



Research paper

High-resistance strength training does not affect nerve cross sectional area – An ultrasound study



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ABSTRACT

Objective: The aim was to study the effect of high-resistance strength training on peripheral nerve morphology, by examining properties of peripheral nerves as well as distal and proximal muscle thickness with ultrasound, comparing healthy individuals who perform and do not perform high-resistance strength training.

Methods: Neuromuscular ultrasound was used to examine cross sectional area (CSA) of the median and musculocutaneous nerves, and muscle thickness of the abductor pollicis brevis muscle, biceps brachii muscle, quadriceps muscle and extensor digitorum brevis muscle, in 44 healthy individuals, of whom 22 performed regular high-resistance strength training.

Results: No difference in nerve CSA was found between trained and untrained individuals although trained individuals had thicker biceps brachii muscles. The CSA of the median nerve in the forearm correlated with participants' height and was significantly larger in men than women.

Conclusions: In this cohort, CSA of the median and musculocutaneous nerves was not affected by strength training, whereas gender had a prominent effect both on CSA and muscle thickness.

Significance: This is the first study to examine the effect of high-resistance strength training on peripheral nerves with neuromuscular ultrasound.

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1. Introduction

The application of ultrasound in the diagnostic evaluation of neuromuscular disorders is becoming increasingly common and important. Although the more traditional methods of electroneurography and electromyography are still routinely used as diagnostic tools for the nerve and the motor unit, ultrasound is a useful complement in yielding morphological information about the nerve and its surrounding tissues (Suk et al., 2013). Moreover, the structure of peripheral nerves may be affected by trauma and tumors, and the cross sectional area (CSA) is often affected by disorders such as carpal tunnel syndrome/entrapment and neuropathies (Hobson-Webb and Padua, 2016). Several ultrasound studies have evaluated peripheral nerve morphology in arms and

legs, contributing reference values and examining the relationship between CSA and factors such as height, weight, age and body mass index (BMI) (Cartwright et al., 2008, 2013, Kerasnoudis et al., 2013, Qrimli et al., 2016).

It is well known that high-resistance strength training (HRST) causes changes in skeletal muscles (Jones and Rutherford, 1987, D'Antona et al., 2006, Folland and Williams, 2007, Seynnes et al., 2007), as well as adaptations of the central nervous system (Moritani and deVries, 1979, Yue and Cole, 1992, Zijdwind et al., 2003). Upper limb muscles gain a greater hypertrophy response to HRST than lower limb muscles (Wilmore, 1974, Cureton et al., 1988). Further, the hypertrophy response of arm muscles is greater in men than women (Kadi et al., 2000), most likely due to the fact that these muscles possess more androgen receptors. Women have approximately 60–80% of the muscle fiber area compared to men (Edwards et al., 1977), while elderly individuals have smaller muscles and fewer muscle fibers compared to younger individuals (Welle et al., 1996). Nevertheless, there is limited knowledge about if and how HRST affects the morphology of peripheral nerves. One previous study examined the skeletal muscle adaptation to resistance training and found a greater increase in muscle thickness of arm muscles compared to leg muscles (Abe et al., 2000).

Abbreviations: APB, abductor pollicis brevis muscle; BMI, body mass index; CMAP, compound motor action potential; CSA, cross sectional area; EDB, extensor digitorum brevis muscle; HHD, hand-held dynamometer; HRST, high-resistance strength training.

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Only one case study has examined the subacute effects of strenuous exercise on nerve remodeling with ultrasound, where both the CSA and the conduction velocity of several peripheral nerves, including the median nerve, were increased following a marathon (Kerasnoudis, 2016). If this holds true in a larger cohort, it could potentially cause misdiagnosis of neuropathy in individuals having completed strenuous exercise. To the authors' knowledge, no other study has assessed how strength training or cardiovascular exercise affects the appearance of peripheral nerves.

The aim of this study was to examine whether individuals who perform HRST on a regular basis have a larger CSA of peripheral nerves than individuals who do not perform HRST. Firstly, we hypothesized that the CSA of the median and musculocutaneous nerves would be larger in trained individuals compared to untrained individuals. Secondly, we hypothesized that trained individuals would have thicker biceps and quadriceps muscles than untrained individuals, and that men would have thicker muscles than women.

