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Effects of neuromuscular electrical stimulation in people with spinal cord injury

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Abstract

Introduction: Muscle force production is usually impaired in people with spinal cord injury (SCI). The use of high-intensity neuromuscular electrical stimulation (NMES) strength training can help promote metabolically active lean muscle mass and thus, increase muscle mass and improve physical health and quality of life (QoL). Nonetheless, NMES is usually used at low-stimulation intensities and there is limited evidence on the effects of high-intensity NMES strength training into improving muscle force and mass, symptoms of spasticity or physical health and quality of life (QoL) in people with SCI.

Methods: Five individuals with chronic SCI completed five 10-repetition sets of high-intensity knee extension NMES strength training sessions for 12 weeks in both quadriceps muscles. Quadriceps femoris (QF) knee extensor torque was measured on a dynamometer and cross-sectional area (CSA_{QF}) was measured with extended-field-of-view ultrasonography. Venous blood samples were collected for blood lipid profiling and c-reactive protein (CRP) analyses. The Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET) was used to assess symptoms of spasticity and the quality of life index (QLI) SCI version III was used for QoL measures.

Results: QF tetanic knee extensor torque increased on average by 35% (2 - 92%) and CSA_{QF} increased by 47% (14 - 145%). A significant increase in the HDL/LDL cholesterol ratio ($p < 0.001$), a mean significant improvement of 4.8% ± 2.3% (absolute value = 0.26) in SCI-SET score was observed, whilst QoL showed a near-significant improvement in the health & functioning domain (15.0 ± 4.2; 17.3 ± 5.1; $p = 0.07$).

Keywords: physical health; quadriceps femoris; muscle mass; muscle force; quality of life; spasticity.

Conclusions: High-intensity NMES-strength training in people with SCI may improve muscle strength, mass, physical health and QoL. However, replication of these results is necessary before clinical implementation.

Introduction

Spinal cord injury (SCI) is a devastating lesion that leads to a marked reduction in muscle force production and commonly evokes symptoms of spasticity, which can profoundly impair physical health and quality of life (QoL) (1, 2). Muscle force production capacity is clearly influenced by skeletal muscle mass (3), which is reduced up to 50% when compared to able-bodied controls (4) and plays a crucial role in reducing the risk of premature all-cause mortality (5). Thus, people with SCI are at a higher risk of developing cardiovascular diseases and dyslipidemia (6) and are thus faced with decreased life expectancy (7, 8).

Muscle strength training stimulates gains in muscle mass and strength, reduces systemic inflammation and enhances longevity and QoL (9-11). More specifically, high-intensity strength training, which refers to the imposition of sufficient loading to evoke near-maximal motor unit activation (12), can impose a strong mechanical stimulus that enhances the hypertrophic response and generates optimum muscle strength gains (13) leading to physical health benefits (14). However, such training may not be feasible in patients with neuromuscular injury or disease, such as those with SCI, who may not be able to sufficiently activate the muscles to generate the necessary forces during training. In these individuals, neuromuscular electrical stimulation (NMES) methods have been used, commonly in the form of functional electrical stimulation (FES), to overcome muscle weakness and improve muscle strength and mass with the consequent benefits in physical health (15-17). Nonetheless, the intensity of muscle contraction is low during FES and optimum hypertrophy and other outcomes are not obtained. Whilst the use of NMES as a strength training modality has previously been shown to stimulate muscle hypertrophy (16, 18-20), the use of NMES as a high-intensity strength training mode has not been extensively investigated and, due to the

limited evidence supporting its use for increasing muscle strength (21, 22) is not commonly used in clinical practice. Importantly, some essential outcomes, such as muscle force and physical health improvements, muscle and bone plasticity (23, 24) effects on intramuscular fat (4, 25) and symptoms of spasticity and QoL, have not been extensively explored in people with SCI undertaking NMES strength training interventions (21, 26) and specifically in response to high-intensity muscle strength training. Furthermore, there is a lack of evidence relating to the use of isometric (27), near-maximal (high-intensity) short duration (2-s) muscle contractions and a wide-pulse width (1000 μs) in people with SCI. Thus, a larger body of work is required to more clearly define the adaptations to NMES-high intensity strength training to allow for clearer cost-benefit decisions by clinicians.

