Nerve Cross-Sectional Area in Extremes of Height and Weight

BY

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Dedication and Acknowledgements

For Thomas, thank you for giving me strength.

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Table 1. Demographics.

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Sex (% Female)	40%	17%	56%	64%
Race (%Caucasian)	80%	67%.	89%	NA
Age	21.67 (19-35) [3.96]	20.83 (19-23) [1.72]	22.22 (19-35) [4.97]	42.4
Height (cm)	190.58 (172.72-213.36) [11.40]	189.44 (172.72-203.2) [10.05]	191.35 (177.9-213.4) [12.76]	168.00
Weight (kg)	102.72 (52.16-148.78) [31.22]	125.58 (92.99-141.5) [16.78]	87.49 (61.24-148.8) [29.62]	74.50
BMI	28.01 (16.5-37.1) [7.46]	34.88 (31.22-38.54) [2.76]	23.42 (16.58-36.93) [5.77]	26.20

BMI = body mass index; STD = standard deviation;

*Normal population derived from previous studies (Cartwright et al, 2013) (Cartwright et al, 2008).

Table 2. Left-sided Nerve Cross-sectional Areas.

Nerve Site	**All Participants (n =15) Mean (Range) [STD]**	**Heavy (n =6) Mean (Range) [STD]**	**Tall (n = 9) Mean (Range) [STD]**	**Controls (n = 140)* Mean (Range) [STD]**	**T-Test Heavy vs. Tall P-value**
Median wrist	10.4 (7-15) [2.23]	11.83 (9-15) [2.14]	9.44 (7-12) [1.81]	9.8 (NA) [2.4]	0.0363
Median forearm	8.73 (7-12) [1.53]	9.83 (8-12) [1.60]	8.00 (7-10) [1.00]	7.6 (NA) [1.7]	0.0166
Ulnar elbow	10.27 (7-20) [3.17]	11.50 (8-20) [4.42]	9.44 (7-12) [1.88]	6.1 (NA) [0.9]	0.2319
Radial groove	10.87 (7-16) [2.75]	12.33 (7-16) [3.27]	9.89 (7-13) [1.96]	7.9 (NA) [2.7]	0.0915
Fibular knee	12.5 (8-19) [3.15]	13.17 (8-19) [3.60]	11.83** (9-17) [2.79]	11.3 (NA) [3.3]	0.4896
Tibial ankle	12.86 (7-18) [2.98]	14.5 (12-18) [2.59]	11.63*** (7-16) [2.77]	13.7 (NA) 4.3	0.0720
Sural ankle	4.00 (3-6) [1.00]	4.67 (4-6) [0.82]	3.56 (2-5) [0.88]	5.3 (NA) [1.8]	0.0287

*Normal population derived from Previous studies (Cartwright et al, 2013) (Cartwright et al, 2008). **(n = 6) ***(n = 8)

Table 3. African American vs Caucasian Left-sided Nerve Cross-sectional Area

Nerve Site	**All Participants (n =15) Mean (Range) [STD]**	**African American (n = 3) Mean (Range) [STD]**	**Caucasian (n = 12) Mean (Range) [STD]**	**Controls (n = 140)* Mean (Range) [STD]**	**T-Test P-value AA vs Cauc**	**Regression P-value Race to nerve area (weight adjusted)**
Median wrist	10.4 (7-15) [2.23]	11.67 (10-13) [1.53]	10.08 (7-15) [2.31]	9.8 (NA) [2.4]	0.2875	0.7175
Median forearm	8.73 (7-12) [1.53]	10.33 (8-12) [2.08]	8.33 (7-10) [1.15]	7.6 (NA) [1.7]	0.0378	0.0890
Ulnar elbow	10.27 (7-20) [3.17]	14.33 (11-20) [4.93]	9.25 (7-12) [1.66]	6.1 (NA) [0.9]	0.007	0.0177
Radial groove	10.87 (7-16) [2.75]	14.33 (13-16) [1.53]	10.00 (8-14) [2.26]	7.9 (NA) [2.7]	0.0083	0.0161
Fibular knee	12.5 (8-19) [3.15]	13.00 (11-14) [1.73]	12.33* (8-19) [3.57]	11.3 (NA) [3.3]	0.7671	0.8740
Tibial ankle	12.86 (7-18) [2.98]	13.67 (12-16) [2.08]	12.64** (9-17) [3.23]	13.7 (NA) 4.3	0.6159	0.8337
Sural ankle	4.00 (3-6) [1.00]	3.67 (3-4) [0.58]	4.08 (2-6) [1.08]	5.3 (NA) [1.8]	0.5387	0.1351

P values from two sided T test are listed for heavy versus tall participants at each nerve site.*n=9 **n=11

