in an intermittent isokinetic

(300°/s) task (Palillo et al., 2012). The difference in the results between these studies and the current results could originate from the muscle of interest and the contraction properties including type, load, and contraction to rest ratio (Enoka & Duchateau, 2008). Intermittent and isokinetic fatiguing contractions are based more on aerobic energy supplies compared to sustained endurance (Russ et al., 2002), which restricts blood circulation to the muscle and therefore relies on anaerobic supplies.

In addition to the differences in endurance capacity, the relationship between obesity and TA functional performance impairment was evident in motor unit activation after fatigue. A negative effect of fatigue on neural drive to motor units and consequent balance control difficulties due to insufficient force has been established (Hakkinen, 1995). A significant contribution of central activation to fatigue development in TA during sustained isometric maximum voluntary exertions for 4 min has been previously found for young non-obese adults (Kent-Braun, 1999).

Adding the obesity effect, Maffiuletti et al. (2007) reported that motor neuron potentiation with ES resulted in comparable fatigue between obese and non-obese groups even though impaired voluntary fatigue resistance was observed for the obese group. This led the authors to conclude that a central activation failure of the quadriceps with obesity had occurred. However, their task involved low levels of exertion and stimulation. In this study, a lower post-CAR was observed with obesity.

CAR measures force enhancement evoked by superimposed ES relative to the MVIC. A smaller CAR or greater muscle twitch shows a higher proportion of motor units which has not been activated voluntarily by the CNS. Previously, central fatigue of the TA was diagnosed in 5 out of 12 healthy adults during a sustained isometric foot inversion endurance at 100% MVC (Vie et al., 2013). In a study by Kent-Braun (1999), a ~20% contribution of central fatigue was estimated for the TA muscle of non-obese subjects. Based on the results of the current study, this proportion might be higher for individuals who are obese. Also in the Kent- Braun (1999) study, a reduction in

CAR after the fatiguing task was suggested indicating an increase in the twitch values or inactivated motor neurons or central activation failure. In the current study, while pre-CAR was not significantly affected by obesity, post-CAR differed, which suggests that fatigue impairs central activation for individuals who are obese.

In a study of adolescents (Blimkie et al., 1990), a similar reduction of central activation was observed for obese adolescents compared to a non-obese group as a sign of reduced motor performance. Incomplete motor unit recruitment is a result of twitch-like motor unit response (Belanger & McComas, 1981). Whether the observed central activation impairment with obesity was due to signal generation or signal propagation is not clear.

4.5.2 Limitations

Interpretation of the results of this study may be limited by the small sample size of males, having primarily participants with Class I obesity, and the method for twitch detection. Twitch response diminishes during maximal contractions and torque fluctuation makes the twitch responses less visible (Behm et al., 1996). TA also has shorter, smaller, and faster twitch responses compared to plantar-flexor muscle (Belanger & McComas, 1981), which could further obstruct the twitch detection. Moreover, the straps used to secure the foot in the footplate may have absorbed some of the ES torque increment. In addition, intra-subject variability of size and location of the motor units may reduce the ES effect (Knaflitz et al., 1990). The method of force generation associated with using the TA muscle is another potential limitation. Complete isolation of the TA is difficult due to contribution of the toes and synergistic muscles in maximum force output (Behm et al., 2001). The methods used in the study were controlled across all participants, minimizing the potential for confounding of the results.

4.6 Conclusion

The results indicated an inverse relationship between the obesity measures and TA functional capacity in healthy young males during maximum voluntary exertions and a sustained isometric endurance task. Overall, higher BMI was associated with lower fatigue resisting ability (shorter endurance), in addition to lower central activation once fatigued. This shows the importance of fatigue prevention interventions, especially for individuals who are obese, to prevent injuries resulting from muscle dysfunction due to signal generation impairment and transmission.

Superimposed ES was used in this study to investigate central fatigue of the TA. Using both superimposed and potentiated ES is recommended in future research to find obesity-related differences in the contribution of central versus peripheral fatigue of the ankle dorsiflexor muscles. Moreover, the practical effect of fatigue resistance impairment with obesity on balance control would be an interesting supplement to this research. Comparing the center of pressure oscillation between obese and non-obese individuals after a TA fatiguing task would further reveal the implications of this impairment.

4.7 Disclosure statement

No potential conflict of interest was reported by the authors.

Chapter 5

5. Reliability Analyses of BMI-Specific Isometric Hand Grip, Shoulder, and Trunk Strengths

5.1 Abstract

Mixed findings on the effect of obesity on muscle strength question the reliability of the results, which has not been reported in any of the obesity-related studies of muscle strength. Therefore, the main goal of this study was to test whether the frequently reported altered maximum muscle strength with obesity reliably persists considering various sources of variability. For three tasks of hand grip, shoulder flexion, and trunk extension, 142 healthy subjects, in three body mass index (BMI) groups of non-obese, overweight, and obese, repeated three maximum voluntary isometric contractions replicated across four days and in two sites. Absolute and relative reliabilities of the hand grip and shoulder flexion strength measures were verified by having coefficient of variation < 10% and intraclass correlation coefficient > 0.9, respectively. For these two tasks, comparable strengths among the groups were found. Also, shoulder flexion strength positively and significantly correlated with BMI ($p=0.017$). For practical purposes, minimum detectable strength changes and true estimation of the muscle strength, with 95% confidence, as well as percentile values are presented for each task, overall and for each group of participant.