Therefore, the purpose of the present study was to investigate the effects of high-intensity strength training performed under isometric conditions using low-to-moderate-frequency (30 Hz) NMES (i.e. standard clinical conditions) on muscle force and mass, physical health, symptoms of spasticity and QoL in people with SCI. The hypothesis was that 12-weeks of high-intensity strength training performed under isometric conditions using low-to-moderate-frequency (30 Hz) NMES will improve muscle force and mass, physical health, symptoms of spasticity and QoL in people with SCI.

Methods

Subjects

Five subjects (4 males, 1 female; see Table 1 for subject's characteristics: subject's levels of injury, completeness of lesion, time since injury, AIS scale score, medication type and, wheelchair user or community walker and use of functional electrical stimulation (FES) routinely) completed a 12-week intervention. Prior to the study, the subjects were given

113 detailed information about the procedures and risks of participation and then read and signed
114 a written informed consent document. The subjects completed the Physical Activity
115 Readiness Questionnaire (PAR-Q), provided a medical certificate to ensure safe exercise
116 participation, and refrained from vigorous exercise (48 h), alcohol (24 h) and stimulant
117 consumption (e.g. caffeine, energy drinks, 6 h) prior to testing. Subjects were asked to
118 replicate the same physical activities for each session. This study was approved by the Edith
119 Cowan University Ethics Committee (project number: 11623).

120 **Procedures**

121 The study duration was 14 weeks and assessments were performed identically on
122 three different occasions at the same time of the day and under the same experimental
123 conditions. In the first two weeks of the study the subjects completed a control phase where
124 they did not perform any experimental training but continued their regular physical activities.
125 This followed a familiarisation session performed the week before the first training session.
126 Training was performed twice a week (with at least one rest day in between) for 12 weeks.
127 All assessments were completed at -1 week ("Control period"), 0 week (0-wk) and 12 weeks
128 (12-wk), except for resting blood samples which were taken at 0-wk and 12-wk only. Post-
129 training assessments were taken 4-6 days after the last training session to allow for recovery
130 of acute, residual effects of intense exercise. The procedures used in this study were similar
131 from the methodology used in a previous study in healthy individuals (28) and adapted for
132 people with SCI.

Outcome measures

Knee-extension torque measurements (NMES protocol)

Subjects were seated with hip and knee joint angles of 85^{o} and 90^{o}, respectively (0 ^{o}=full extension), with the thigh and trunk secured to a standard dynamometer chair (Biodex System 3 Pro, Ronkonkoma, NY) and the knee joint aligned with the centre of rotation of the dynamometer. If any voluntary contractions were visualized and a torque recorded, then a standardised warm-up protocol was performed. However, if no voluntary contraction was observable then the subjects were instructed to attempt three maximal voluntary isometric contractions (MVICs) with no additional warm-up efforts. This method was used because all subjects were instructed to consciously think about performing an MVIC in the knee extensors for 3 seconds and relax to be consistent among the whole cohort of participants.

Subsequently, two electrical square-wave stimuli (two 1000-μs square-wave pulses with 5-ms interpulse interval) were delivered to the subjects' right and left legs by a high-voltage constant-current electrical stimulator (400 V, DS7A, Digitimer Ltd., Welwyn Garden City, UK) every 20 s, increasing in current from 30 to 99 mA in 10-mA increments until a plateau in the peak twitch (doublet) torque was observed. This was defined as the maximal peak twitch torque ($\tau_{tw,p}$) and was used as the "target torque" during the subsequent training session. A second, submaximal twitch torque ($\tau_{tw,sub}$) recording was obtained at a current intensity of 40 mA. Subsequently, a maximum of three NMES trains were provided at different stimulation (current) intensities until reaching the closest value to the target torque**.** The NMES protocol consisted of repeated 30-Hz trains of 58 symmetric biphasic pulses (0.033-s inter-pulse interval; 1000 μs) and the inter-train interval was 2 s (i.e. 2-s on and 2-s off).

