



Skeletal Muscle Hypertrophy and Decreased Intramuscular Fat After Unilateral Resistance Training in Spinal Cord Injury: Case Report

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Abstract

Background: Skeletal muscle atrophy is a common adaptation after spinal cord injury (SCI) that results in numerous health-related complications. Neuromuscular electrical stimulation (NMES) has been recognized as an effective tool, which attenuates atrophy and evokes hypertrophy.

Objective: To investigate the effects of NMES resistance training (RT) on individual muscle groups and adipose tissue of the right thigh after stimulation of the knee extensor muscle group in a man with chronic SCI.

Participant: A 22-year-old man with a complete SCI sustained in a motorcycle accident 5 years prior to participation in this study.

Methods: The participant underwent training twice a week for 12 weeks, including unilateral progressive RT of the right knee extensor muscle group using NMES and ankle weights. The stimulation was applied to knee extensors while the participant was sitting in his wheelchair. A series of T1-weighted magnetic resonance images were acquired for the whole right thigh prior to and after training. Skeletal muscle cross-sectional areas were measured of the whole thigh, knee extensors, hip adductors, hamstrings, and sartorius and gracilis muscle groups. Additionally, intramuscular fat and subcutaneous fat of the thigh were measured.

Results: At the end of 12 weeks, the participant was able to lift 17 lbs during full knee extension. Average skeletal muscle cross-sectional areas increased in all of the measured muscle groups (12%–43%). Hypertrophy ranging from 30% to 112% was detected in multiaxial slices after the NMES RT protocol. Intramuscular fat decreased by more than 50% and subcutaneous fat increased by 24%.

Conclusion: Unilateral NMES RT protocol evoked hypertrophy in the knee extensor and adjacent skeletal muscle groups and was associated with a reduction in intramuscular fat in a person with a chronic SCI. Additionally, subcutaneous adipose tissue cross-sectional areas increased in response to RT.

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Key Words: Skeletal muscle atrophy; Neuromuscular electrical stimulation; Resistance training; Exercise; Spinal cord injuries; Tetraplegia; Body composition; Glucose intolerance; Hyperlipidemia; Cardiovascular disease; Osteoporosis; Metabolic syndrome

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INTRODUCTION

Spinal cord injury (SCI), considered one of the most devastating injuries, often has significant health-related consequences (1,2). Following injury, skeletal muscle atrophy is a key adaptation resulting from disuse and immobilization in both complete and incomplete SCI (3,4). A few weeks postinjury, skeletal muscle cross-sectional area (CSA) can be as low as 30% to 50% compared with able-bodied controls (3,4). Moreover, skeletal muscle atrophy has been associated with increasing infiltration of intramuscular fat (IMF) (3,5), a repository of fat that is associated with glucose intoler-

ance and insulin resistance after SCI and in other clinical populations (5). The detrimental effects of atrophy also include altered body composition (6), glucose intolerance and type 2 diabetes mellitus (7), hyperlipidemia (8), cardiovascular disease (9), osteoporosis (10), and increased incidence of metabolic syndrome (11).

Resistance training (RT) has been proposed as an effective type of exercise that induces muscle hypertrophy and promotes the development of metabolically active lean muscle mass that could enhance glucose homeostasis and improve the lipid profile in able-bodied individuals (12). The principle of loading the paralyzed muscles to mimic RT has been previously applied during static actions, cycling, and lifting ankle weights (13–15). Dudley et al showed that loading the paralyzed muscle 48 weeks postinjury could reverse the process of skeletal muscle atrophy (13). Neuromuscular electrical stimulation (NMES) was used to evoke RT of the paralyzed knee extensors for 8 weeks and resulted in regaining 75% of the CSA at 6 weeks postinjury (13). In a brief report, unilateral NMES RT was applied for 12 weeks to the paralyzed knee extensor muscle group and evoked skeletal muscle hypertrophy up to 39% (15). Both reports investigated the extent of hypertrophy in the knee extensor muscle group without considering the adjacent skeletal muscle groups. Moreover, none of these reports investigated the impact of the training on IMF or subcutaneous adipose tissue.