5.2 Introduction

A shift in the adult population to include ~1.9 billion obese ($30 \leq$ body mass index (BMI) kg/m^2) and overweight ($25 \leq$ BMI < 30 kg/m^2) worldwide (World Health Organization, 2015) has had negative consequences of increased risk of injuries with obesity (Matter et al., 2007). Increasing BMI has been shown to be associated with impaired back extensor muscle function (Dedering et al., 1999; Mbada et al., 2010) and shoulder pain complaints (Rechardt et al., 2010) during physical resistance tests. In a meta-analysis of 33 publications in Medline and Embase databases, overweight and obesity have been linked with chronic low back pain (Shiri et al., 2010). Sedentary lifestyle and lower physical activity among individuals who are obese may contribute to weaker muscle strength. However, this negative effect can be counterbalanced with a favorable chronic weight-bearing effect as a result of increased body mass (Lafortuna et al., 2005).

Mixed findings have been reported in the literature on the effect of obesity on muscle strength. Most studies have reported a higher absolute isometric strength of the trunk and lower extremity muscles (Miyatake et al., 2000; Hulens et al., 2001; Rolland et al., 2004; Maffiuletti et al., 2007; Abdelmoula et al., 2012) as well as upper extremity muscles (Cavuoto & Nussbaum, 2013[a,b]; Fogelholm et al., 2006; Mehta, 2016; Miyatake et al., 2000; Kitagawa & Miyashita, 1978) for an obese compared to non-obese group. However, for similar muscle groups other studies reported reduced (Kitagawa & Miyashita, 1978) or unchanged (Hulens et al., 2001; Rolland et al., 2004) strength with obesity, which increases concerns about sources of variability such as experimental protocol, equipment settings and calibration, postures, experimenters and subjects. To guard against various sources of errors, reporting the reliability or repeatability of the strength measurements is critical (Atkinson & Nevill, 1998), which has been neglected in the previous studies of strength differences with obesity.

Interpretability of the strength results in design, clinical and rehabilitation decision making and practice depends on the reliability of the measurements, particularly when participants with a wider range of BMI are included, as this increases the between-subject variability. Within-subject variability such as biological changes due to fatigue, either physically or mentally, and learning effect could also affect the results (Hopkins, 2000), and this effect can vary between subject groups. For example, lack of motivation, mental fatigue, or central nervous system-related issues have been reported to be more apparent for fatigued obese individuals (Mehta, 2015; Pajoutan et al., 2016[b]). Therefore, a reasonable number of subjects and trials is needed to have a higher inter- and intra-individual reliability of the measures (Hopkins, 2000).

During repeated measurements, relative reliability reflects the degree of maintaining each individual's rank relative to a sample of subjects, and absolute reliability shows the amount of within-subject variability (Edouard et al., 2013). In this study, three repeated measures of maximum voluntary contraction (MVC) replicated across four sessions, each on a different day, and in two sites in a large heterogeneous (wide range of BMI) sample of subjects enabled measuring the relative and absolute reliabilities as well as inter- and intra-site variability of isometric strength measures. Verifying the reliability in this study enables generalization of the findings more reliably to other conditions and individuals. Therefore, the first objective of this study was to test whether the altered maximum muscle strength with obesity, suggested by many studies in the literature, reliably persists during repeated and replicated measurements. Three tasks of hand grip, shoulder flexion, and trunk extension were selected for the purpose of strength measurement. These muscle groups were selected for the high frequency of shoulder and hand use during activities of daily living and the role of trunk extensor strength in supporting the more anterior center of mass, due to accumulated fat tissues around the abdomen, for individuals who are obese. The second objective of this study was to capture strength differences between subject groups and identify significant predictors of strength. It was hypothesized that strength is affected by BMI and this effect is task-dependent.

5.3 Methods

5.3.1 Subjects and Ethical Approval

As part of a larger study on functional capacity changes related to obesity, 142 healthy subjects participated. Participants were recruited into three groups: 49 (24 males, 25 females) normal weight ($18 \leq$ BMI < 25 kg/m^2), 50 (25 males, 25 females) overweight ($25 \leq$ BMI < 30 kg/m^2) and 43 (22 males, 21 females) obese ($30 \leq$ BMI kg/m^2). All participants completed demographic, health history, and physical activity questionnaires prior to the experiment. Only healthy individuals who did not perform extensive physical activity more than one hour per day (> 3 times/week) were included in this experiment. Detailed demographic and anthropometric information for the participants, divided by group, is provided in Table 5.1. All study protocols were approved by the University at Buffalo and Texas A&M University Institutional Review Boards and all participants provided informed consent prior to participation.