Cross Sectional Nerve Area of Heavy and Tall Subjects

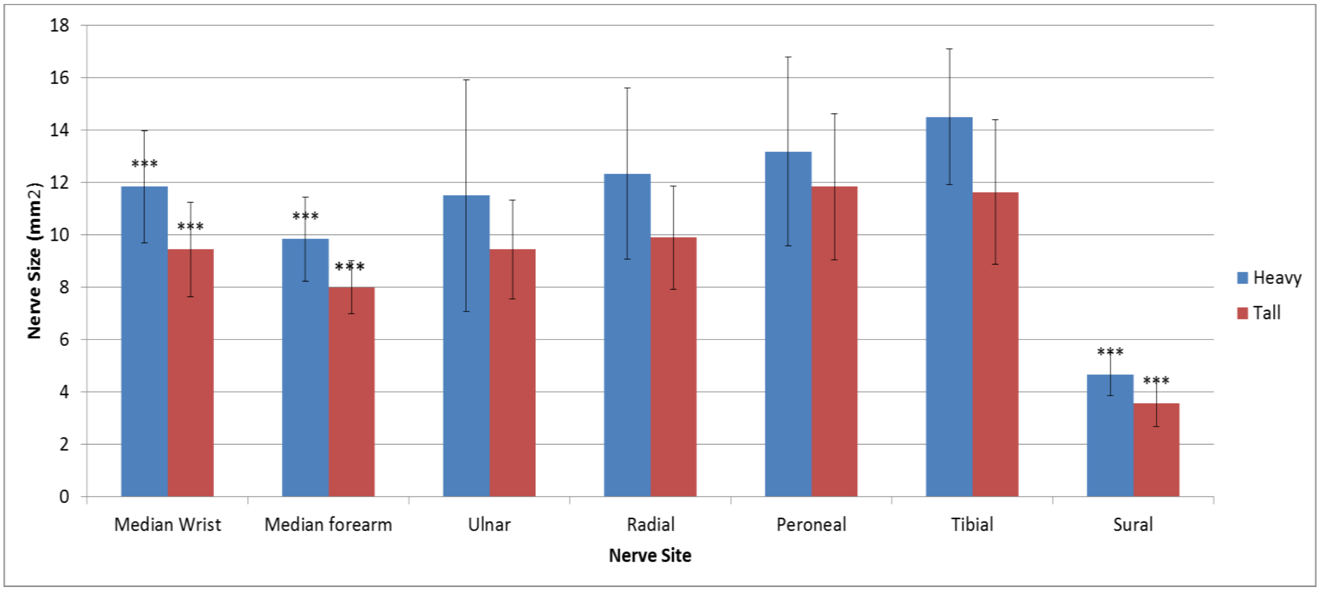

Figure 1. At every nerve site, average cross sectional nerve area was larger for heavy subjects when compared to the tall cohort. Heavy participants had significantly larger cross sectional nerve area at three sites; median at the wrist, median at the forearm and sural (indicated by *** above bar).

Abstract

Introduction: Cross-sectional nerve area reference values have been reported for many populations including pediatric, geriatric, and middle-aged, however few studies have investigated extremely tall and heavy individuals. Previous studies are conflicting; some suggest height and others weight as the key variable influencing nerve size.

Methods: Six heavy (5 males and 1 female) and 9 tall participants (4 males and 5 females) were enrolled. These subjects have no reported history of neurologic disorder and nerves were measured bilaterally using ultrasound at the following sites: median at the wrist and forearm, ulnar at the elbow, radial at the spiral groove, fibular at the knee, tibial at the ankle, and sural at the ankle.

Results: Nerve cross-sectional area has a higher correlation with weight than height. Ancillary analyses show there are no differences in nerve area between Caucasians and African Americans after controlling for weight.

Conclusions: Nerve cross-sectional area is more closely correlated with weight than height. This data is important to take into consideration when using ultrasound to evaluate patients of different body habitus.

Keywords: Height, weight, nerve cross-sectional area, ultrasound, ethnicity

INTRODUCTION

A. Background

Over the past twenty years, uses for ultrasound have grown immensely in all specialties in the diagnosis and treatment of patients (McDonagh et al, 2015). Specifically in the peripheral nervous system, ultrasound provides a detailed perspective of the muscles, vessels, nerves, and tissues of the body (Perikh et al, 2004). Pathology of the peripheral nervous system, whether benign or malignant, may affect nerves in a variety of ways. Enlargement of the peripheral nerves may occur due to conditions including blunt trauma, entrapment, tumors, and inflammatory responses (Cartwright et al, 2011). Quantifying the effect of these disorders on nerve size and function is paramount in developing more efficient diagnostic and treatment techniques.

Recently, studies have investigated the diagnostic and treatment utility of neuromuscular ultrasound for disorders ranging from carpal tunnel syndrome to amyotrophic lateral sclerosis (Sugimoto et al, 2014)(Cartwright et al, 2011). These investigations have had great success in elucidating the vast utility and potential of ultrasound techniques in medicine. Currently, reference values for nerve cross-sectional area have been obtained at many nerve sites in healthy adult, child, and geriatric populations (Cartwright et al, 2007). From these initial reference studies, ancillary analyses have investigated correlation with the body habitus factors height and weight. The results are conflicting, with some labs suggesting height is the most significant indicator of nerve area while others showing that weight is the best predictor (Kim et al, 2012)(Zaidmen et al, 2009). Solving this issue would allow healthcare providers to more effectively interpret nerve pathology in tall and heavy patients using neuromuscular ultrasound in the future.