156 **Muscle cross-sectional area (CSA)**

157 Quadriceps femoris (QF) CSA was measured using B-mode axial-plane
158 ultrasonography (Aloka SSD-α10, software 6.1.09, Aloka Co., Ltd., Tokyo, Japan). Subjects
159 rested supine for 15 min before testing to minimise fluid shifts before images were captured
160 with a 10 MHz linear-array probe (60-mm width) using the extended field-of-view technique
161 (EFOV; (29)). A line from the central point of the patella to the medial aspect of the anterior
162 superior iliac spine (ASIS) was marked to obtain the images (29). One line perpendicular to
163 this was marked at 50% of the distance from the greater trochanter to the lateral epicondyle
164 (29). Two continuous single view scans were then obtained by moving the probe transversely
165 across the thigh on the marked line. Minimal pressure was applied with the probe to avoid
166 compression of the muscle. CSA_{QF} was measured using ImageJ digitising software (1.46r,
167 Wayne Rasband, National Institutes of Health, USA) for the whole quadriceps femoris (QF)
168 with the mean of the two images taken as CSA_{QF}.

169 **Blood biomarkers for blood lipid profile and CRP concentration**

170 Resting venous blood samples were collected from a superficial vein on the
171 antecubital aspect of the arm. A needle and vacutainer setup were used with the subject
172 seated following a 12 h overnight fast, blood samples were collected at the same time of day
173 on each testing occasion. Whole blood samples were collected in 5-ml serum separator (SST)
174 vacutainers. The SST sample was centrifuged for 15 min at 5,000 rpm, with 500 µL aliquoted
175 and stored at -80^{o}C before being sent to a local pathology laboratory for blood lipid profiling
176 and c-reactive protein (CRP) analysis.

Spasticity and quality of life (QoL) measures

The Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET) (30) was used to obtain subjective and objective measures of symptoms of spasticity and how these interfere with specific areas of life. The quality of life index (QLI) SCI version III (31) was used to obtain measures of both satisfaction and importance regarding various aspects of life.

Muscle strength training intervention: electrical stimulation and training progression (NMES training-intervention)

NMES was delivered by a high-voltage constant-current electrical stimulator (400 V, DS7A, Digitimer Ltd., Welwyn Garden City, UK) under the same conditions as the assessment (refer to "Knee extension torque measurements" section) through four self-adhesive stimulation electrodes (Axelgaard, PALS, USA) placed over the rectus femoris (RF), vastus lateralis (VL), and vastus medialis (VM). Two 5×10 cm electrodes were placed over RF and one 5×5 electrode was placed on each of the VM and VL approximately at their motor points using a split end cable (outlet cable which delivered current through 2 electrodes emanating from each positive and negative terminal on the stimulator), to increase the surface area of stimulation. The electrodes were placed to elicit the greatest twitch response with a low stimulation intensity. Long quadriceps muscle length was chosen to elicit greater hypertrophy (27).

Each session commenced with a "warm-up" period consisting of paired electrical square-wave stimuli (two 1000 μs square-wave pulses, 5–ms interpulse interval) followed by a maximum of three tetanic trains ($\tau_{t,40mA}$) delivered to each leg separately every 20 s while the stimulation current was increased from 30 mA in 10-mA increments until a plateau in the maximum peak twitch torque was observed or the maximal current intensity was 99 mA. This

200 plateau was defined as the maximal peak twitch torque ($\tau_{tw,p}$) and was used as the target
201 torque during the training session. Subsequently, a tetanic train of NMES at 40 mA ($\tau_{t,40mA}$)
202 was delivered followed by a maximum of three trains of NMES performed at different
203 stimulation current intensities until reaching the closest value to the target torque. These
204 assessments were repeated at the beginning of every NMES training session to assess the
205 level of the current needed to evoke a near-maximal muscle contraction.