2. Material and methods

2.1. Subjects

This study was performed at the Department of Clinical Neurophysiology, Uppsala University Hospital, between April and June 2016. Participants who had previously participated in a study on the use of compound motor action potential (CMAP) as a neurophysiological parameter for HRST (Molin and Punga, 2016) were asked to participate in this follow-up study. For the previous study, participants were divided into two groups based on training regimen: (1) the "trained group", consisting of individuals who reported performing HRST \geq two times per week for at least one year, and (2), the "untrained group", which consisted of participants who reported no strength or cardiovascular training at all or who reported cardiovascular training but no HRST. Exclusion criteria were a family history of neurological disorders, use of muscle relaxant medication or symptoms of muscle fatigue. For this study, the criterion for remaining in the trained group was that the training intensity was *not less* than when participating in the previous study. To stay in the untrained group, participants had to confirm that they had not started performing HRST. Height and weight were once again noted to update these values from the previous study.

CMAP amplitude and area were assessed with motor neurography, with stimulation of the median, musculocutaneous, femoral and peroneal nerves, with recordings of the abductor pollicis brevis, muscle, biceps brachii muscle, rectus femoris muscle and extensor digitorum brevis muscle. The isometric muscle strength of these muscles was assessed with a hand-held dynamometer. Full details on the methods are available in the original article (Molin and Punga, 2016).

The study was approved by the Uppsala Ethical Review Board (Case No. 2014/430), performed in accordance with the ethical standards of the ICMJE and conformed to the recommendations of the Declaration of Helsinki. All participants signed a written informed consent form before participating in the study.

2.2. Ultrasound examination

The ultrasound examinations were performed with a stationary ultrasound device (LOGIQ S8; GE Healthcare). Measurements were performed by either C.J.M., J.W. or biomedical technicians at the Neurophysiology clinic at Uppsala University Hospital. C.J.M. participated in all evaluations in order to gain uniform judgments.

Three nerve sites were chosen for examination: median nerve at the wrist, just proximal to the carpal ligament; median nerve in the

forearm, 12 cm proximal to the carpal ligament; and musculocutaneous nerve at the axillary fossa, in the crest between the biceps and deltoid muscle. The probe was adjusted so that it was perpendicular to the nerve. The CSA was measured with the tracer tool, measuring just inside the epineurium. At each predetermined measurement level, we aimed to assess the largest CSA. Three consecutive images and measurements were recorded, and the mean value of these three measurements was used for analysis. Usually there were only minimal differences between the three measurements. The largest CSA was chosen, since this is the parameter commonly used in clinical practice when evaluating neuropathies.

The thickness of four muscles was also measured: the abductor pollicis brevis (APB) muscle, the biceps muscle, the quadriceps muscle and the extensor digitorum brevis (EDB) muscle. Subjects lay supine with muscles relaxed during the examination. The APB and biceps muscle were examined with the forearm supine. The APB muscle was examined with the probe perpendicular to the first metacarpal bone, and was measured from the superficial fascia down to the tendon of the flexor pollicis longus muscle. The biceps muscle was measured approximately two thirds of the distance from the acromion to the elbow crease, and the quadriceps muscle was measured approximately in the middle between the anterior superior iliac spine and the proximal edge of the patella. For all muscles, measurements were taken at the thickest part of the muscle belly. In order to obtain a correct muscle thickness, the transducer was held against the skin with minimal pressure, with a visible layer of ultrasound gel between the transducer and the skin on the ultrasound image, i.e. the transducer had no direct contact with the skin. The largest measured diameter was recorded. Once again, three consecutive images and measurements were performed, and the mean was calculated. The measurements of the biceps brachii muscle also included the brachialis muscle, since the muscle belly was measured from the superficial part of the fascia, down to the part of the fascia adjacent to the humerus. The measurements of the APB muscle also included the superficial head of the flexor pollicis brevis muscle. For the quadriceps muscle, the vastus intermedius muscle belly and the rectus femoris muscle belly were measured individually. The values were then added together in order to obtain a total value of the quadriceps muscle thickness. Unless participants reported sensory or motor symptoms in the right-side extremities, the right arm and leg were examined. For the median nerve, APB and EDB muscles, an L8-18i MHz linear-array transducer was used. For the musculocutaneous nerve, biceps and quadriceps muscles, a ML6-15 MHz linear-array transducer was used. Participants were sitting up during examination of the median nerve and the APB muscle and lay supine with extended legs during examination of the biceps muscle, musculocutaneous nerve, quadriceps muscle and EDB muscle. When measuring the musculocutaneous nerve, participants were asked to place their right hand behind their head while laying supine, in order to expose the crest between the biceps and the deltoid muscle. Participants who reported symptoms of carpal tunnel syndrome (numbness, paresthesias, tingling) were excluded from the examination of the median nerve at the wrist. No participant reported symptoms or showed any signs of any other peripheral neurological disorder.