B. Health Disparities

In addition to the lack of clarity in the literature regarding the influence of body habitus on nerve size, many studies lack diversity in subject recruitment and are thus limited in generalizability for minority populations (Gilbert et al, 2016). The majority of medical research in the past several decades has enrolled subjects which are Caucasian, well-educated, and in good socioeconomic standing (Sue et al, 2006). Therefore, conclusions drawn from investigations without ample subject diversity are limited in accuracy for the population as a whole. By 2044 it is projected that more than half of all Americans will belong to a minority group, so it is of the utmost importance to include more heterogeneous cohorts now so that the medical literature will reflect the US population in the future (Colby et al, 2014).

However the issue is not only the need to recognize that health disparities are a problem in the practice and research of medicine, but also that the lack of trust that often exists in underserved populations makes it exceedingly difficult to recruit subjects. When investigators attempt to directly recruit a racially diverse cohort, they encounter many boundaries that prevent the inclusion of minority groups. Barriers to recruitment for these populations often include: lack of access to healthcare, lack of trust in the healthcare system, disparities in medical education, and inability to effectively communicate with the community (Cuevas et al, 2017). In order to overcome this, researchers find ways to engage the broader community in order to appeal to minority groups and improve the investigation generalizability. Connecting with church and community leaders, handing out flyers at community events, providing free transportation to study site, hosting informational sessions, and maximizing transparency are a few of the ways that investigators use in order to recruit disparate groups (Magnani et al, 2005). This investigation will utilize these various techniques to recruit a racially diverse cohort. Multivariate analyses will be performed in order to determine if there are any interracial differences in nerve cross-sectional area.

C. Literature Review

Recent investigations involving the determinants of cross-sectional nerve area have produced mixed results. Body habitus factors, height and weight, and age have all shown correlation to some extent with nerve area in various studies. Determing which factor is most closely correlated with nerve size has produced conflicting reports. A few investigations into the matter purport that age is the most significant variable, stating that body habitus factors are also closely related to nerve area (Cartwright et al, 2013). Other studies have yielded results that show height as the most significant factor, with age having only minor correlation and weight being negligible (Zaidmen et al, 2009). And still other inquiries into this matter have regarded age, height, and weight as equivalent significant predictors of nerve area (Kerasnoudis et al, 2013). The lack of consensus on this subject has created an opportunity for this study to clarify this issue and better elucidate nerve area as a correlate of body size. Our investigation recruited subjects in the extremes of height and weight in the population in order to determine which body habitus factor is most significant.

D. Study Impetus

This investigation was designed and implemented in order to compare cross-sectional nerve area in extremely tall and heavy individuals in the population. Recruiting subjects that exhibit body habitus factors in the upper end of the distribution bell curve will allow us to better evaluate the correlation between height and weight on nerve size. Previous studies have produced reference nerve size data at many sites by recruiting all age groups (Cartwright et al, 2007). This data will be compared to our heavy and tall cohorts in order to determine trends. We expect to observe that weight is more significantly correlated with nerve area than height, based on clinical observations. We hypothesize that individuals with larger body mass indices will have a greater need for innervation and larger nerve area when compared to someone of lesser mass. This need for more innervation will stimulate neurons to develop within the nerve bundle, increasing nerve area, which eventually leads to an improved ability of the nerves to innervate the "additional mass". The findings from this study may be used to better interpret issues in the development and function of the peripheral nervous system in tall and heavy patients. Using results derived from this study, physicians may one day be able to use body habitus factors as a correlate to determine proper nerve area in extreme patients.

E. Significance

The implications of this investigation may improve the ability for healthcare providers to use neuromuscular ultrasound in the diagnosis and treatment of nerve disorders in tall and heavy patients. The reference data generated by this study could aide in the compilation of a nerve growth chart for this specific cohort of patients. Healthcare providers may then be able to compare a patient's age, height, and weight to a proper nerve area data compiled from studies like this one. In this way neuromuscular ultrasound could become a better way to visualize peripheral nervous system disorders in an efficient and non-invasive manner.

Additionally, this study will analyze nerve size as a correlate of race between African American and Caucasian subjects. The data produced will not only add reference values to the body of literature on an underrepresented minority group in medicine but also provide insight into interracial differences in nerve area. The results could eventually be used to compile a normal curve for nerve growth for each race, tailoring the medical observation and treatment of pathology to a specific individual. Health equity in medicine is a significant issue in the modern world and this study will act as a champion for underrepresented groups. This investigation may inspire further research being conducted regarding correlates to nerve area as well as disparities in medical research.