206 After the warm-up period the NMES session commenced with electrically-evoked
207 muscle contractions being elicited at the target torque for 5 sets of 10 repetitions on each leg,
208 with a 1-min rest between sets (duty cycle 2s on-2 s off). To determine the actual training
209 intensity either one of two methods was used. The first method was by evoking the maximal
210 peak twitch torque ($\tau_{tw,p}$) and setting the current so the tetanic torque was equal to $\tau_{tw,p}$.
211 However, if $\tau_{tw,p}$ showed a decrease compared to previous sessions, a second method was
212 used whereby the starting current was set to be equal to the highest current used in the
213 previous training session. Within each session, the current was increased by 2 mA per each
214 set of 10 repetitions to maintain a high torque production as fatigue developed; thus, if the
215 second method was chosen, the current selected for set 1 was the same as that used in the
216 final set of the previous session. Using this method, the torque produced in set 1 of training
217 was always higher than that performed in any set of the previous session, so the evoked
218 torque increased incrementally.

219 The training volume progression was based on the total torque-time integral (TTI)
220 over the 24 sessions. Maximum levels of torque evoked in the first contractions during the
221 first week of training (i.e. between 0 and 1 wk) and in the last five contractions during the last
222 week of training (between 11 and 12 wk) were calculated for analysis of training progression
223 and to measure the levels of work capacity over the weeks of training.

All training sessions were conducted by the same trained researcher, who was a senior Physiotherapist and were additional to any other rehabilitation exercise. The subjects were asked to keep their physical training routine consistent for the duration of the experiment. All subjects were asked to consciously attempt to contract their QF muscles while the NMES protocol was being delivered, due to evidence showing that consciously thinking about moving a part of the body activates a part of the cerebral cortex and may allow for a better sensory integration of the information (32).

Statistical analysis

Wilcoxon non-parametric tests were used to separately examine changes in control and experimental periods (-1 and 0: control period and between 0 and 12-weeks: intervention) in peak twitch torque ($\tau_{tw,p}$), evoked tetanic torque ($\tau_{t,40mA}$), cross-sectional area (CSA_{QF}), body composition, biochemical measures for lipid profile and CRP, symptoms of spasticity and QoL outcomes. Reliability of the outcome measures between the control period (-1-wk) and 0-wk was assessed using the intra-class correlation coefficient (ICC). Values are reported as mean ± SD and statistical significance was set at an alpha level of 0.05; however, due to the moderate sample size used and issues surrounding the use of stringent cut-off limits, results associated with p values <0.1 are also highlighted as near-significant.

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Results

Muscle strength: peak twitch torque ($\tau_{tw,p}$) and evoked tetanic torque ($\tau_{t,40mA}$)

Although mean maximal peak knee extensor twitch torque ($\tau_{tw,p}$; sum of right and left quadriceps; QF) did not change significantly (p=0.08) between 0-wk (50.4±14.3 Nm) and 12-wk (44.8±11.7), QF evoked tetanic torque ($\tau_{t,40mA}$) showed a significant increase of 31.8±24.8% between 0 and 12-wk (from 0-wk: 44.2 ± 15.0 Nm to 12-wk: 56.7±17.4 Nm; p=0.04, Z score=-2.0) (see Figure 1). The intra-class correlation (ICC) coefficient for $\tau_{tw,p}$ for the right leg was 0.96 and for left leg 0.87 when assessed between -1 and 0-wk. The level of torque developed during 'fatigue' at the end of the training period was statistically greater (35.2±27.9 Nm) than the non-fatigued torque developed in week 1 (29.1±20.2 Nm). Mean TTI at session 24 was statistically greater than week 1 (percentage difference: 126±131%; p=0.03).