A NMES RT protocol that could evoke hypertrophy of the exercised and the adjacent skeletal muscle groups would be more attractive and may suggest a possible influence on overall body composition and metabolic profile after SCI. Hypertrophy of the adjacent skeletal muscle groups could be stimulated through the actions of circulating growth factors (16–18). Therefore, the purpose of the current case study was to investigate the impact of 12 weeks of a unilateral NMES RT protocol on individual skeletal muscle groups, IMF, and subcutaneous adipose tissue of the right thigh. Additionally, the CSAs of individual muscle groups and fat were measured across multi-axial slices of magnetic resonance imaging (MRI). One of the hypotheses is that individual skeletal muscle groups, antagonists and synergists of the knee extensors, will demonstrate hypertrophy. Additionally, it was postulated that training would result in reduction of IMF in chronic complete SCI.

CASE REPORT

A 22-year-old man had suffered a complete SCI (C5–C6, ASIA A) secondary to a motorcycle crash 5 years prior to this study. He had been using his power wheelchair for mobility and had limited right-side hand function that was nevertheless sufficient to drive his wheelchair using a standard joystick. Additionally, he had an indwelling catheter and used digital stimulation for bowel movement. The participant (weight: 60 kg, height: 193 cm; body mass index: 17 kg/m^2) had no previous history of

orthopedic, cardiovascular, or metabolic conditions. The participant enrolled in the study after signing a consent form that was approved by the Institutional Review Board of Indiana University.

Training was performed at Indiana University in the Clinical Research Laboratory located at the Department of Physical Therapy. The training protocol was twice a week for 12 weeks using surface NMES and ankle weights. The weights were progressively increased by 2 lbs on a weekly basis after 40 repetitions of full knee extension were achieved in a session. Failure to attain full knee extension of 4 sets \times 10 repetitions resulted in maintaining the same load until the desired repetitions were achieved. Training sets were separated by 2-minute rest intervals to minimize muscle fatigue. For the first 2 weeks, no ankle weights were used to ensure achievement of full knee extension against gravity and to protect against skeletal muscle damage. The training involved concentric/eccentric paradigms of the knee extensor muscle group. When the current increased, knee extensors contracted and dynamically moved the leg and the weights against gravity. After full extension was maintained for 3 seconds, the current was slowly decreased and the leg was returned to the starting position.

A Theratouch NMES unit (Richmar, Inola, OK) was used in the training along with conductive adhesive gel electrodes, which were replaced with new pairs every 3 weeks. NMES was applied via large (8- \times 10-cm) electrodes. The edge of one electrode was placed on the skin 2 to 3 cm above the superior aspect of the patella over the vastus medialis muscle, and the other was placed lateral to and 30 cm above the patella over the vastus lateralis muscle. Parameters were set at 30 Hz and 450- μ s pulse duration and a contraction/relaxation time of 5 s on/5 s off (13,15). With the participant in a sitting position in his power wheelchair, the current amplitude was progressively increased until full knee extension was attained, and the position was maintained for 3 seconds.

Whole thigh, knee extensor, hamstrings, hip adductors, sartorius, and gracilis skeletal muscle CSAs were measured before and after training (1 week after the last training session) using MRI (3–5). Images of the right thigh were collected with a 1.5-T magnet (repetition time 550 ms, echo time 14 ms, field of view [FOV] 20 cm, matrix size 256 \times 256). Transaxial images, 10 mm thick and 5 mm apart, were obtained from the hip joint to the knee joint using the whole body coil. The location of the scan was specifically identified by placing a mark 6 inches proximal to the patella and matched for the follow-up scan after 3 months to ensure similar position in the magnet. Images were downloaded and analyzed using the computer program Win Vessels (Ronald Meyer, Michigan State University), as has been previously described (3,5).