Nerve Cross-Sectional Area in Extremes of Height and Weight

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INTRODUCTION

Ultrasound can be utilized to provide insight into the status of peripheral nerves, muscles, vessels, tendons, and other tissues, which may be beneficial in the diagnosis and treatment of conditions affecting the peripheral nervous system (Kerasnoudis et al, 2013)(Perikh et al, 2004). Peripheral nerve enlargement is common in entrapment, inflammation, trauma, tumors and other conditions (Cartwright et al, 2011). Many laboratories have established reference values for normal nerve cross-sectional area in healthy adults and children, and at various anatomic sites (Cartwright et al, 2007)(Cartwright et al, 2009). In healthy individuals, studies have yielded conflicting information regarding the body habitus factor most closely associated with nerve cross-sectional area, with some showing a closer association with height and others with weight. (Zaidmen et al, 2009)(Kim et al, 2012). Clarifying this issue will help in the interpretation of nerve enlargement in tall and heavy patients, so this study was designed to determine if height or weight is more important in predicting nerve cross-sectional area.

In addition to analyzing the potential determinants of nerve area in this “extreme” population, ancillary analyses will be performed to assess for nerve area differences between African American and Caucasian individuals. It has been well documented that there are significant health disparities in medical research regarding African American populations (Gilbert et al, 2016). The majority of medical research focuses on cohorts that are primarily Caucasian, in higher socioeconomic standing, and well-educated (Sue et al, 2006). Thus the results of these studies, lacking in diversity, have limited generalizability for minority populations (Williams et al, 2009). This study aims to include African American participants, as well as Caucasian, in an attempt to better elucidate any interracial differences that may exist in regards to nerve cross-sectional area.

METHODS

Participants. This study was approved by the Wake Forest School of Medicine Institutional Review Board before any data collection occurred, and all participants provided written informed consent. Based on the National Health and Nutrition Examination Survey of 2011-2012, more than 95% of all males fall under 188.2 cm (6 ft 2 in) in height and 124.3 kg (274 lbs) in weight, while more than 95% of all females fall under 173.7 cm (5 ft 7 in) in height and 80% of females are less than 90.7 kg (200 lbs) in weight (NHANES, 2011-2012). In order to examine the nerve area of tall and heavy individuals in the population, the minimum recruitment criteria were set as: males over 188.2 cm and/or 124.3 kg (6 ft 2 in and/or 274 lbs) and females over 173.7 cm and/or 90.7 kg (5 ft 10 in and/or 200 lbs). The female criterion for weight was lowered from the 95th percentile to the 80th percentile in order to allow for recruitment of sufficient participants.

Subjects volunteered and mainly consisted of students from Wake Forest University and volunteers from the medical center. All participants were asked if they had symptoms associated with the peripheral nervous system and, if so, were not included. In most cases all nerve sites were measured on each participant, but time and clothing constraints limited this on some participants. Age, height, weight, race, and handedness were recorded for every participant.

Ultrasound. The patients were seated and nerves studied. A portable ultrasound device (Biosound MyLab 25; Esaote Group, Genoa, Italy) with an 18-MHz linear array transducer was used to obtain images. Seven nerves sites were identified at the commencement of the study as regions of interest. These sites were chosen since they are commonly sites of entrapment neuropathy and sites at which one can typically provide reproducible nerve images. The nerves imaged were: the median at the distal wrist crease and mid-forearm, the ulnar at the medial epicondyle, the radial at the spiral groove, the peroneal just proximal to the fibular head, the tibial at the ankle, and sural just proximal to the lateral malleolus. The smallest cross-sectional area was obtained by carefully positioning the transducer so it was perpendicular to the nerve. The “freehand” trace tool of the ultrasound device was then used to measure the nerve area.

Data analyses.

Using baseline measures and demographics, descriptive statistics were generated in Table 1 for all subjects included in this study. In order to evaluate nerve size at each nerve site, only left side measurements were used to limit intra-observer dependence. Side-to-side comparisons were calculated at each nerve site by dividing the difference between the side-to-side areas by the smaller area. A two-sided two-sample T test was performed at each nerve site between heavy and tall participants. Multivariate linear regression was performed with height and weight as independent variables and nerve size as dependent variables in order to determine which factor correlated more closely with nerve area. Ancillary analyses were performed between African American and Caucasian participants; mean nerve area was compared at each site and multivariate analysis was performed to determine if race was a significant correlate of nerve size.

RESULTS

Fifteen participants were recruited; 9 male and 6 female. The demographics for participants are compiled in Table 1, including mean height, mean weight, percent female, and racial distribution. The mean nerve cross-sectional area, standard deviation, and number of nerves evaluated for heavy and tall participants are included in Table 2. Data from previous studies have also been included in order to provide a metric for comparisons to be drawn from this cohort (Cartwright et al, 2012)(Cartwright et al, 2008). Figure 1 shows the trend in mean nerve area for individuals in the tall and heavy cohorts at the seven nerve sites.