2.3. Statistical analysis

Statistical analysis was performed with R version 3.2.4 (R Core Team, 2016). A two-tailed independent *t*-test was performed to compare parametric data between the trained vs. the untrained group, and between men and women. Correlation analysis between CSA and age, height and weight was performed with Pearson's product-moment correlation coefficient. Multivariable linear regression was performed to assess the effect of age, height

and weight, with CSA as the dependent variable, and also to control for training status when comparing men and women. BMI was neither included in the correlation analysis nor the multivariable linear regression, since BMI does not take into account an individual's ratio between muscle tissue and body fat, which can be especially misleading in trained individuals. Correlation analysis with Pearson's correlation coefficient was also performed to assess the relationship between CSA and CMAP amplitude, CMAP area and muscle strength of the biceps muscle (previously collected data (Molin and Punga, 2016)), and between CMAP amplitude and muscle thickness. A multivariable linear regression with CMAP amplitude of the biceps muscle in the trained cohort as the dependent variable was also performed, to assess the relationship with isometric muscle strength and muscle thickness. Data are presented as mean \pm SD unless otherwise stated. A p -value < 0.05 was considered significant.

3. Results

3.1. Clinical features of participants

The cohort consisted of 44 healthy participants (29 women and 15 men) within the age range of 23–68 years (mean \pm SD: 41 ± 12.4). The trained and untrained groups each consisted of 22 individuals. Participant characteristics are stated in Tables 1 and 2. The untrained group was significantly older than the untrained group ($p = 0.043$; Table 1). All participants performed regular weight lifting ≥ 2 times per week with free weights and/or weight machines in the gym (Table 1). None of the participants had an occupation that considerably affected their muscle strength. The most common medication in the untrained group was hypertensive agents, followed by antidepressants. No medication in the trained group had a modal value of more than 1. There was only one smoker in the untrained group and none in the trained group.

3.2. Ultrasound

Three measurements of the median nerve at the wrist level (two in the untrained group, one in the trained group) were removed from further analysis, due to clinical symptoms of carpal tunnel syndrome. One measurement of the median nerve was further removed from the untrained group, due to anomalous anatomy. No difference was found in CSA of the median and musculocutaneous nerves between trained and untrained individ-

uals. Trained individuals had a significantly thicker biceps brachii muscle than untrained individuals ($p = 0.019$; Table 3; Fig. 1). No other muscles were significantly thicker in the trained group.

Men had significantly larger CSA of the median nerve in the forearm than women ($p < 0.001$), also when controlling for training status and body habitus ($p = 0.045$). Additionally, men had significantly greater thickness of the APB muscle ($p < 0.001$), biceps brachii muscle ($p < 0.001$; Fig. 1) and quadriceps muscle ($p < 0.002$; Table 4). These differences persisted when controlling for training status ($p < 0.001$ for APB and biceps muscle; $p < 0.01$ for quadriceps). No differences in muscle thickness or nerve CSA were found when comparing trained to untrained individuals within the same gender.

A significant correlation between CSA of the median nerve in the forearm and height was found ($p < 0.001$; Fig. 2; Table 5). A significant correlation was also found between CMAP amplitude and muscle thickness of the EDB muscle ($r = 0.3$, $p = 0.048$). No correlation was found between CSA of the musculocutaneous nerve and CMAP amplitude, CMAP area or isometric muscle strength of the biceps muscle (data not shown). The multivariable analysis of CMAP amplitude and muscle strength and muscle thickness of the biceps muscle in the trained cohort did not show a relation between the variables ($p > 0.05$).

The correlation between height and nerve CSA of the median nerve in the forearm persisted after controlling for multiple variables ($p < 0.001$; Table 5).

4. Discussion

4.1. The effect of HRST on nerve CSA

This is the first study that examines whether HRST alters the CSA of peripheral nerves. The main finding was that HRST did not affect cross sectional area of the median nerve or the musculocutaneous nerve in this cohort. In case the acute and sub acute effects of training include nerve enlargement that remains several days after strenuous exercise, the use of neuromuscular ultrasound could potentially cause misdiagnosis of neuropathies in patients. Therefore, the present study provides valuable data that long-term effect of regular HRST on peripheral nerves does not influence ultrasound diagnostics of neuropathies using CSA as a parameter.