Table 5.3 Participants' information presented as mean (SD). Those groups that do not share a letter (in the order of normal, overweight and obese) are significantly different at $p < 0.05$ based on a *t*-test

	Normal (n = 49)	Overweight (n = 50)	Obese (n = 43)
Age (yr)	31.4(8.5)	33.4(9.8)	31.4(9.4)
Body mass (kg)$^{A, B, C}$	64.8(8.4)	76.7(8.1)	100.8(15.5)
Stature (cm)	169.3(8.4)	168.2(8.4)	169.8(7.5)
BMI (kg/m^2)$^{A, B, C}$	22.6(2.1)	27.1(1.4)	34.8(3.8)
Body fat (%)$^{A, B, C}$	21.7(8.8)	29.9(7.7)	36.5(7.5)
Fat free mass (kg)$^{A, A, B}$	50.9(10.1)	54.0(10.0)	64.0(12.9)
Waist circumference (cm)$^{A, B, C}$	79.8(10.6)	90.8(7.8)	108.1(12.0)
Hip circumference (cm)$^{A, B, C}$	95.3(12.5)	103.2(7.4)	118.5(13.3)
Waist to hip ratio$^{A, B, C}$	0.84(0.06)	0.88(0.06)	0.91(0.06)

5.3.2 Experimental Setup and Protocol

Three repeated measures MVC of hand grip, shoulder flexion and trunk extension were replicated across four sessions. Sessions were separated by at least 48 hours to minimize the effect of any residual fatigue on performance, and task order was counterbalanced across subjects. To measure and reduce the sources of variability related to lack of motivation and inability to fully activate motor neurons, the MVCs were repeated three times and the maximum of them was selected as a measure of muscle strength for each subject in each session. Reproducibility or repeatability of the observed values was also tested across replicated sessions. In each session, participants warmed up before each task with repeated grip, shoulder, and trunk flexion, extension, and rotation. The three isometric MVCs, each five seconds with two minutes of rest in between, were then performed. Tasks were separated by at least 10 minutes.

An isokinetic dynamometer (Cybex Humac NORM, Ronkonkoma, NY, USA) was used to measure the shoulder flexion and trunk extension torque. Shoulder flexion of the right arm was tested with participants laying supine on the dynamometer chair with a seat belt around the pelvis and arm flexed at 90º with extended elbow (Figure 5.1a). The dynamometer's axis of rotation and shoulder adaptor height were set with respect to the acromion process and arm length, respectively. The forearm was kept parallel to the shoulder adaptor grasping a handle with the wrist in a neutral position. Participants were allowed to release the handle during the rest periods. For trunk extension, participants stood upright on the dynamometer footplate with slightly flexed (< 5°) trunk against the sacral pad (Figure 5.1b). The dynamometer's axis of rotation was aligned based on the iliac crest and L5/S1 location. The scapular and chest pads were fastened in parallel across the center of the scapulae and against the subject's chest. The feet were placed in a fixed position against footplate heel cups separated at about shoulder width. The thigh pad, tibial pad, and pelvic belt was attached to help firmly securing the lower body minimizing the confounding effect of other muscles during trunk extension.

Hand grip force was tested with a grip dynamometer (SS25LA, BIOPAC Systems, Inc, Aero Camino Goleta, CA, USA) and data acquisition system (BIOPAC Student Lab (MP36), BIOPAC Systems, Inc, Aero Camino Goleta, CA, USA) with the sampling rate of 1 KHz. Participants were seated upright on the dynamometer chair with their arms at their side, resting the lower arm on a stabilizer tube, with the shoulder joint in a neutral position, and the elbow flexed at 90º (Figure

5.1c). The forearm was kept parallel to the ground with the wrist in a neutral position while grasping the dynamometer.

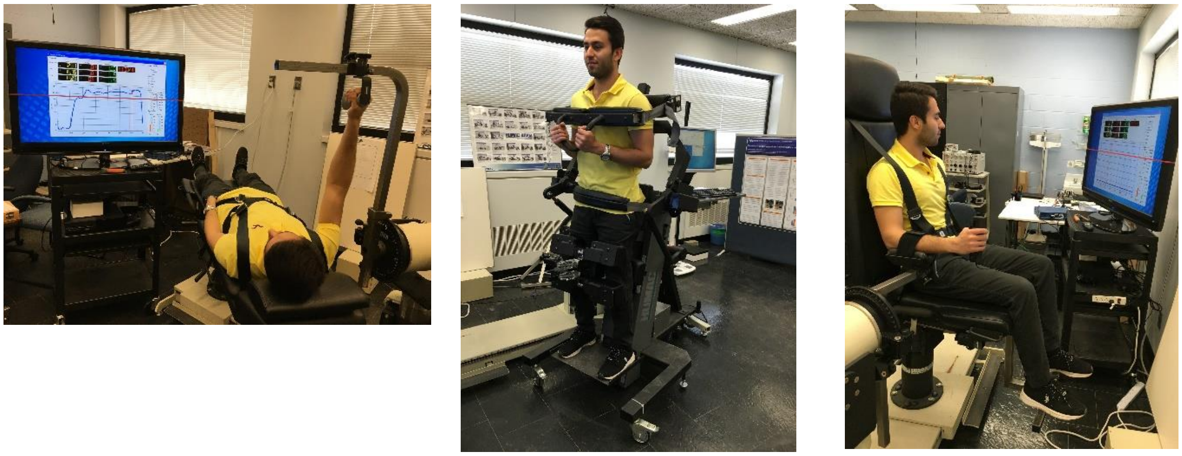

Figure 5.3 Experimental set-up: a: shoulder flexion, b: trunk extension, c: hand grip