Data from the left side of the body were used for major analyses and side-to-side comparison with data from the right side of the body revealed that nerve cross-sectional area differences ranged from 2.2% at the peroneal nerve in the tall cohort to 21% at the ulnar nerve in the heavy cohort. Mean cross-sectional nerve area was larger in the heavy group than the tall cohort at every nerve site measured, and this was significant at 3 nerve sites (median forearm, median wrist, sural). Multiple regression analysis was performed, adjusted for race and sex, showing that neither height nor weight had a significant (alpha = 0.05) correlation with nerve area at any of the 7 sites; however, weight held more significance than height when regressed by nerve size at four out of seven of the nerve sites measured (ulnar, peroneal, tibial, sural). Ancillary analysis of racial differences in mean nerve size at each site revealed African American mean cross sectional nerve area was larger than the Caucasian cohort at six out of the seven sites measured (all excluding sural). Significant differences were observed at three of the nerve sites (median forearm, ulnar, radial). Multiple regression analysis was performed at each nerve site to determine if race was a significant contributor to nerve area after controlling for weight, and this yielded non-significant results at five out of seven nerve sites (median wrist, median forearm, tibial, peroneal, sural).

DISCUSSION

This investigation evaluated nerve cross-sectional area at 7 predetermined sites using neuromuscular ultrasound on subjects that were extremely tall and heavy. The impetus behind this inquiry was to elucidate which body habitus factor, height or weight, is a more significant predictor of nerve cross-sectional area. Weight appears to be the better indicator of nerve size, although our sample size limited power to demonstrate this relationship. Individuals in the heavy cohort had larger mean nerve area than tall subjects at all sites measured, with significantly larger nerves at 3 out of 7 sites. When multivariate regression was performed, weight held more significance than height at four out of seven of the nerve sites. However since the controlled multivariate regression yielded non-significant results for both weight and height correlating to nerve size, we are unable to make definitive conclusions regarding this matter.

Weight may not be significantly correlated with nerve size in our regression model but it appears to be a more significant indicator of nerve area than height. This outcome does make sense physiologically. With more body mass, larger nerves may be needed for the musculature to function properly. More neurons may be contained within the nerve bundle leading to larger cross-sectional nerve area in heavier individuals. It is also possible that heavier individuals simply have more tissue everywhere, including in the nerves. Nerves have some connective tissue and this may be driving the increased cross-sectional area in heavier individuals.

We found that race does not appear to be a significant indicator of nerve size, as it was not a significant predictor of nerve size at the majority of sites measured during regression analysis. However, African Americans had significantly larger mean nerve area at 3 out of the seven sites (median forearm, ulnar and radial). This finding was most likely driven by the difference in weight distribution in the racial cohorts.

Previous inquiries into the determining factors of nerve size have yielded conflicting results, especially when pertaining to height and weight. Some studies have purported that age is most closely associated with nerve size, although height and weight are significantly associated with nerve area as well (Cartwright et al, 2013). Others have suggested that height is the most significant indicator of nerve size, with age having minimal correlation (Zaidmen et al, 2009). And yet other investigations have produced results that have produced results showing height, weight, and age as significant indicators of nerve size (Cartwright et al, 2007)(Cartwright et al, 2008)(Kerasnoudis et al, 2013). Our investigation looked specifically at height and weight in the extremes of the population in order to elucidate which factor is a more significant indicator of nerve size.

This inquiry has provided detailed data regarding nerve area in extremely large and heavy individuals, but there are limitations inherent in this study. The small sample size limited the power present in our analyses. Including more subjects in a similar study in the future would increase power of the investigation and chances of finding statistically significant results. Finally, during data collection, not all subjects underwent every nerve area measurement due to physical limitations, clothing restrictions, etc. and this may have limited analyses at some nerve sites.

Even though this investigation has inherent limitations, we have provided a detailed analysis of the most significant indicators of nerve size. Seven predetermined nerve sites were examined using neuromuscular ultrasound in extremely tall and heavy participants. Although the small sample size limited power, we found that weight appears to be a better indicator of nerve area at the majority of sites measured when compared to height. Heavier individuals also had larger nerves than taller subjects at most sites. Also race did not appear to be a significant indicator of nerve area at the majority of nerve sites measured in our model. More studies must be done in the future in order to investigate viable applications of the determinants of nerve size such as enrolling patients in a longitudinal study in order to compile a nerve growth chart as a correlate of height, weight, and age which then may be used as a quick test for nervous system health for healthcare practitioners in the future.