Muscle cross-sectional area (CSA_{QF})

Mean quadriceps femoris CSA (CSA_{QF}, sum of right and left legs) increased by 45±25% (p=0.04, Z score=-2.0) from 0-wk (80.0±33.8 cm^2) to 12-wk (113.1±42.8 cm^2) (see Figure 2A). Between-subject differences were qualitatively observed, where the greatest response (increase in CSA_{QF} of 145%, right leg), was observed in subject E who had not been exposed to electrical stimulation training previously, whereas the least response (increase of 15%, right leg) was observed in subject C with an incomplete lesion (T_{12}, AIS D) who was a community walker (walked with one crutch). The intra-class correlation (ICC) coefficients for $\tau_{tw,p}$ for both right and left leg separately were 0.99 between -1-wk and 0-wk. An example

of the cross-sectional area (CSA_{QF}) of the (left) quadriceps measured in subject A at 0-wk and 12-wk using extended-field-of-view ultrasonography can be found on Figure 2B.

Blood biomarkers for blood lipid profile and CRP

A near-significant decrease in low density lipoprotein concentration (p=0.06; Z score=-1.8) and a significant increase in the cholesterol HDL/LDL ratio (p=0.04; Z score=-2.0) were observed, whilst a near-significant decrease in cholesterol/HDL ratio (p=0.08; Z score=-1.7) was detected. Plasma c-reactive protein (CRP) concentration did not change significantly (p=0.50; Z score=-0.6) however two subjects with CRP concentrations higher than the recommended levels showed clear reductions after the 12-wk of training (subject A: 73% decrease; subject E: 95% decrease). Mean changes in blood biomarkers are shown in Table 2 (blood biomarkers at 0-wk and 12-wk and percent change within group).

Spasticity symptoms and quality of life (QoL)

Symptoms of spasticity measured using the spasticity evaluation tool (SCI-SET 7-day recall: positive vs negative effects of spasticity; -3-+3) were significantly reduced by 5%±2% (0-wk: -0.7±0.4; 12-wk: -0.4±0.3; p=0.04; Z score=-2.0, see Figure 3: seven-day recall score at -1, 0 and 12 weeks).

The Quality of life index (QLI) for SCI version III total score (QLI) and subscales domains did not change significantly from 0-wk to 12-wk. However, there was a near-significant change towards an improvement in the health & functioning domain (0-wk: 15.0±4.2; 12-wk: 17.3±5.1; p=0.08, Z score=-1.7). The intra-class correlation coefficients were 0.94 for QLI, 0.97 for HF, 0.85 for SOC, 0.87 for FAM and 0.97 for PSP when measured from -1-wk and 0-wk. Subject C and D showed a change in QLI greater (20% and

16%, respectively) than the mean percentage difference from -1 and 0-wk (12%) and thus showed notable responses.

Discussion

The main results of this study are that high-intensity NMES strength training induced substantial increases in evoked tetanic knee extensor torque (i.e. muscle strength) and quadriceps cross-sectional area (i.e. muscle size). These changes were observed even in subjects who also used other forms of electrical stimulation-based training (e.g. FES) regularly. It was of specific interest that the mean evoked torque increased from 0-wk to 12-wk. This result was also evidenced by the evoked torque measured in the last contractions in the final week, which were either equal to or higher in all subjects than the first contractions in the first week. These results in evoked torque revealed a notable increase in muscle work capacity in paralysed muscles after the high-intensity NMES strength training intervention. Another interesting observation was that tetanic muscle force (QF tetanic torque ($\tau_{t,40mA}$)) increased significantly whilst mean maximal peak twitch torque ($\tau_{tw,p}$) did not change significantly. One possibility is that $\tau_{tw,p}$ can be affected by factors such as series elastic component stiffness or changes in the relationship between Ca^{2+} release and force production in paralysed muscle, and thus may not be a reliable longitudinal measure of muscle force (33) particularly in clinical populations. Nonetheless, the substantial (mean=32%) increases in tetanic torque revealed a clear improvement in muscle force generating capacity after the training.

