Chapter 5

Functional recovery and muscle properties after stroke: a longitudinal study

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Submitted
Summary

The main aim of this study was to determine whether alterations in strength and speed of the thigh muscles and voluntary activation capacity of patients with stroke relate to changes in functional performance. Fourteen patients performed functional performance tests on average 3.5 months after stroke (t=0) and 3 (n=8), 6 (n=5) and 12 months (n=3) thereafter (resp. follow-up (F)1, F2 and F3). Maximal voluntary isometric torques of knee extensors (MVCe) and flexors (MVCf), maximal triplet response maximal rate of torque development during voluntary (MRTDvol) and electrically evoked contractions (MRTDstim) and the degree of voluntary activation of knee extensors were estimated.

Five subjects were measured at t=0, F1 and F2. The scores at all but one functional performance tests improved over time. Significant correlations (|r|>0.7) were found between ΔMRTDstim (i.e., MRTDstim at F2 minus MRTDstim at t=0) of the paretic lower limb (PL) and ΔFugl-Meyer (FM) (r=0.99, p=0.01), between Δtriplet of PL and ΔFM (r=0.90, p=0.04), between Δtriplet of PL and ΔRivermead Mobility Index (r=0.92, p=0.03), between ΔMVCf of the non-paretic lower limb (NL) and ΔBerg Balance Scale (r=0.92, p=0.03) and between ΔMVCf of PL and Δ10 m walk test (r=0.99, p=0.002). In conclusion, improvements in functional performance up to 9 months after stroke were shown. Most importantly, changes in muscle variables correlated significantly with improvements in functional performance of patients with stroke.
Introduction

Almost all stroke patients experience a certain degree of functional recovery within the first six months after stroke. These functional gains in patients with stroke are primarily attributable to spontaneous recovery (improvements which occur naturally over time). The period of spontaneous recovery may range from two to twelve months with 80% or more of the process occurring within six months after the stroke. It is further suggested that most of the overall improvement occurs already within the first month after acute stroke. Recovery from motor impairments and development of behavioral compensation strategies have been found to extend beyond six months post stroke. Rehabilitation is devoted to enlarge and precipitate this functional recovery in order to improve quality of life after stroke. Therefore, rehabilitation programs adapted to objectives as allowed by the state of the neuromuscular system are important.

Many daily activities, especially locomotion, require sufficient function of thigh muscles. A number of studies reported that lower extremity muscles are weaker in stroke patients compared to healthy controls. Furthermore, the inability to generate normal amounts of force has been suggested to be the major limitation of physical activity. More specific, intrinsic strength capacity as well as the ability to maximally activate the knee extensors correlate strongly with functional performance (daily activities) in patients with stroke. In addition, a recent study showed a significant association between paretic lower limb strength and balance both cross-sectionally in acute patients with stroke as well as longitudinally in post-acute patients. Besides a reduction in maximal muscle strength, the ability to generate torque as fast as possible, is also impaired after stroke. Rate of torque development is an important determinant of e.g. risk of falling and (again) for controlling balance. Recent work from our group has shown lower maximal rates of torque development during electrically stimulated as well as during voluntary contractions of the paretic and non-paretic knee-extensors. Decreased ability to rapidly develop knee
extension torque contributes more to lower walking speed after stroke than does maximal strength\textsuperscript{48}.

In summary, there is clear evidence that difficulties in executing daily tasks in stroke patients are related to both impaired strength and speed of paretic and/or non-paretic muscles. Nevertheless, most studies are performed at one point in time\textsuperscript{1,31,10,41,45,37}. It is not fully elucidated whether the improvements in functional performance at the activity level of stroke patients during rehabilitation relate to changes in specific contractile function of the thigh muscles. Therefore, the present study reports on longitudinal changes in functional performance in a group of stroke patients during the first year after stroke. Furthermore, it is determined whether these changes relate to alterations in strength and speed characteristics of the paretic and non-paretic thigh muscles and voluntary activation capacity of patients with stroke.