The CSA values of the median nerve in the study by Kerasnoudis (2016) were normal before the marathon run, but became indicative of median nerve neuropathy at the wrist 24 h after the race (according to the authors' own reference material). Similar observations were found in the ulnar, tibial and sural nerves. Nevertheless, in this previous study the CSA of the median nerve was only increased at the wrist level, whereas it remained unchanged in the forearm and actually was reduced at the upper arm level. In the current study, we found no significant differences in CSA of any nerves between the trained and the untrained group. Obviously, this could be due to the fact that endurance running, such as marathon, is a different form of training than resistance training. Furthermore, the values obtained in the previous marathon study represent the acute and subacute effect of training in merely one participant, while the present study focused more on long-term effects on peripheral nerves at a group level.

While HRST did not significantly alter CSA, gender appears to have a significant effect on the CSA, considering that men had a larger CSA of the median nerve in the forearm compared to women. This is in line with previous studies (Bathala et al., 2014, Qrimli et al., 2016), in which the median nerve in the forearm was found to be larger in men than women. On the contrary, one previous study (Kerasnoudis et al., 2013) reported no difference in CSA of the median nerve between men and women. The lack of a differ-

Table 1
Participant characteristics of trained and untrained group.

	Trained group (N = 22)	Untrained group (N = 22)
Sex male/female (N)	10/12	5/17
Age (years)	37.2 (11.4)	44.7 (12.4)
Weight (kg)	70.9 (10.1)	72.8 (13.1)
Height (cm)	174 (8.6)	170 (9.3)
Body mass index	23.4 (2.4)	25.3 (3.7)
Concomitant medication	6 (27%)	9 (41%)
<i>Training parameters</i>		
Weight training times/week	3 (2–6)	n.a.
Weight training duration (years)	7 (1–20)	n.a.
Free weights/training machine (N)	18 (82%)	n.a.
Kettle bells/suspension training	10 (46%)	n.a.
Crossfit/circle training	2 (9%)	n.a.
Aerobic cardiovascular training	21 (96%)	6 (27%)

Values represent mean (SD). Medication intake and type of training is stated as N (%) of subjects. For weight training times/week and duration, median (range) is stated. n.a., not applicable. Experimental settings were similar for the two groups.

Table 2
Participant characteristics of trained and untrained group by sex.

	Trained group (N = 22)		Untrained group (N = 22)	
	Men (N = 10)	Women (N = 12)	Men (N = 5)	Women (N = 17)
Age (years)	33 (10.1)	40.8 (11.6)	42.4 (17.7)	45.5 (11.0)
Weight (kg)	80.2 (5.6)	63.2 (5.2)	83.8 (10.1)	69.6 (12.3)
Height (cm)	181.2 (6.0)	167.6 (4.4)	183.2 (4.9)	165.5 (5.6)
Body mass index	24.5 (2.2)	22.5 (2.2)	25.1 (3.1)	25.4 (3.9)
<i>Training parameters</i>				
Years performing HRST	6 (6)	9 (4)	n.a.	n.a.
Mean number of repetitions	32 (14)	27 (10)	n.a.	n.a.
Upper arms (N)	6 (60%)	11 (92%)	n.a.	n.a.
Lower arms/hands	6 (60%)	7 (58%)	n.a.	n.a.
Legs/thighs	10 (100%)	12 (100%)	n.a.	n.a.
Lower legs	9 (90%)	12 (100%)	n.a.	n.a.

Values represent mean (SD). Mean number of repetitions represents the total number of repetitions (all sets) during a specific exercise. Muscle groups are stated as N (%) of subjects focusing on this group when performing HRST. n.a., not applicable. Experimental settings were similar for the two groups.

Table 3
Nerve cross sectional area and muscle thickness in the trained and untrained group.

	Trained group (N = 22)			Untrained group (N = 22)			p-value
	N	Mean (SD)	Range	N	Mean (SD)	Range	
<i>Nerve (mm²)</i>							
Median wrist	21	8.3 (1.5)	5.4–10.3	19	7.9 (1.5)	5.3–10.8	0.39
Median forearm	22	6.1 (1.3)	3.9–9.5	22	5.6 (1.1)	3.5–8.4	0.22
Musculocutaneous	22	3.4 (1.2)	1.4–6.8	22	3.0 (0.8)	1.6–5.0	0.21
<i>Muscle (mm)</i>							
APB	22	18.8 (2.8)	13.2–23.3	22	18.1 (2.5)	14.6–25.3	0.34
Biceps brachii	22	34.8 (5.5)	26.6–47.8	22	31.0 (5.0)	23.6–41.2	0.019
Quadriceps	22	45.9 (9.8)	26.4–66.2	22	42.5 (8.3)	30.9–62.8	0.22
Vastus intermedius		21.4 (6.2)	10.3–36.0		20.1 (5.7)	12.4–34.6	
Rectus femoris		24.5 (5.2)	16.1–39.3		22.4 (3.5)	16.3–29.0	
EDB	22	8.5 (1.8)	5.8–12.9	22	7.6 (1.6)	4.5–11.1	0.08