Briefly, the outer perimeter of the thigh muscle groups was traced, and then pixel signal intensity within

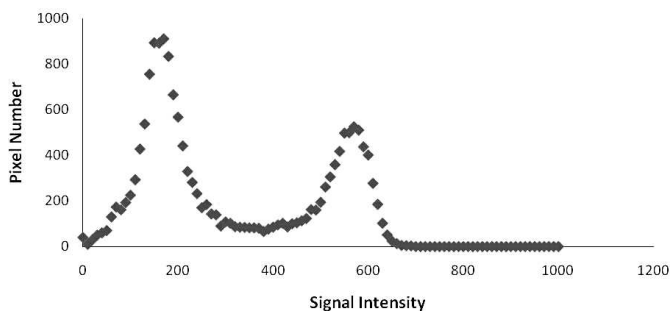


Figure 1. A bimodal histogram of a region of interest around the whole thigh. Skeletal muscle peak is on the left and fat peak is on the right. A midpoint between the 2 peaks indicates the cutoff point between muscle pixels and fat pixels.

this region was automatically determined (3,5). Next, a bimodal histogram of 2 peaks was plotted. The first peak represents the muscle peak and the second represents the fat peak (Figure 1). A midpoint between the 2 peaks separates muscle pixels from fat pixels. The CSAs were calculated using the following equations: Muscle CSA (cm^2) = total number of pixels of muscle \times (FOV/matrix size) 2 ; IMF CSA (cm^2) = total number of pixels of IMF \times (FOV/matrix size) 2 . Subcutaneous fat CSA was considered as the area between the muscle border and the outer perimeter of the thigh.

RESULTS

At the end of the 12 weeks of training, body weight was measured using a hospital bed scale and showed an increase from 60 to 61.3 kg. The participant was able to lift 17 lb (7.7 kg) with full knee extension for 4 sets \times 10 reps. The average CSAs of the individual skeletal muscle groups are presented in Table 1. Skeletal muscle hypertrophy was detected across multiaxial slices in both knee extensor and adjacent muscle groups (antagonist and synergists) (Figures 2 and 3), with the range of hypertrophy differing among the measured groups (Table 1).

After 12 weeks of training, IMF dropped from $8.3 \pm 5.5 \text{ cm}^2$ to $3.8 \pm 2.0 \text{ cm}^2$ (53%). Relative IMF (IMF CSA/skeletal muscle CSA \times 100) decreased from $6.1\% \pm 5.5\%$ to $3.9\% \pm 2\%$. Surprisingly, thigh subcutaneous fat

increased from $49.18 \pm 18 \text{ cm}^2$ to $61 \pm 23 \text{ cm}^2$ (Figure 4). The ratio of subcutaneous fat CSA to whole thigh skeletal muscle decreased, from 0.85 ± 0.2 to 0.81 ± 0.2 ; this suggests that skeletal muscle CSA increased at a greater rate when compared to subcutaneous fat after training.

DISCUSSION

This case study documented several novel findings in response to a 3-month NMES RT protocol for a person with a chronic SCI: (a) Skeletal muscle hypertrophy was reported not only in the activated muscles but also in adjacent muscle groups (hip adductors, hamstrings, sartorius, and gracilis) following loading of the knee extensors; (b) skeletal muscle hypertrophy was evident across multiaxial slices that extend proximally from the hip joint to the knee joint distally; (c) training was accompanied by a reduction in IMF accumulation, a repository of fat that has been shown to interfere with glucose metabolism and cause insulin resistance; and (d) increases were observed in subcutaneous adipose tissue across multiaxial slices.

The increase in muscle CSA of the knee extensors is similar to that seen in a previous report that used a comparable NMES protocol (15). In the current study, short, intermittent, high-force loading evoked myofiber hypertrophy in the knee extensor as well as the adjacent muscle groups. Previous reports have shown that insulin-like growth factor-binding proteins have increased after an RT protocol that employed 2 bouts of NMES in individuals with chronic SCI and able-bodied controls (16). It is possible that insulinlike growth factor 1-activated signaling pathways or mechanical stretch applied to the antagonist muscles may be responsible for evoking hypertrophy (17,18). It is also documented that approximately 50% of knee extensors can be activated in healthy volunteers, even after maximizing NMES parameters (19); however, in SCI, activation can exceed 80% because the muscle CSA is smaller compared with able-bodied controls (20). Therefore, it is possible that larger electrodes may have resulted in the activation of adjacent muscle groups during the training program, whether intentional or not, and caused hypertrophy.