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DISCUSSION

A. Interpretation of Results

The primary objective of this investigation was to elucidate correlation between body habitus factors and cross-sectional nerve area as well as to determine whether height or weight is a more significant indicator of nerve size. Heavy subjects showed larger mean nerve size data than tall participants at all sites, being significantly larger at 3 sites (median at the forearm, median at the wrist, and sural at the ankle). Multivariate regression analysis yielded non-significant results for both height and weight at all sites, most likely due to the small sample size recruited in this investigation. However, we observed that weight was a more significant indicator of cross-sectional nerve area than height at four out of seven of the measured sites (ulnar, peroneal, tibial, sural). So although our regression model did not produce results that were conventionally significant (alpha $\leq$ 0.05), it still allowed us to observe trends in the data. As expected, weight was a better determinant of nerve area when compared to height in our cohort. A similar investigation with significantly more participants is needed to provide more support for our current findings and would most likely increase the significance of the results. Ancillary analysis regarding interracial differences in nerve size showed that race was not a significant predictor of nerve size at the majority of sites measured (median wrist, median forearm, tibial, peroneal, sural). The mean cross-sectional nerve areas in the Caucasian and African American cohorts were only significantly different at 3 nerve sites (median forearm, ulnar and radial), at which the African American subjects had larger nerves. This difference was can most likely be attributed to the weight distribution between the racial cohorts; the African American cohort had a heavier distribution of subjects while the Caucasian had a taller distribution. This most likely skewed our results slightly, toward a finding of larger nerves at each site in the African American cohort. Recruiting a more even distribution of tall and heavy subjects in each racial cohort would improve the validity of the results. Our study was sufficiently geared to observe basic trends in the data and from this we confirmed our hypothesis that weight is a better indicator of nerve area than height in this extreme cohort.

B. Physiological Plausibility

In terms of plausibility, the results from this investigation make logical sense. From our study we have shown that heavy individuals have larger nerve area, on average, than tall individuals and that weight appears to be the most significant indicator of nerve area. When compared to subjects that are of average height and weight, individuals in the upper extremes of weight have significantly more body mass. This extra body mass contains more muscle tissue (as well as fat, ligaments, and tendons) which requires more innervation from the proper nerve fibers. The need for more innervation, most likely induces the development of more neurons within the nerve fiber bundle leading to the extra muscle tissue. The increased number of neurons in the nerve bundle directly increases the cross-sectional nerve area; therefore heavier individuals have larger nerves. This interpretation of the results is a pragmatic physiological explanation, however is not without limitations. It is possible that heavier individuals simply have more tissue everywhere in the body, including more nerve connective tissue and Schwann cells within the nerve bundle itself. This would falsely increase nerve cross-sectional area in heavier individuals when compared to normal populations, without actually increasing the amount of neurons or neuronal density within the nerve fiber. An ancillary investigation comparing nerve size in extremely heavy individuals who are of a higher muscle to fat ratio and those of a low muscle to fat ratio would elucidate the role of body fat in nerve area in this population. DEXA may be used in this hypothetical investigation in order to measure the exact level of fat in the body. Using neuromuscular ultrasound, nerve area may be compared to determine if fat/muscle content directly influences nerve area at various sites. If the findings show that individuals with higher muscle/fat ratio have larger cross sectional nerve area, it would support our physiological explanation for heavier individuals having larger nerves. More muscle means a greater need for innervation to that tissue, resulting in more neurons being contained in the bundle.

C. Addition to scientific literature

Currently in regards to the determinants of nerve area, the medical literature purports conflicting results as aforementioned in the introduction. Some studies have shown that height and weight are equal determinants, some show that height is the most indicative variable and yet others have found that both of these variables are insignificant with age being most indicative of nerve area. In 2013, Cartright et al published an investigation into the cross-sectional nerve areas of thirty-two children (3 months to 16 years) and 20 geriatric adults (67–92 years) at multiple nerve sites. They purported that age was significantly correlated with nerve area with Pearson correlation coefficients ranging from 0.51 to 0.85 (Cartwright et al, 2013). Another recent study performed by Zaidmen et al in 2009 used 190 subjects, with and without neuropathy, in order to investigate nerve cross sectional area at the median and ulnar nerves. They purported that in healthy children and adults, nerve cross sectional area was significantly greater with increasing height with ($P<0.05$). Also an inquiry by Kerasnoudis et al in 2014 into the factors related to ulnar cross sectional areas in 65 healthy subjects (mean age 45.6, SD ± 7.5, 30 women) resulted in weight (p=0.001) and height (p=0.04) both being significantly correlated. Our investigation provides more clarity on this topic and provides sufficient objective evidence that weight is a more significant indicator of nerve area than height. This supports evidence from previous nerve conduction velocity investigations that purport taller individuals have slower conduction velocities than shorter individuals (Rivner et al, 2001)(Stetson et al, 1992). An investigation by Rivner et al retrospectively examined nerve conduction velocities at multiple nerve sites in 3969 subjects ranging from 20 to 95 years in age. They found that height was inversely correlated with nerve conduction velocity, with correlation coefficients ranging from -0.278 at the ulnar nerve to -0.420 in the peroneal nerve (Rivner et al, 2001). These studies show that height is inversely correlated with nerve conduction velocity, possibly due to longer axons reducing speed of transmission or smaller nerve area that provides more resistance to action potential flow. Our investigation purports that taller individuals have smaller nerve area than heavy individuals, and this makes sense according to nerve conduction velocity studies that show tall individuals have slower nerve conduction that may be attributed to smaller nerve area. Also our interpretations of the results are rationally sound and provable in the physiological realm. Ancillary investigations are needed in order to provide more definitive support for our findings, however. Our addition to the literature on this subject will allows healthcare practitioners in the future to more accurately interpret and treat nerve pathology in tall and heavy subjects. The data from this study may one day be compiled into standard values for nerve area according to height and weight of the patient. Eventually this may act as a “nerve growth chart” allowing physicians to use body habitus factors in order to determine proper nerve area. This may improve and expedite the diagnosis of nervous system disorders. Although more research must be done in order to provide more definitive data on the subject, the potential impact of this study is profound by providing a definitive body habitus metric, weight, that has been proven to be an indicator of proper nerve size.