5.3.3 Statistical Analysis

For each task, intraclass correlation coefficient (ICC) was used to evaluate the level of agreement among four replicated MVCs within each person relative to the between-subject variability. Within each site, intra-site ICCs were calculated using one-way random model. Inter-site ICCs were also calculated using 2-way random (i.e., 4 trials crossed with subjects and 2 sites) model. For the sake of generalizability, the levels of site and trials were considered to be a random sample of all possible levels. The ICCs, as a measure of relative reliability, were then averaged and the 95% confidence interval (CI) was calculated for the overall sample of subjects as well as for each obesity group since a heterogeneous sample of subjects increases between-subject variability which might conceal the between-trial variability (Weir, 2005). A high agreement (ICC > 0.9; Edouard et al., 2013) would enable using the average of the replicated MVCs as a measure of strength for each person within each task.

Absolute reliability of the strength measurements across the replicated MVCs was also tested by standard error of measurement (SEM) and coefficient of variation (CV, SD/mean) in addition to its 95% CI, as suggested by Atkinson & Nevill (1998). For each task, SEM and CV were used to quantify the precision of each individual measure across trials and were suggested as measures of absolute reliability (Looney, 2000). Standard deviations less than 10% of the mean (CV < 10%) verify the absolute reliability of the strength and indicate that about 68% of the measures are within 10% of the mean (Strike, 1991). For each task, SEM was calculated overall and within each obesity group using the relevant ICC and standard deviation of the sample strength measures ($SEM = SD\sqrt{(1\text{-}ICC)}$. SEM eliminates the effect of inter-individual variability calculated in ICC (Atkinson & Nevill, 1998). The SEMs then used to provide 95% CIs for the true strength measurements quantified as strength ± 1.96(SEM) for each task and overall population. In addition, minimum detectable change (MDC) was calculated as $SEM \times 1.96 \times \sqrt{2}$, which shows minimum considerable real change in the performance (Weir, 2005).

Between-group effects of obesity and its interaction with gender controlling for age and blocking for site, on strength outcome and reliability measures, wherever relevant, of each task were tested by separate analyses of covariance (ANCOVA). Significant interactions were followed up by Tukey's pairwise comparison tests. In addition, regression analysis was performed for each task in order to find the linear trend of strength changes with increasing BMI and age.

For ANCOVA and regression analyses, the assumptions of normality, homogeneity of variance, and independence of residual errors were checked by using Shapiro-Wilk test, Leven's and Durbin-Watson tests, respectively. In order to meet the assumptions, natural log transformation was used for the hand grip, and Box-Cox transformations with $\lambda = 0.25$, $\lambda = 0.58$ were applied on the shoulder flexion and trunk extension data, respectively. Finally, strength data (untransformed) was used to provide the percentile values of strength for each task overall as well as for each obesity group. The variability of the strength in the commonly used submaximal percentiles (i.e., 5th, 10th, 25th, etc) in design was considered. All statistical analyses were conducted in SPSS Ver. 24 (IBM Corporation) and the level of significance was set at $\alpha = 0.05$.

5.4 Results

The ICC and CV with 95% CIs and SEM results are presented in Table 5.2. A very high relative reliability was observed for each of the three tasks with all mean inter- and intra-site ICCs exceeding 0.92. The lower bound values of the 95% CI for ICCs were above 0.85, which occurred for the overweight group for trunk extension. Therefore, the average of the replicated MVCs can be reliably used. CVs (%) ranged 1.08-28.39 for the hand grip, 1.24-26.42 for the shoulder flexion and 2.54-43.30 for the trunk extension task. Generally, higher CVs were observed for the trunk extension compared to the hand grip and shoulder flexion tasks. For this task, the normal group had significantly (p = 0.003) lower CV compared to the overweight and obese groups. Measures of strength for the shoulder flexion task were the most reliable, which is evident from the lower SEM. Among obesity groups, SEM changed from 12-14.88 (N) for the hand grip task, 2.42-2.64 (Nm) for the shoulder flexion and 9.44-12.69 (Nm) for the trunk extension task.