Table 1. Mean Values \pm SDs of Skeletal Muscle CSAs Pretraining and Posttraining Across Multiaxial Slices from Iliac Crest to the Knee Joint

Skeletal Muscle	Pretraining CSA (cm^2)	Posttraining CSA (cm^2)	% Change ^a	Min % Change	Max % Change
Whole thigh	55.7 ± 10	72.4 ± 11	30%	14%	39.5%
Knee extensor	26.5 ± 3	38 ± 5	43%	18%	54%
Hamstrings	12 ± 3.5	13.6 ± 5	12%	1.5%	30%
Adductors	13 ± 7	17 ± 8	40%	8%	94%
Sartorius	1.8 ± 0.12	2.5 ± 0.4	38%	9.6%	50%
Gracilis	2.2 ± 0.9	2.6 ± 0.8	20.5%	0.4%	112%

^a % Change = $([\text{posttraining CSA} - \text{pretraining CSA}]/\text{pretraining CSA}) \times 100$.

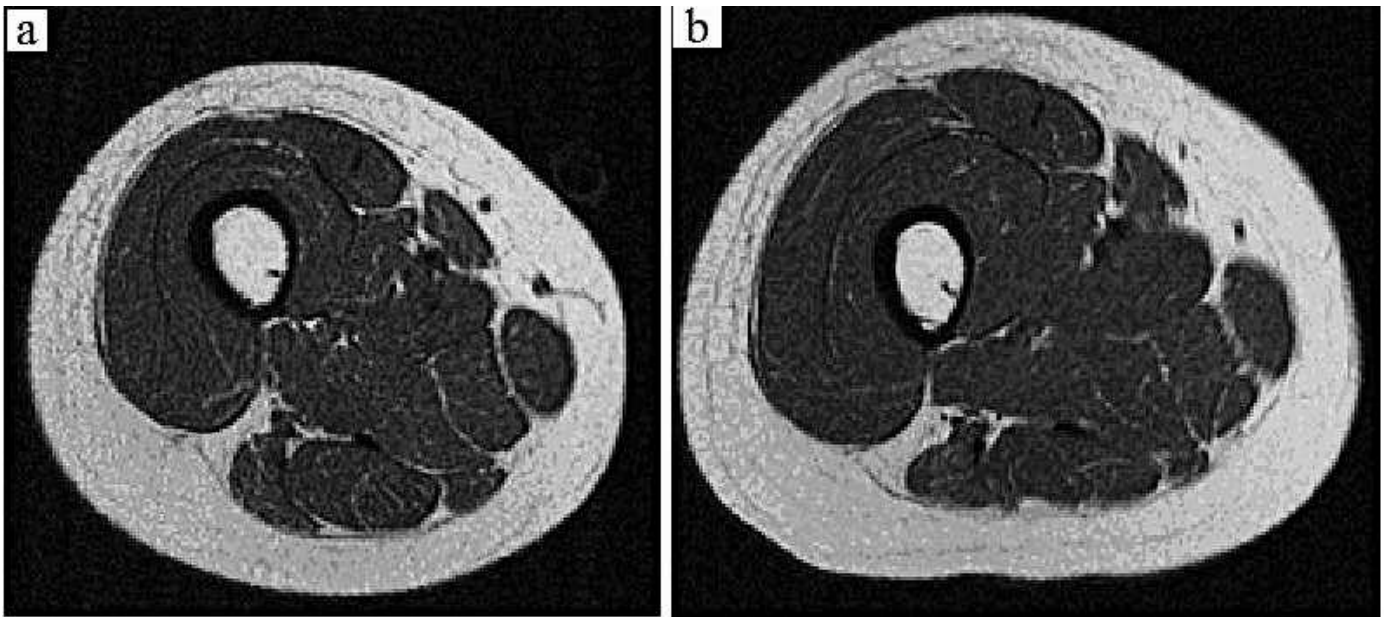


Figure 2. A representative T1-weighted MRI of the midthigh (a) pretraining and (b) posttraining in an individual with complete SCI. Bony and soft tissue landmarks were used to match pretraining and posttraining images to ensure the exact anatomical location.