\textbf{Methods}

\textbf{Subjects}

A total number of fourteen patients were included in the study. Patients (characteristics: see Table 5.1), all with first-ever stroke and a hemiparesis of the lower extremity, entered the study on average 3.5 months after stroke and 2 months after admission in the rehabilitation centre (Figure 5.1: t=0). Data on muscle function in relation to functional performance of these patients on inclusion are reported elsewhere\textsuperscript{31}. They were invited for measurements again 3 (n=8), 6 (n=5) and 12 (n=3) months after the first measurement (Figure 5.1: follow-up (F)1, F2 and F3 respectively). Because of drop-out of a number of subjects, data will be largely descriptive.

Before participation, each subject was thoroughly informed about the procedures, completed a health questionnaire and signed an informed consent.
The exclusion criteria were medical complications (such as unstable cardiovascular problems), severe cognitive and/or communicative problems preventing understanding verbal instructions or limiting performance of the requested tasks (e.g. aphasia, hemineglect) and contra-indications for electrical stimulation (unstable epilepsy, cancer, skin abnormalities and pacemaker). The project carried the approval of the institutional review board (Medical Ethical Committee) of the VU University Medical Centre, Amsterdam, The Netherlands.

**Figure 5.1: Time frame with measurement points.** First measurement point (t=0) is 3.5 months after stroke and the three follow-up measurements (F1, F2, F3) were executed 3, 6 and 12 months after t=0, respectively.

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<th>Time after admission (days)</th>
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**Experimental set-up**

Body function and activity-participation level were assessed with different clinical tests (‘functional performance’ tests). In addition, muscle function characteristics of the knee-extensors and -flexors were assessed in both limbs. The measurements were spread over four different days with at least one day of rest in between.

**Experimental procedures**

**Functional performance tests**

The following tests were performed by the subjects under supervision of a physiotherapist (except for the Rivermead Mobility Index, which was carried out by one of the researchers):

- **Berg Balance Scale (BBS)** assesses sitting and standing balance and exists of 14 test-items, scored on an ordinal 5-point scale (0-4). It gives an estimation of the chance that patients with stroke will fall\(^3\)-\(^5\).

- **Brunnstrom Fugl-Meyer (FM), lower extremity**, is a test for evaluation of patellar, knee flexor and Achilles reflexes, flexor and extensor synergies, isolated movements of knee flexor and ankle dorsal flexor function and normal reflex activity of the quadriceps and triceps surae muscles in the paretic lower limb hemiplegic patients\(^23\). Maximal possible score is 34.

- **Rivermead Mobility Index (RMI)** comprises a series of 14 questions and one direct observation, and covers a range of activities from turning over in bed to running. It is a measure of mobility disability which concentrates on body mobility\(^14\).

- **Timed “get-up-and-go” test (TUG)** requires patients to stand up from a chair, walk 3m, turn around, return, and sit down again. Time to fulfil this test is measured\(^47\). The shorter the time needed to do this test, the better; for all other tests applies the higher the score, the better.

- **10 meter walk test (10m)** is performed at comfortable (self selected) walking speed by patients who are able to walk independent with or without mobility aid and/or orthesis. Time to walk 10m is measured and averaged over three
• **Motricity Index (MI)** evaluates the arbitrary movement activity and maximum isometric muscle force. Possible scores are 0-9-14-19-25-33 at each of the three parts of the test for lower extremities\(^{20,15,12}\).

• **Functional Ambulation Categories-score (FAC)** evaluates the measure of independence of walking of the patient. Categories are scored on a six-point scale (0-5)\(^{28,29}\).

**Force measurements**

The procedures for the measurements as well as the calculation of variables are described in detail elsewhere\(^{31}\). Briefly, maximal voluntary and electrically evoked isometric torques of the knee extensors and maximal voluntary isometric torques of the knee flexors were measured while subjects were seated on a custom built Lower EXtremity System (LEXS)\(^{31}\). The lower leg was strapped tightly to a force transducer just above the ankle by means of a cuff at a knee flexion angle of 60° (0° = full extension). Electrical stimulation, used for the knee extensors only, was applied via two surface electrodes placed over the quadriceps muscles with a computer-controlled constant current stimulator (Digitimer DSH7, Digitimer Ltd., Welwyn Garden City, UK).