Table 5.4 ICC and CV with 95% CI, and SEM results

	ICC			CV (%)	SEM
	Inter-site	Intra-site			
		Site 1	Site 2		
Grip					
Overall	0.98 (.978, .987)	0.98 (.976, .989)	0.98 (.968, .985)	7.51 (6.83, 8.20)	13.63
Normal	0.98 (.974, .990)	0.99 (.976, .993)	0.97 (.945, .986)	7.33 (6.28, 8.38)	14.13
Overweight	0.98 (.971, .988)	0.98 (.968, .991)	0.97 (.949, .987)	8.36 (6.96, 9.76)	14.88
Obese	0.98 (.976, .991)	0.98 (.959, .991)	0.99 (.978, .994)	6.72 (5.65, 7.77)	12.00
Shoulder					
Overall	0.98 (.970, .982)	0.97 (.963, .983)	0.98 (.969, .986)	8.93 (8.10, 9.77)	2.53
Normal	0.97 (.961, .985)	0.98 (.964, .991)	0.97 (.941, .985)	8.58 (7.14, 10.02)	2.64
Overweight	0.98 (.967, .987)	0.97 (.946, .985)	0.98 (.968, .992)	9.06 (7.51, 10.60)	2.42
Obese	0.98 (.967, .988)	0.97 (.944, .988)	0.98 (.955, .989)	9.20 (7.78, 10.62)	2.46
Trunk					
Overall	0.96 (.948, .970)	0.93 (.902, .955)	0.97 (.961, .982)	15.66 (14.25, 17.07)	10.86
Normal	0.96 (.944, .978)	0.94 (.888, .970)	0.98 (.962, .991)	12.36 (10.59, 14.13)	9.44
Overweight	0.96 (.936, .975)	0.92 (.851, .959)	0.98 (.955, .989)	17.25 (14.58, 19.91)	11.93
Obese	0.95 (.921, .973)	0.95 (.891, .977)	0.96 (.926, .983)	17.62 (14.91, 20.33)	12.69

The ANCOVA showed that obesity and its interaction with gender were not significant in any of the analyses. However, age (p = 0.02) and site (p = 0.04) effects were significant covariates for only the trunk extension strength.

Regression analyses revealed that hand grip and trunk extension strength measures are significantly linked with age (p = 0.016 and 0.002 respectively). Shoulder flexion strength was significantly associated with BMI (p = 0.017). All three regression models were significant. The results are presented in Table 5.3 and the trends of strength changes based on significant predictors for each task were illustrated in Figure 5.2.

Table 5.3 Unstandardized coefficients and 95% CI are presented. Significant p-values are marked by *

Factor	Coefficient (95% CI)	p-value
Grip		
Regression		0.036*
BMI	1.58 (-1.56, 4.73)	0.262
Age	-2.21 (-4.09, -0.34)	0.016*
Constant	358.91 (254.76, 463.06)	< 0.001*
Shoulder		
Regression		0.054*
BMI	0.59 (-0.08, 1.09)	0.017*
Age	-0.11 (-0.41, 0.19)	0.554
Constant	34.14 (17.46, 50.82)	< 0.001*
Trunk		
Regression		0.010*
BMI	0.12 (-1.52, 1.76)	0.996
Age	-1.51 (-2.49, -.54)	0.002*
Constant	156.71 (102.51, 210.91)	< 0.001*