Nerve cross sectional area values are given in mm². Muscle thickness values are given in mm. Statistical comparison with *t*-test between the trained and untrained group. APB, abductor pollicis brevis muscle; EDB, extensor digitorum brevis muscle. Significant p-values are marked in bold.

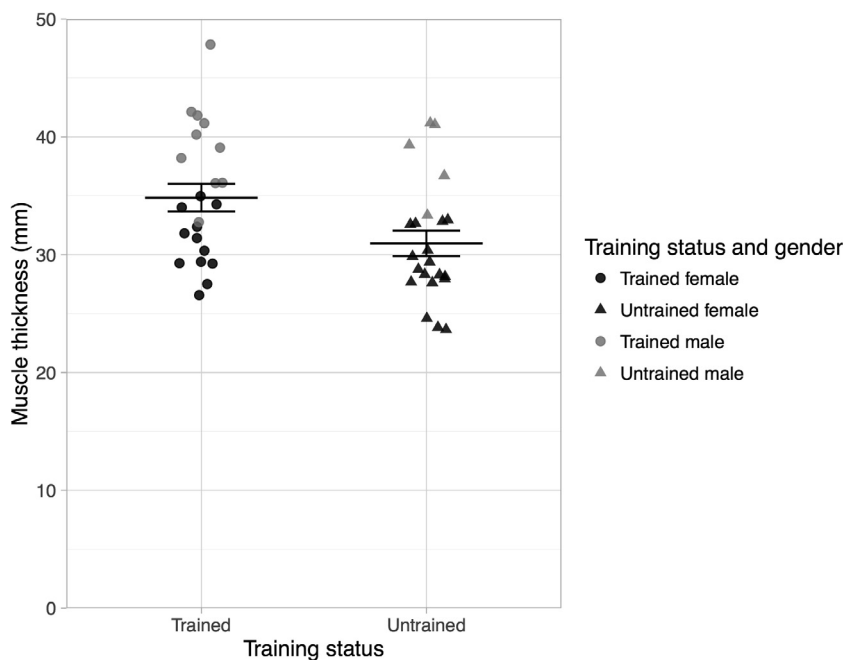


Fig. 1. Greater thickness of the biceps brachii muscle in the trained cohort compared to the untrained cohort. Data presented as mean \pm SEM. $p = 0.019$.

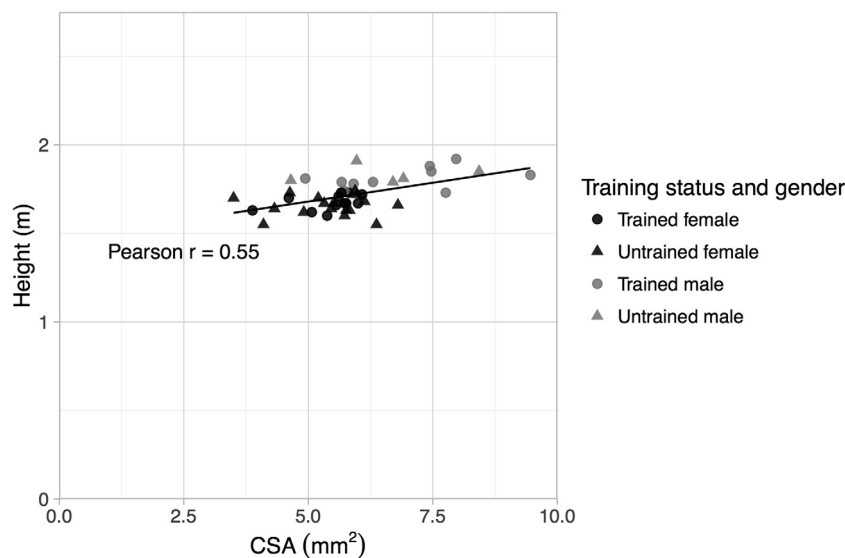
ence in CSA between trained and untrained individuals when men and women were analyzed separately may be due to the fact that the low number of participants restricted this subgroup analysis.