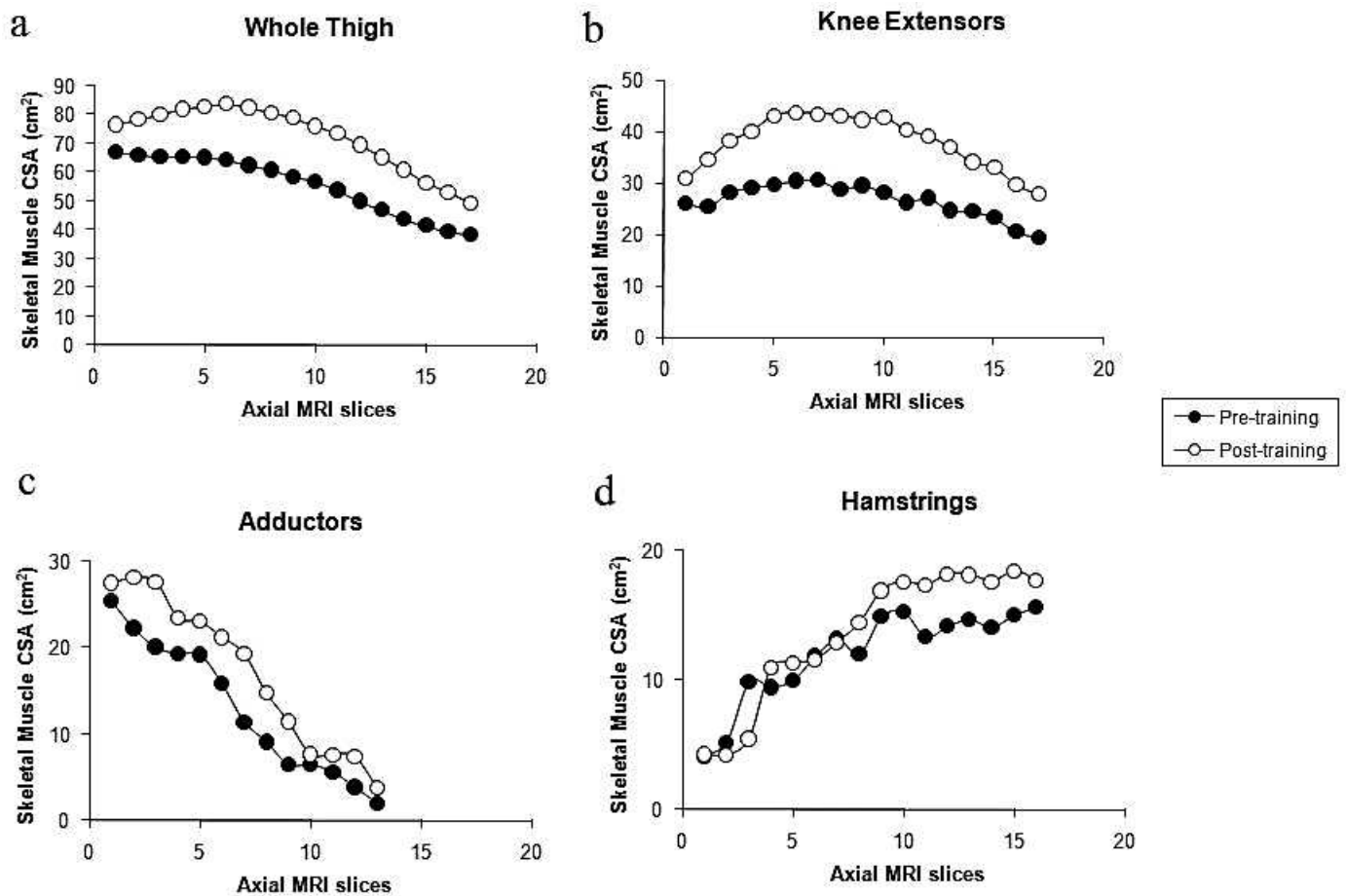


Figure 3. CSAs across multiaxial slices from the hip (slice #1) to the knee joints (13–17) of (a) whole thigh, (b) knee extensors, (c) adductors, and (d) hamstring muscles pretraining and posttraining.