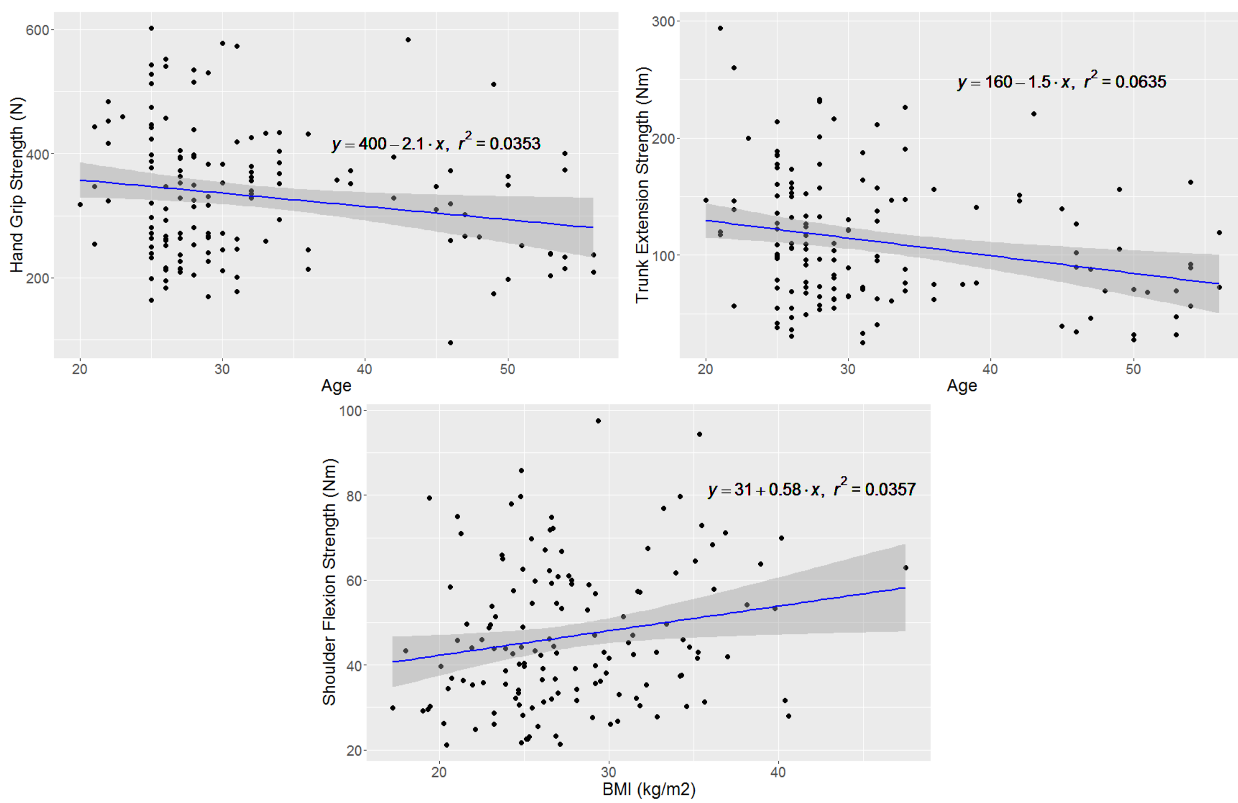

Figure 5.4 Linear predictors of the strength for each task

For practical purposes, strength percentiles of each task, overall and for each obesity group, are provided in Table 5.4. Additionally, mean, 95% CI of the true strength estimates, and MDC for the overall sample of subjects and for each task are presented in Table 5.5. MDCs are 11.4%, 15.0% and 27.0% of the mean for hand grip, shoulder flexion, and trunk extension tasks, respectively. Figure 5.3 schematically illustrates box-plots of the strength outcomes.

Table 5.4 Strength distributions for hand grip, shoulder flexion and trunk extension.

	Overall	Normal	Overweight	Obese
Hand Grip (N)				
5	195.69	197.1	174.2	187.9
10	209.70	213.4	202.1	222.7
25	250.44	248.7	238.9	258.5
50	325.12	314.4	322.4	347.1
75	394.88	396.5	385.6	403.4
90	482.17	512.9	508.9	456.6
95	540.05	557.0	535.5	538.1
Shoulder Flexion (Nm)				
5	23.47	23.19	22.51	26.86
10	27.72	26.31	23.55	28.61
25	33.43	31.39	34.12	34.82
50	43.30	42.66	42.99	45.60
75	58.94	52.66	59.39	63.13
90	71.10	75.08	69.43	72.43
95	77.88	79.53	73.42	79.24
Trunk Extension (Nm)				
5	33.53	34.19	32.82	32.16
10	45.99	54.64	44.63	39.70
25	68.97	70.18	68.18	65.43
50	104.07	105.07	101.47	106.34
75	150.13	154.46	146.44	150.45
90	187.32	185.75	176.44	214.80
95	216.11	200.92	251.17	228.12

Table 5.5 95% CI for true strength values

Task	Mean	95% CI	MDC
Hand Grip (N)	331.75	(305.03, 358.46)	37.78
Shoulder Flexion (Nm)	46.77	(41.82, 51.73)	7.01
Trunk Extension (Nm)	111.31	(90.03, 132.60)	30.10