Table 4

Nerve cross sectional area and muscle thickness in men and women.

Nerve (mm ²)	Men (N = 15)			Women (N = 29)			p-value
	N	Mean (SD)	Range	N	Mean (SD)	Range	
Median wrist	14	8.5 (1.7)	5.4–10.8	26	7.8 (1.4)	5.3–9.9	0.18
Median forearm	15	6.8 (1.3)	4.7–9.5	29	5.4 (0.8)	3.5–6.8	<0.001
Musculocutaneous	15	3.4 (1.3)	1.4–6.8	29	3.1 (0.9)	1.6–5.0	0.34
<i>Muscle (mm)</i>							
APB	15	21.0 (2.1)	17.7–25.3	29	17.1 (1.7)	13.2–20.0	<0.001
Biceps	15	39.1 (3.8)	32.8–47.8	29	29.7 (3.0)	23.6–35.0	<0.001
Quadriceps	15	49.9 (9.3)	37.9–66.2	29	41.3 (7.7)	26.4–58.0	0.002
Vastus intermedius		23.4 (6.7)	16.0–36.0		19.4 (5.1)	10.3–29.5	
Rectus femoris		26.5 (4.8)	21.2–39.3		21.9 (3.5)	16.1–29.0	
EDB	15	8.6 (2.1)	4.5–12.9	29	7.8 (1.4)	5.0–11.1	0.13

Nerve cross sectional area values are given in mm². Muscle thickness values are given in mm. Statistical comparison with *t*-test between the men and women. APB, abductor pollicis brevis muscle; EDB, extensor digitorum brevis muscle. Significant *p*-values are marked in bold.

**Fig. 2.** Correlation between cross sectional area (CSA) of the median nerve in the forearm and height in the whole cohort (N = 44).**Table 5**

Correlation analysis and multivariable linear regression between CSA and age, height and weight in whole cohort.

Nerve site	Age		Height		Weight	
	r	p-value	r	p-value	r	p-value
<i>Correlation analysis</i>						
Median wrist	0.15	0.34	0.26	0.10	0.28	0.09
Median forearm	0.005	0.97	0.55	<0.001	0.24	0.12
Musculocutaneous	0.13	0.41	0.26	0.09	0.30	0.16
<i>Multivariable linear regression</i>						
Median wrist	0.020	0.33	3.1	0.38	0.019	0.47
Median forearm	6.6e–05	0.99	8.4	<0.001	–1.7e–02	0.33
Musculocutaneous	0.010	0.44	3.1	0.17	–0.0022	0.90

r = Pearson product-moment correlation coefficient. β = regression coefficient. CSA, cross-sectional area. N = 44. Significant *p*-values are marked in bold.

4.2. Nerve and muscle measurements

In this cohort, we found a significant correlation between the CSA of the median nerve in the forearm and height. No correlation was found with age or weight. Further, no correlation was observed for any of the included variables and CSA of the median nerve at the wrist or the CSA of the musculocutaneous nerve. The literature is somewhat ambiguous regarding the correlation between CSA of nerves and other variables. Correlations exist between median nerve CSA at the wrist and BMI, weight and age

(but not between the CSA and height), as well as between CSA and BMI for several other nerves (Qrimli et al., 2016). Another study instead found that height and weight correlated most strongly with the CSA of the median nerve, although no effect was seen of neither age nor BMI (Zaidman et al., 2009). This is in contrast to another study, which found significant correlations between nerve CSA and age in the median, ulnar, radial, sciatic, peroneal, tibial and sural nerves (Cartwright et al., 2013). In another study by partly the same authors (Cartwright et al., 2008), there was a stronger correlation between nerve CSA and

weight as well as BMI, while the association with age and height was weaker. Contrary to these findings, one study (Kerasnoudis et al., 2013) actually found that the median nerve at the axilla decreased with increasing age, while no correlation was found with age at other sites of the median nerve. Considering the lack of scientific consensus in this area, it remains difficult to draw the correct conclusions. The reason that the CSA of the median nerve in the forearm more often correlates with other variables than the CSA at wrist level could be explained by the latter being a common entrapment site, causing carpal tunnel syndrome and thereby nerve enlargement.