**Familiarization session**

During the familiarization session, measurements were performed with the non-paretic lower limb to check whether the instructions were understood by the subject. After a warming-up (existing of 5 submaximal contractions) subjects were trained to perform maximal isometric knee flexion (MVCf) and extension (MVCe) contractions and fast voluntary knee extensions. Subsequently, the subjects were familiarized with electrical stimulation. During the follow-up measurements, no familiarization session was performed.
**Muscle strength and speed**

Subjects were asked to maximally generate isometric knee extensions for 3-4 s to determine MVCe. Alternately, MVCfs were performed, as described in Horstman *et al.*[^31]. Thereafter, subjects were asked to perform knee extensions as fast as possible[^31] with the command: 3, 2, 1 GO! They were encouraged to reach a peak force of at least 70% of their MVC and were not allowed to make a countermovement (flexion) or have pretension before the fast extension[^19]. The same measurements as performed with the paretic lower limb (PL) were repeated with the non-paretic lower limb (NL), carried out on a separate day. Control subjects just performed one session, with the right leg only.

**Triplet stimulation and voluntary activation**

A modified super-imposed stimulation technique was used in which electrically evoked triplets (pulse train of three rectangular 200 μs pulses applied at 300 Hz) were used to establish the subjects’ capacity to voluntarily activate their muscles[^38]. Measurements started with PL in a knee angle of 60° knee flexion. First, stimulation current was increased until supramaximal stimulation was ensured. Next, subjects underwent measurements consisting of a triplet superimposed on the plateau of the force signal of the MVC. Subsequently, these measurements were performed with NL.

**Data analysis of muscle function**

*MVC torque* (Nm) was determined as the peak force from the force plateau multiplied by the external moment arm. MVCe and MVCf were assessed. *Maximal rate of torque development* was defined as the steepest slope of torque development during fast voluntary contractions (MRTDvol)^[^19] and during a pulse train of 80 ms, 300 Hz (MRTDstim). MRTDvol was normalized to MVCe torque in order to correct for the number of parallel muscle fibers (‘muscle thickness’) to get a fair comparison of contractile speed of muscles between different subjects independent of absolute maximal torques. MRTDstim was therefore expressed as a percentage of 150 Hz torque (obtained at the same stimulation intensity as the 300 Hz pulse train).
Voluntary activation is defined as the completeness of skeletal muscle activation during voluntary contractions and was calculated by means of a modified interpolated twitch technique\textsuperscript{38}. Voluntary activation (%) = \[ 1 - \left( \frac{\text{superimposed triplet}}{\text{rest triplet}} \right) \] * 100.

Here the superimposed triplet is the force increment during a maximal contraction at the time of stimulation and the control triplet is that evoked in the relaxed muscle\textsuperscript{53}. Supramaximal triplet torque of the relaxed muscle is used as a measure for the maximal (intrinsic) torque capacity of the knee extensors, independent of voluntary activation.

Pearson correlations were calculated between changes (Δ, between t=0 and F2) in scores at the tests of functional performance and changes in the 6 muscle variables (MVCe, MVCf, MRTDvol, MRTDstim, triplet and voluntary activation).

Results

Only a part of the total number of 14 subjects participated in the follow-up measurements. Most important reasons given were that travelling from their (nursing) home to the rehabilitation centre was too time-consuming for the patients. Some experienced the measurements (especially the electrical stimulation and the duration of the experiments) as too uncomfortable. Other patients missed the follow-up measurements due to severe illness. One patient decided to spend the winter abroad. Moreover, data were not complete for some of the patients due to unreliability, e.g. concentration problems (one subject dozed off a few times during the measurements), no force plateau during the MVCs or subjects did not reach 90% of their MVC during the familiarization session. Therefore, the data will be mainly descriptive and hardly any statistical analyses were performed.

Functional performance

Figure 5.2 shows the course of the scores of the subjects with stroke at two important (see below, Table 5.4) tests of functional performance, namely the Berg Balance Scale
(BBS), a measure of ability-activity level, and at the Fugl Meyer (FM), an impairment (bodily functions) measure developed to assess physical recovery after stroke

Figure 5.2: Course of all individual scores at the Berg Balance Scale (BBS) and Brunnstrom Fugl-Meyer, lower extremity (FM) at 4 measuring times (t=0, F1, F2, F3). Note that t=0 is on average 3.5 months after stroke.