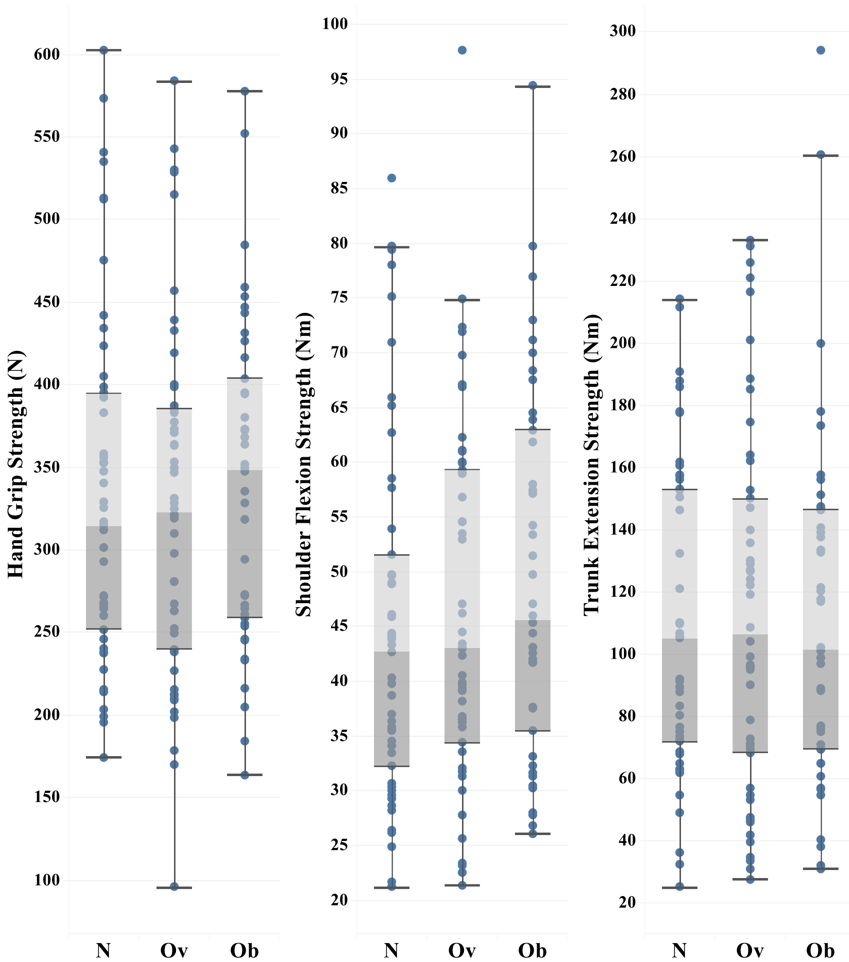

Figure 5.5 Strength outcomes during the hand grip, shoulder flexion and trunk extension tasks for obese (Ob), overweight (Ov), and normal weight (N) groups.

5.5 Discussion

Absolute and relative reliabilities of the hand grip and shoulder flexion strength measures were verified by having CVs < 10% and ICCs > 0.9, respectively. For those tasks, the higher absolute strengths for obese compared to non-obese individuals frequently reported in the literature were not observed in this study. The effect of various sources of errors was not reported in previous obesity-related studies, which limits the generalizability and reliability of their findings. In this study, however, the reliability of the measures was verified even in a large and homogeneous sample of subjects, representative of the population. However, the results of this study can only be extended to Class I and Π obesity ($30 < \mathrm{BMI} < 40$ kg/m^2) and younger healthy adults, for the specific tasks tested.

For the trunk extension task, however, the absolute reliability of the measures was not valid (CV% > 10%). For this task, the normal group had a significantly ($p = 0.003$) lower mean CV (12.4%) compared to the obese (17.6%) and overweight (17.3%) groups. The heterogeneous sample over a larger BMI range resulted in an increased variability in the trunk strength and this variability is even more apparent for the overweight and obese individuals for whom, there is an increased fat accumulation around pelvic area without contractile support in force generation. Added variability during trunk exertions was previously reported as a result of complex muscle involvements and co-contractions (Ma et al., 2009). Adding to the sources of variability in this study, a systematic site effect ($p = 0.04$) was observed for the trunk extension task, which could be due to the performance of the experimenters in the two sites in instructions or stabilization of the subjects. In conclusion, measuring trunk extensor strength in other postures or settings, such as a seated posture, might be required to increase stability and minimize unintended activation of antagonist muscles, and therefore increase the reliability and precision of the measures.

Comparable trunk extension strength between obese and non-obese groups was also previously reported in some studies (Kitagawa & Miyashita, 1978; Cavuoto & Nussbaum, 2013[b]). However, the former classified obesity based on body fat percentage (%BF) rather than BMI, and overweight individuals were not considered in either of the studies. For the hand grip task, comparable strength was also observed previously (Hulens et al., 2001; Rolland et al., 2004; Mehta & Shortz, 2014). In a large study of 1443 elderly subjects in all three BMI categories, isometric grip strength remained intact with obesity (Rolland et al., 2004). Rather than obesity, they found that recreational physical activity is the determinant of the handgrip force capacity. Our sample includes both recreationally active and sedentary individuals. It is recommended that future studies take this into consideration. Additionally, Mehta & Cavuoto (2015) found that the higher muscle strength with obesity for the hand grip task held true for younger subjects (20-35 years old), whereas, the current sample includes subjects aged from 20 to 56 years and a negative linear effect of age on the hand grip strength was apparent ($p = 0.016$). Age was also a significant negative linear predictor of the trunk extension strength ($p = 0.002$). For the shoulder flexion strength, however, only BMI was a positive linear determinant ($p = 0.017$). This supports our hypothesis of a task-dependency of the effect of BMI on strength measures. The increasing trend of shoulder torque with increasing BMI could be due to an increase in the proportion of fast-twitch muscle fibers at higher BMI (Tanner et al., 2002) suitable for short powerful outcomes (Saltin et al., 1977), where the effect of blood occlusion as a result of denser fat tissues is negligible.

In general, findings of this study suggest that individual changes in strength equal or greater than 10-30% can be considered a real change rather than random noise. More specifically, with 95% confidence, changes of 11.4%, 15.0% and 27.0% of the mean above or below the previous score can be interpreted as a real change for hand grip, shoulder flexion, and trunk extension tasks, respectively. These MDCs help in clinical decision-makings and performance assessments, for example as a result of trainings on athletes (Weir, 2005). The results of this study suggest that, with 95% confidence, the true maximum muscle strength is between 305.0-358.5 (N) for the hand grip, 41.8-51.7 (Nm) for the shoulder flexion, and 90.0-132.6 (Nm) for the trunk extension task.