Regarding the musculocutaneous nerve, a previous study (Cartwright et al., 2008) found no correlation between nerve CSA and height, weight, BMI or age, which is in line with our current findings. The mean CSA values of the musculocutaneous obtained in this study are however noticeably smaller compared with two previous studies, where mean values of 6.9 mm² (Cartwright et al., 2008) and 6.8 mm² (Schafhalter-Zoppoth and Gray, 2005) were obtained. The discrepancy may have several causes, including different ultrasound device, site of measurement and high individual variance. The use of a zoom function generally increases the obtained nerve CSA (Jelsing et al., 2015). In this study, we used a read-zoom function for some of the musculocutaneous measurements, which may have affected our values. It has been considered important for each ultrasound laboratory to obtain its own reference values, because of the high discrepancy between different reference values found in the scientific literature (Kerasnoudis et al., 2013).

The finding that women have thinner muscles, as measured with ultrasound, could be expected. The biceps brachii muscle was thicker in trained individuals despite the fact that men and women were analyzed together, which proves that the resistance training indeed has a considerable effect on muscle thickness. This is in line with previous studies stating that upper limb muscles have a greater hypertrophy response compared to lower limb muscles (Wilmore, 1974, Cureton et al., 1988). However, the untrained group consisted of more females, which may be one explanation that we did not see the same relationship for the other examined muscles. The reason why we did not see the same result in muscle thickness when comparing trained and untrained men and women separately is probably due to the number of participants being too low when dividing the cohort into subgroups. The finding that the CMAP amplitude of the EDB muscle correlates with muscle thickness in the whole cohort is in line with a previous study (Seok et al., 2016), and similar correlations has also been found in foot muscles of diabetic patients (Severinsen and Andersen, 2007).

4.3. Drawbacks and conclusion

One drawback of the study was that the untrained group was older than the trained group. This may be important to keep in mind, since several studies have found a correlation between increasing nerve CSA and age. If such a correlation held true, the untrained group would have larger nerve CSA. Since the trained group was younger, an increase in CSA from resistance training would be matched by a larger CSA in the untrained group due to age, potentially resulting in a lack of difference between the two groups. Another drawback is the difference in gender between the two groups, where the untrained group predominantly consisted of women. Further, the lack of correlation between CSA and the previously measured parameters of CMAP amplitude, area or muscle strength in this cohort may be due to the fact that the CSA and the other values were obtained on different occasions, or because the study group was too small. As stated previously, correlations between CMAP amplitude and muscle thickness have

been found. However, CMAP is a measurement of the muscle response to nerve stimuli, not necessarily related to nerve CSA, whereas the CSA is of course affected by a plethora of physiological parameters, and does not necessarily always correlate to nerve function or muscle thickness.

Future prospective cohort studies should include measurement of CSA of peripheral nerves before the onset of, and after a training program, as well as immediately before and after a single training session. This would provide a more controlled environment, ensuring that the amount of training is the same for all participants, while also studying the acute effects of HRST.

In conclusion, this is the first study to examine whether the nerve CSA differs between individuals who perform or do not perform HRST. The main finding was that there was no significant difference between the two groups regarding CSA. Furthermore, this article contributes reference values for the musculocutaneous nerve, on which data are sparse compared to other peripheral nerves. Further research is needed, both to examine the effect of resistance training on peripheral nerves, but also to investigate which physiological parameters truly correlate with nerve CSA.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Conflict of interest statement

None of the authors have potential conflicts of interest to be disclosed.

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References

- Abe, T., DeHoyos, D.V., Pollock, M.L., Garzarella, L., 2000. Time course for strength and muscle thickness changes following upper and lower body resistance training in men and women. *Eur. J. Appl. Physiol.* 81, 174–180.
- Bathala, L., Kumar, P., Kumar, K., Shaik, A., Visser, L.H., 2014. Normal values of median nerve cross-sectional area obtained by ultrasound along its course in the arm with electrophysiological correlations, in 100 Asian subjects. *Muscle Nerve* 49, 284–286.
- Cartwright, M.S., Passmore, L.V., Yoon, J.S., Brown, M.E., Caress, J.B., Walker, F.O., 2008. Cross-sectional area reference values for nerve ultrasonography. *Muscle Nerve* 37, 566–571.
- Cartwright, M.S., Mayans, D.R., Gillson, N.A., Griffin, L.P., Walker, F.O., 2013. Nerve cross-sectional area in extremes of age. *Muscle Nerve* 47, 890–893.
- Cureton, K.J., Collins, M.A., Hill, D.W., McElhannon Jr., F.M., 1988. Muscle hypertrophy in men and women. *Med. Sci. Sports Exerc.* 20, 338–344.
- D'Antona, G., Lanfranconi, F., Pellegrino, M.A., Brocca, L., Adami, R., Rossi, R., et al., 2006. Skeletal muscle hypertrophy and structure and function of skeletal muscle fibres in male body builders. *J. Physiol.* 570, 611–627.
- Edwards, R.H., Young, A., Hosking, G.P., Jones, D.A., 1977. Human skeletal muscle function: description of tests and normal values. *Clin. Sci Mol. Med.* 52 (1977), 283–290.
- Jelsing, E.J., Presley, J.C., Maida, E., Hangiandreou, N.J., Smith, J., 2015. The effect of magnification on sonographically measured nerve cross-sectional area. *Muscle Nerve* 51, 30–34.
- Folland, J.P., Williams, A.G., 2007. The adaptations to strength training: morphological and neurological contributions to increased strength. *Sports Med.* 37, 145–168.
- Hobson-Webb, L.D., Padua, L., 2016. Ultrasound of focal neuropathies. *J. Clin. Neurophysiol.* 33, 94–102.