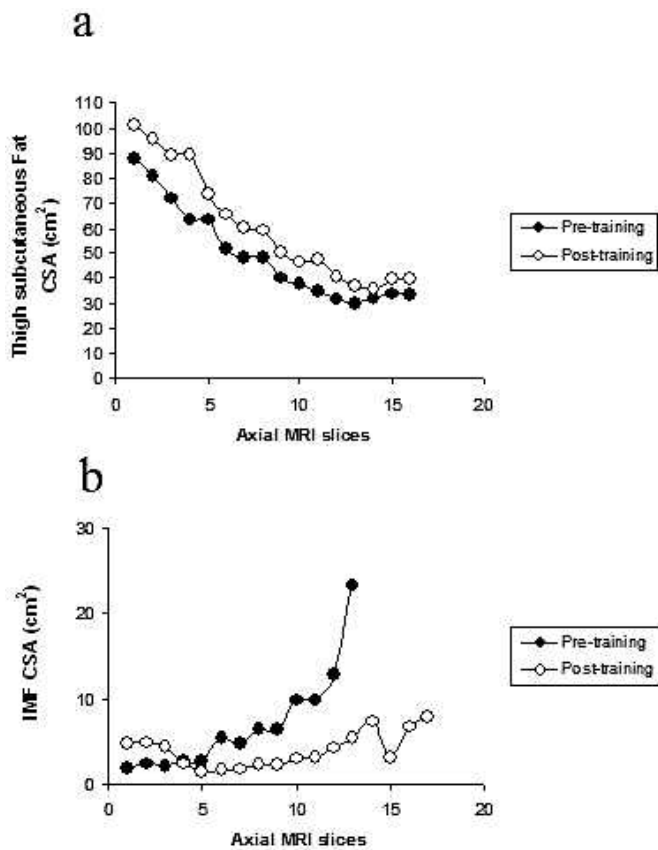


Figure 4. CSAs across multi-axial slices from the hip (slice #1) to the knee joints (15–17) of (a) thigh subcutaneous fat and (b) IMF pretraining and posttraining.

It is clear that effectively loading the paralyzed skeletal muscle could result in reduction of IMF. The findings may also suggest improvement in the metabolic profile after SCI. The assumption was based on previous work that showed a strong relationship between IMF and glucose intolerance in individuals with complete SCI (5). Additionally, improvement in glucose homeostasis was observed after training knee extensor muscle groups using a similar protocol (15). Compared to the established knowledge of RT on subcutaneous adipose tissue (12), the result of the current case study is perplexing and novel; subcutaneous fat, a major storage repository of the circulating fatty acids, increased by 24%. Increased circulating fatty acids have been shown to be responsible for insulin resistance in obese and nonobese individuals (21). Therefore, reducing fatty acids by storage in subcutaneous fat may be considered a benefit to RT. A recent finding showed that persons with type 2 diabetes mellitus have more IMF and less subcutaneous adipose tissue compared to healthy controls; this profile exacerbates insulin resistance (22). Altering this profile by reducing IMF and increasing subcutaneous adipose tissue could potentially improve insulin sensitivity. Moreover, the results suggest that subcutaneous adipose tissue

atrophy could result in an altered metabolic profile in people with SCI.

CONCLUSION

A NMES RT protocol resulted in substantial skeletal muscle hypertrophy in a person with a chronic SCI. The training paradigm was successful in reducing IMF and increasing subcutaneous adipose tissue, a phenotype that has been suggested to benefit the metabolic profile in healthy controls. The reduction in IMF is considered a unique finding that could provide impetus for future trials to determine its impact on the metabolic profile after SCI. The findings may also suggest that appropriate loading of paralyzed skeletal muscles can serve as a stimulus to evoke gross hypertrophy, which can impact whole body composition. Further studies are warranted to investigate the impact of RT on body composition and metabolic profile after SCI.

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