D. Limitations

This investigation pragmatically elucidated the correlation between nerve area and body habitus factors in extremely tall and heavy subjects, however does contain inherent restrictions. Due to time and fiscal constraints, the most glaring limitation is the small sample size recruited. This resulted in lower power for the resulting analysis and decreased generalizability. An additional study that recruits significantly more participants over a longer time period would most likely increase the power and the validity of the results. Also during the data collection phase of the experiment, we were not able to obtain cross-sectional nerve area values at every site due to clothing restrictions, physical limitations, previous injury, time constraints, etc. Fewer data points measured lowered the generalizability of the resulting analysis at that specific nerve site. In the future, studies of the same type and caliber may impose a stricter dress code on the subjects during data collection to ensure ample data points at each nerve site. During data analysis, the unequal gender composition of the tall and heavy cohorts also acted as a potential confounder to our two sided T-test calculations using mean cross sectional nerve area between the two groups. Gender was controlled for in the multivariate analysis and this limited its' potential to confound in the regression analysis. A final limitation that may have had an impact on this investigation was the presence of participants whose body habitus satiated the criteria for both tall and heavy participants. This made it difficult to assign these subjects into one of the study arms and therefore may have influenced the resulting analyses. In this investigation we assigned individuals who met both the tall and heavy criteria into the group into which their height/weight was more "extreme" according to the study defined inclusion criteria.

E. Conclusions

Regardless of this investigation's inherent constraints, our study has provided a pragmatic analysis of the indicators of cross-sectional nerve area in extremely tall and heavy subjects. Neuromuscular ultrasound was used to evaluate and record nerve area at seven predetermined sites in the upper and lower extremities. After the data was collected and analyzed, we found that weight was a more significant indicator of cross-sectional nerve area than height at the majority of nerve sites measured. The small sample size contained within this investigation limited power of the analysis however was still sufficient to observe that heavier subjects tended to have larger nerve area, on average, when compared to taller subjects. Physiologically this result is logical; heavier individuals have more body mass leading to more nerve fibers being contained within the nerve bundle in order to properly innervate the extra mass. An increase in nerve bundle size results and cross-sectional nerve area is increased in these larger subjects when compared to those of lesser body mass. Ancillary analysis showed that race was not a significant indicator of nerve size at the majority of nerve sites measured. In order to provide more support for our results, more investigations of the same caliber are needed into the indicators of nerve area using a significantly larger sample size. This would increase the power and generalizability of these future studies. The implications of this investigation are vast and may one day act as part of the foundation of a nerve growth chart as a correlate of body habitus factors. This growth chart would allow health care practitioners to factor in height, weight and age when evaluating peripheral nerve function and size. This may act be used as an early diagnostic tool for nervous system disorders as well as in the treatment of neuronal abnormalities.

References

1. A Kerasnoudis, K. Pitarokoili. “Ulnar Nerve Reference Values for Cross-Sectional Area, Intranerve Cross Sectional Area Variability and Side to Side Difference Ratio.” *Rheumatology International*, 2013. doi:10.1007/s00296-013-2708-1.
2. Cartwright, Michael S., David R. Mayans, Natalie A. Gillson, Leah P. Griffin, and Francis O. Walker. “Nerve Cross-Sectional Area in Extremes of Age.” *Muscle & Nerve* 47, no. 6 (June 2013): 890–93. doi:10.1002/mus.23718.
3. Cartwright, Michael S., Francis O. Walker, Leah P. Griffin, and James B. Caress. “Peripheral Nerve and Muscle Ultrasound in Amyotrophic Lateral Sclerosis.” *Muscle & Nerve* 44, no. 3 (September 2011): 346–51. doi:10.1002/mus.22035.
4. Cartwright, Michael S., and Francis O. Walker. “Neuromuscular Ultrasound in Common Entrapment Neuropathies.” *Muscle & Nerve* 48, no. 5 (November 2013): 696–704. doi:10.1002/mus.23900.
5. Cartwright, Michael S., Hae W. Shin, Leah V. Passmore, and Francis O. Walker. “Ultrasonographic Findings of the Normal Ulnar Nerve in Adults.” *Archives of Physical Medicine and Rehabilitation* 88, no. 3 (March 2007): 394–96. doi:10.1016/j.apmr.2006.12.020.
6. Cartwright, Michael S., Martin E. Brown, Patrick Eulitt, Francis O. Walker, Victoria H. Lawson, and James B. Caress. “Diagnostic Nerve Ultrasound in Charcot-Marie-Tooth Disease Type 1B.” *Muscle & Nerve* 40, no. 1 (July 2009): 98–102. doi:10.1002/mus.21292.
7. Cartwright MS, Passmore LV, Yoon JS, Brown ME, Caress JB, Walker FO. Cross-sectional area reference values for nerve ultrasonography. Muscle Nerve 2008;37:566–571.
8. Cartwright, Michael S., Samantha Demar, Leah P. Griffin, Nikhil Balakrishnan, Jessica M. Harris, and Francis O. Walker. “Validity and Reliability of Nerve and Muscle Ultrasound.” *Muscle & Nerve* 47, no. 4 (April 2013): 515–21. doi:10.1002/mus.23621.
9. Cartwright MS, Shin HW, Passmore LV, Walker FO. Ultrasonographic reference values for assessing the normal median nerve in adults. J Neuroimaging 2008;19:47–51.
10. Colby, Sandra L. and Jennifer M. Ortman. “Projections of the Size and Composition of the U.S. Population: 2014 to 2060” Current Population Reports, P25-1143, U.S. Census Bureau, Washington, DC, 2014.
11. Cuevas, Adolfo G., Kerth O’Brien, and Somnath Saha. “What Is the Key to Culturally Competent Care: Reducing Bias or Cultural Tailoring?” Psychology & Health, February 6, 2017, 1–15. doi:10.1080/08870446.2017.1284221.
12. Gilbert, Keon L., Rashawn Ray, Arjumand Siddiqi, Shivan Shetty, Elizabeth A. Baker, Keith Elder, and Derek M. Griffith. “Visible and Invisible Trends in Black Men’s Health: Pitfalls and Promises for Addressing Racial, Ethnic, and Gender Inequities in Health.” *Annual Review of Public Health* 37 (March 18, 2016): 295–311. doi:10.1146/annurev-publhealth-032315-021556.
13. Height and Weight Growth Charts." Center for Disease Control. CDC, 20 Apr. 2001. Web. 23 Mar. 2017. https://www.cdc.gov/growthcharts/data/set1clinical/cj41cs017c.pdf.