A large (mean=45%) increase in CSA_{QF} was observed, which is clinically important since the muscle atrophy that is typically associated with chronic SCI has detrimental effect on metabolic, cardiovascular and functional systems (6) which meaningfully impact life

309 expectancy (6, 34). Previous researchers have reported less increase (20%) after an 8-week
310 intervention (19) and others reported similar large increases in CSA after NMES training
311 (35%-45%) after 12 to 24 weeks of training, albeit using different pulse widths (250/600 μs)
312 at similar frequencies (30-35 Hz) (16, 18, 20, 35). Thus, our training stimulated the same
313 increase in CSA (45%) in 12 weeks as others have obtained after a similar period using
314 currents up to 200 mA (18), although the maximum current intensity in our study being 99
315 mA. This improvement in CSA_{QF} with lower current intensities may speculatively be
316 attributed to three important differences in the present study: (a) the use of isometric rather
317 than concentric contractions that were performed at a long muscle length (27), (b) the use of
318 near-maximal muscle contractions that could be performed with less fatigue due to the short
319 duration (2-s) contractions when compared to other studies (e.g. 5-s contractions), and (c) the
320 use of wide-pulse width NMES (1000 μs) instead of narrow pulses widths. The use of
321 isometric contractions may have generated higher muscle forces at a given activation level
322 and therefore a greater mechanical load would have stimulated muscle hypertrophy (36).
323 Two-second contractions were chosen as optimal after pilot testing results, and thus used in
324 the present study to allow for higher stimulation intensities to be used without the
325 development of rapid muscle fatigue. Thus, this type of contraction at a long muscle length
326 may speculatively be a main factor driving the positive outcomes; however, this hypothesis
327 needs to be more explicitly examined in future studies by comparing adaptations to training
328 using different exercise protocols. Finally, the use of wider pulse widths could have
329 generated muscle contractions through central mechanisms (i.e. using Ia afferents) and, thus
330 may have generated higher forces or delayed muscle fatigue (37, 38). However, further
331 testing of the specific effects of each training variable is needed to provide valuable and
332 informative information for future clinical implementation.

Changes in blood-based biomarkers of physical health were observed, including a significant decrease in LDL and an increase in HDL/LDL ratio. These improvements in physical health outcomes are thought to be associated with an increased life expectancy in people with SCI (6). Similar findings of improvement in the lipid profile were previously reported (11, 35), however, in contrast with the findings of Gorgey, changes in total cholesterol levels and triglycerides were not found in the current study. As dietary intake was not strictly controlled, it is not possible to determine whether nutritional factors influenced this result, however it is also possible that additional muscle groups allowed for greater systemic changes to be elicited. Additionally, two subjects with initial high CRP concentration levels obtained normal CRP levels after the intervention in the current study. This result might suggest a protective effect of the muscle contractions evoked by high-intensity NMES strength training, which promotes anti-inflammatory myokine release and may attenuate low-grade inflammation reducing cardiovascular disease risk (9, 39). However, other more specific markers, such as interleukin 6 (IL-6) (9), should be included in future studies to better understand the metabolic response. Possibly longer duration interventions or targeting more muscle groups in combination with a controlled diet intake may evoke robust reductions in systemic inflammation.

Of final note, an important finding of the present study was that the subjects reported improvements in their symptoms of spasticity. This relevant finding emphasises the potential benefits of high-intensity NMES strength training for improving the perception of spasticity symptoms, which represents a negative influence in QoL in people with SCI (2). However, no overall improvements in QoL were reported and the change observed in the spasticity symptoms may not be clinically significant (30). Nonetheless, a near-significant value was observed toward an increase in the health and functioning subscale of the QoL index (0-wk: 15.0±4.2; 12-wk: 17.3±5.1; $p=0.07$) and two subjects showed a change in QLI score greater

(20% and 16%) than the mean percentage difference observed from -1 and 0-wk (12%), indicating clear improvements. In future, it will be important to understand the perceptions of people with SCI of feeling physically active and experiencing muscle contractions of the paralysed muscles (40). As an example of this, one subject who was a former competitive surfer expressed that he that he was enjoying having a "leg day at the gym" as he used to have before his injury. Thus, the present results provide evidence that the high-intensity NMES strength training intervention had a positive impact on the subject's perceptions of their physical disability.