5.6 Conclusion

Absolute and relative reliabilities of the hand grip and shoulder flexion tasks in this study including a large healthy subjects representing the general population and various sources of errors (e.g., sites, repeated and replicated measurements) were met. This along with findings of comparable strength measures between obesity groups raised concerns about the reliability of previous studies that found otherwise. However, a positive linear association of shoulder flexion task with BMI suggests a task-dependency nature of the force-BMI relationship. The findings of this study for the shoulder flexion and hand grip tasks can be reliably used for practical purposes to estimate the required strength and allowances in product design and performance evaluation.

5.7 Acknowledgement

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Chapter 6

6. Summary and Future Research

The goal of this dissertation was to test the effect of obesity on muscle functional capacity and fatigue development both centrally and peripherally. For this purpose, first the force-endurance relationship was assessed, in Chapter 2, and higher fatigue rates with obesity were found. The source(s) of faster fatigue development with obesity, in terms of central and peripheral fatigue, were studied at an upper extremity (shoulder) and a lower extremity (ankle) joint in Chapters 3 and 4, respectively; and central fatigue impairment with obesity was found in both studies. The reliability of the strength findings from Chapter 2 was investigated in Chapter 5 for generalizability. The results of this dissertation can be applied for practical purposes to design preventive measures to reduce injury rates and to compare, predict and assess performance.

In Chapter 2 updated joint-specific force-endurance models accounting for demographic changes in the population were provided. These models can be used in predicting endurance time relative to estimated submaximal exertions. The faster fatigue rates during hand grip, shoulder flexion and trunk extension found for obese compared to normal weight individuals suggest an altered fatigue development with obesity. To postpone fatigue initiation, assistive devices such as arm-rest supports or wearable exoskeletons can be designed for individuals who are obese.

The main finding of this dissertation, from Chapters 3 and 4, was a reduced ability of the obese individuals compared to their non-obese counterparts to activate their motor units once fatigued. Central fatigue can happen as a result of improper nutrients or insufficient physical exercise, and might serve as a mechanism to prevent physical injuries. Taking supplements and stimulants such as oral intake of branched-chain amino acid (BCAA; Newsholme & Blomstrand, 2006) has been suggested to decrease a subjective feeling of fatigue. In addition, physical strength training was suggested to adapt the nervous system and increase voluntary motor unit activation (Sale, 1987). Moreover, psychological factors such as fear of musculoskeletal injuries was suggested as a precautionary movement strategy for obese individuals during dynamic tasks (Davis et al., 2009; Pajoutan et al., 2016[c]). During static exertions, voluntary reduction of motor unit activation could be a mechanism to prevent overexertion injuries, which are more common with obesity (Matter et al., 2007).

In Chapter 5, the reproducibility of the strength measures from the first study (Chapter 2) were tested for the practical implications. Guarding against various sources of errors in this study, absolute and relative reliability of the strength results for the hand grip and shoulder flexion tasks were verified. Therefore, strength results for these two tasks, overall and for each obesity group, can be reliably used in performance assessment, ergonomics applications, clinical and rehabilitation decision making, and design for commonly used percentile values. In addition, a comparable muscle strength for the young healthy obese compared to non-obese group was observed. For the trunk extensor strength, obesity impairment was evident in the strength per unit body mass and fat-free mass, which was reported in a separate study (Pajoutan et al., 2016[a]).

Despite their applicability, the results of this dissertation are limited to static isometric exertions and sustained submaximal endurance for the specific tasks tested as well as young to middle-aged, healthy individuals who were only recreationally active. Also, obese individuals were limited to Class I and Π obesity ($30 < \mathrm{BMI} < 40$ kg/m^2) only since extremely obese individuals only consist ~6% of the population (Flegal et al., 2010). Generalizing the results to other postures, tasks, populations, absolute target loads and other individual factors requires further research.

In addition, there are some limitations associated with using electrical stimulation as a means of detecting muscle twitches to quantify central and peripheral fatigue. These challenges include detecting small twitch responses, complete isolation of the muscle of interest, finding the right locations of motor units, and avoiding co-contractions of antagonist muscles. To deal with these challenges, a custom-written Matlab code and visual inspection was used to detect the twitches and averaged over repeated MVCs, electrodes were cut to fit for each individual's muscle and placed on the right spot found by EMG M-waves, and subjects were secured and strapped. In addition, the same methods used for all participants. However, advanced techniques or devices might be needed to reduce the confounding effects and yield results with a higher confidence.

Future work is needed to explore the underlying reasons of the central fatigue impairment with obesity observed in this dissertation. These reasons include impaired signal generation or propagation, incomplete motor unit activation or recruitment, or lack of motivation. Furthermore, considering the changes in the muscle physiology such as muscle oxygenation concurrently with electrical stimulation is recommended to supplement this research. Going forward, future investigations are encouraged to further investigate the effect of fatigue on movement coordination of obese individuals during dynamic tasks (e.g., Sangachin & Cavuoto, 2016[a]). In addition, the effect of obesity and application of the findings of this dissertation in workplace design such as sitting versus standing workstations (Sangachin et al., 2016[c]) is recommended.

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