14. Kim, Hyoung Seop, Seung Ho Joo, Zee-A. Han, and Yong Wook Kim. "The Nerve/tunnel Index: A New Diagnostic Standard for Carpal Tunnel Syndrome Using Sonography: A Pilot Study." Journal of Ultrasound in Medicine: Official Journal of the American Institute of Ultrasound in Medicine 31, no. 1 (January 2012): 23–29.
15. Magnani, Robert, Keith Sabin, Tobi Saidel, and Douglas Heckathorn. "Review of Sampling Hard-to-Reach and Hidden Populations for HIV Surveillance." AIDS (London, England) 19 Suppl 2 (May 2005): S67–72.
16. McDonagh, Cara, Michael Alexander, and David Kane. "The Role of Ultrasound in the Diagnosis and Management of Carpal Tunnel Syndrome: A New Paradigm." Rheumatology (Oxford, England) 54, no. 1 (January 2015): 9–19. doi:10.1093/rheumatology/keu275.]
17. Parikh, Amish, and Denis Daneman. "Is Carotid Ultrasound a Useful Tool in Assessing Cardiovascular Disease in Individuals with Diabetes?" *Diabetes Technology & Therapeutics* 6, no. 1 (February 2004): 65–69. doi:10.1089/152091504322783440.
18. Rivner, Michael H., Thomas R. Swift, and Khalid Malik. "Influence of Age and Height on Nerve Conduction." Muscle & Nerve 24, no. 9 (September 2001): 1134–41. doi:10.1002/mus.1124.
19. Stetson, Diana S., James W. Albers, Barbara A. Silverstein, and Robert A. Wolfe. "Effects of Age, Sex, and Anthropometric Factors on Nerve Conduction Measures." Muscle & Nerve 15, no. 10 (October 1992): 1095–1104. doi:10.1002/mus.880151007.
20. Sue, Stanley, and Meenu K. Dhindsa. "Ethnic and Racial Health Disparities Research: Issues and Problems." Health Education & Behavior: The Official Publication of the Society for Public Health Education 33, no. 4 (August 2006): 459–69. doi:10.1177/1090198106287922.
21. Sugimoto, Takamichi, Kazuhide Ochi, Naohisa Hosomi, and Masayasu Matsumoto. "[Ultrasonographic diagnosis of inflammatory neuropathies]." *Brain and Nerve = Shinkei Kenkyū No Shinpo* 66, no. 3 (March 2014): 223–28.
22. US National Center for Health Statistics (division of NHANES) http://www.cdc.gov/nchs/data/series/sr_11/sr11_252.pdf
23. Williams, David R., and Selina A. Mohammed. "Discrimination and Racial Disparities in Health: Evidence and Needed Research." *Journal of Behavioral Medicine* 32, no. 1 (February 2009): 20–47. doi:10.1007/s10865-008-9185-0.
24. Zaidman, Craig M., Mohammed Al-Lozi, and Alan Pestronk. "Peripheral Nerve Size in Normals and Patients with Polyneuropathy: An Ultrasound Study." Muscle & Nerve 40, no. 6 (December 2009): 960–66. doi:10.1002/mus.21431.

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