Limitations of this study included the absence of a non-training control group, due to the difficulty in recruiting people with SCI into a study where no intervention is given, and moderate sample size. It would be of great scientific benefit if larger, controlled studies could be conducted in the future to test the findings of the current study.

Conclusion

Twelve weeks of high-intensity NMES strength training of the knee extensor muscles increased evoked tetanic knee extensor torque (i.e. muscle strength) and quadriceps cross-sectional area (i.e. muscle size). Subjects reported reduced symptoms of spasticity. Despite this, however, no overall improvement in QoL was reported, although a near-significant value was observed toward an increase in the health and functioning subscale in the QLI and positive, subjective comments were received from the subjects. High-intensity NMES strength training may be effective for improving muscle force and mass and decreasing perceived symptoms of spasticity, and can be safely implemented in people with SCI. Some evidence also indicated improvements in physical health and quality of life. However, replication of these results in a larger sample of subjects and with a non-training control group is necessary before its implementation in clinical practice.

382 **Declarations**

383 **Ethics approval and consent:** Edith Cowan University Ethics Committee. Reference

384 number: 11623.

385 **Consent for publication**: Not applicable.

386 **Availability of data and materials**: The datasets used and analysed during the current study

387 are available from the corresponding author on reasonable request.

388 **Competing interests**: The authors declare that they have no competing interests.

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391 The authors declare that the results of the study are presented clearly, honestly, and without

392 fabrication, falsification, or inappropriate data manipulation and results of the present study

393 do not constitute endorsement by ACSM.

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Fig. 1. QF evoked tetanic torque ($\tau_{t,40mA}$) measured at 0 and 12-wk

Isometric knee extensor torque (QF; sum of right and left quadriceps) at weeks 0 and 12 (0-wk, 12-wk). QF evoked tetanic torque ($\tau_{t,40mA}$) showed a significant increase of 31.8±24.8% between 0 and 12-wk.
Grey dashed lines represent individual subjects whilst the black solid line represents the group mean. Inset: Percentage change in evoked isometric knee extensor torque (QF) from 0-wk to 12-wk. * Significantly different between 0-and 12-wk ($p<0.05$).

Fig. 2.

A- Cross-sectional area of the quadriceps (CSA_{QF})

Total cross-sectional area of the sum of right and left quadriceps at 0-wk and 12-wk. CSA_{QF} increased significantly ($p=0.04$) by 45.0 ± 25.8% between 0 and 12-wk.
Grey, dashed lines represent individual subjects whilst black, solid line represents the group mean. Inset: Percentage change in $CSA_{QF.}$ * Significantly different from 0-wk and Control ($p<0.05$).

B- Cross-sectional area ultrasound image using extended-field of view technique

Example of the cross-sectional area (CSA_{QF}) measurement of the (left) quadriceps measured in subject A at 0-wk and 12-wk using extended-field-of-view ultrasonography. A significant increase of 45.0 ± 25.8% was observed (mean ± SD) in the group of 5 subjects.

Fig. 3. Spasticity evaluation tool (SCI-SET) results

Seven-day recall score (-3-+3) at -1, 0 and 12 weeks. A significant reduction of 4.8%±2.3% was observed.
* Significantly different at 12-wk from 0 and -1-wk ($p<0.05$). Grey, dashed lines represent individual subjects whilst black, solid line represents the group mean.

Title and legends to tables:

Table 1: Subject's characteristics

Subject's levels of injury, completeness of lesion, time since injury, AIS scale score, medication type and, wheelchair user or community walker and use of functional electrical stimulation (FES) routinely.

Table 2: Blood lipid profile and CRP concentration

Blood biomarkers at 0-wk and 12-wk and percent change within group (mean ± SD).