- Jones, D.A., Rutherford, O.M., 1987. Human muscle strength training: the effects of three different regimens and the nature of the resultant changes. *J. Physiol.* 391, 1–11.
- Kadi, F., Bonnerud, P., Eriksson, A., Thornell, L.E., 2000. The expression of androgen receptors in human neck and limb muscles: effects of training and self-administration of androgenic-anabolic steroids. *Histochem. Cell Biol.* 113, 25–29.
- Kerasnoudis, A., 2016. Ultrasound visualization of nerve remodeling after strenuous exercise. *Muscle Nerve* 53, 320–324.
- Kerasnoudis, A., Pitarokoili, K., Behrendt, V., Gold, R., Yoon, M.S., 2013. Cross sectional area reference values for sonography of peripheral nerves and brachial plexus. *Clin. Neurophysiol.* 124, 1881–1888.
- Molin, C.J., Punga, A.R., 2016. Compound motor action potential: electrophysiological marker for muscle training. *J. Clin. Neurophysiol.* 33, 340–345.
- Moritani, T., deVries, H.A., 1979. Neural factors versus hypertrophy in the time course of muscle strength gain. *Am J Phys Med.* 58, 115–130.
- Qrimli, M., Ebadi, H., Breiner, A., Siddiqui, H., Alabdali, M., Abraham, A., et al., 2016. Reference values for ultrasonography of peripheral nerves. *Muscle Nerve* 53, 538–544.
- R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: <https://www.R-project.org/>.
- Schaffhalter-Zoppoth, I., Gray, A.T., 2005. The musculocutaneous nerve: ultrasound appearance for peripheral nerve block. *Reg. Anesth. Pain Med.* 30, 385–390.
- Seok, J.I., Walker, F.O., Kwak, S.G., 2016. Evaluation of extensor digitorum brevis thickness in healthy subjects: a comparative analysis of nerve conduction studies and ultrasound scans. *Clin. Neurophysiol.* 127, 1664–1668.
- Severinsen, K., Andersen, H., 2007. Evaluation of atrophy of foot muscles in diabetic neuropathy – a comparative study of nerve conduction studies and ultrasonography. *Clin. Neurophysiol.* 118, 2172–2175.
- Seynnes, O.R., de Boer, M., Narici, M.V., 2007. Early skeletal muscle hypertrophy and architectural changes in response to high-intensity resistance training. *J. Appl. Physiol.* 2007 (102), 368–373.
- Suk, J.I., Walker, F.O., Cartwright, M.S., 2013. Ultrasonography of peripheral nerves. *Curr. Neurol. Neurosci. Rep.* 13, 328.
- Welle, S., Totterman, S., Thornton, C., 1996. Effect of age on muscle hypertrophy induced by resistance training. *J. Gerontol. A Biol. Sci. Med. Sci.* 51, M270–M275.
- Wilmore, J.H., 1974. Alterations in strength, body composition and anthropometric measurements consequent to a 10-week weight training program. *Med Sci Sports* 6, 133–138.
- Yue, G., Cole, K.J., 1992. Strength increases from the motor program: comparison of training with maximal voluntary and imagined muscle contractions. *J. Neurophysiology* 67, 1114–1123.
- Zaidman, C.M., Al-Lozi, M., Pestronk, A., 2009. Peripheral nerve size in normals and patients with polyneuropathy: an ultrasound study. *Muscle Nerve* 40, 960–966.
- Zijdewind, I., Toering, S.T., Bessem, B., Van Der Laan, O., Diercks, R.L., 2003. Effects of imagery motor training on torque production of ankle plantar flexor muscles. *Muscle Nerve* 28, 168–173.