Because the outcome of most tests of functional performance seemed to plateau at F2 and because F3 values could only be obtained in three subjects, mean values of the five subjects assessed until F2 are presented in Table 5.2. Overall, the data of the functional performance tests show improvement (except for MI) during the follow-up period.
**Table 5.2:** Median values and 1st quartiles for the Berg Balance Scale (BBS), Motricity Index (MI), Functional Ambulation Categories-score (FAC), Rivermead Mobility Index (RMI) and Brunnstrom Fugl-Meyer (FM) and mean and standard deviations for Timed “get-up-and-go” test (TUG) and 10 meter walk test (10m) at the 3 measurement points 3.5 months after stroke (t=0) and during follow-up (F1 and F2) for the five subjects who participated at these three measurement points (n= 5).

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<td>FM</td>
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<td>17 (14)^</td>
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<td>10m (m/s)</td>
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<td>0.65 ± 0.72^</td>
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<td>TUG (s)</td>
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<td>39.8 ± 26.1</td>
<td>37.3 ± 30.9^</td>
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* significant improvement (p<0.05) compared with t=0
^ trend (p<0.1) compared with t=0

**Muscle variables**

Data were not complete for reasons explained earlier. Furthermore, it is a general experience that subjects, knowing that a superimposed stimulation will be performed, anticipate upon stimulation and perform less when compared with MVC without stimulation. To minimize this effect, which influences the activation results, only data were used when MVCs with superimposed stimulation were more than 90% of their highest attempt. Therefore, variables of muscle functions in Table 5.3 show missing values. The zero values are values from subjects who did perform the measurements but were not able to generate force with their paretic lower limb.

There was a substantial variation between subjects with respect to the outcome of the muscle variables at the start of the study (t=0) as well as with respect to the changes in these variables over time (Table 5.3).
Table 5.3: Data on muscle variables for 5 subjects who were measured during the first measurement (t=0) and 3 and 6 months thereafter (F1, F2 respectively) for the non-paretic (NL) and paretic lower limb (PL). Maximal voluntary extension (MVCe) and flexion (MVCf) torque, maximal rate of torque development during voluntary (MRTDvol) and electrically evoked contractions (MRTDstim), triplet torque and voluntary activation (VA).

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</table>
Correlations between changes in functional performance and muscle function

Table 5.4 shows the potential relevant correlations (n=4 or 5) with $|r|>0.7$ between changes ($\Delta$, i.e., MVCe at F2 minus MVCe at t=0) in scores at tests of functional performance and changes in muscle variables. Figure 5.3 shows the five significant correlations namely the correlations between $\Delta$MRTDstim of PL and $\Delta$FM ($r=0.99$, $p=0.01$, n=4), between $\Delta$triplet of PL and $\Delta$FM ($r=0.90$, $p=0.04$, n=5), between $\Delta$triplet of PL and $\Delta$RMI ($r=0.92$, $p=0.03$, n=5), between $\Delta$MVCf of NL and $\Delta$BBS ($r=0.92$, $p=0.03$, n=5) and between $\Delta$MVCf of PL and $\Delta$10m ($r=0.99$, $p=0.002$, n=5).

Table 5.4: Correlation coefficients between changes (between t=0 and F2) in scores at tests of functional performance and changes in muscle variables for the non-paretic (NL) and paretic lower limb (PL) of 5 subjects. Berg Balance Scale (BBS), Motricity Index (MI), Functional Ambulation Categories-score (FAC), Rivermead Mobility Index (RMI) and Brunnstrom Fugl-Meyer (FM), Timed “get-up-and-go” test (TUG) and 10 meter walk test (10m). Maximal voluntary extension (MVCe) and flexion (MVCf) torque, maximal rate of torque development during voluntary (MRTDvol) and electrically evoked contractions (MRTDstim), triplet torque and voluntary activation (VA).

<table>
<thead>
<tr>
<th></th>
<th>BBS</th>
<th>FM</th>
<th>RMI</th>
<th>10m</th>
<th>FAC</th>
<th>TUG</th>
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<td>(m/s)</td>
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<td>PL</td>
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<tr>
<td>MVC</td>
<td>-</td>
<td>0.843*</td>
<td>0.861^</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.832^</td>
</tr>
<tr>
<td>MVCf</td>
<td>-</td>
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<td>-</td>
<td>0.985*</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>MRTDvol</td>
<td>-</td>
<td>0.750</td>
<td>-</td>
<td>-</td>
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<td>MRTDstim</td>
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<td>0.990*</td>
<td>0.860</td>
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<td>0.897*</td>
<td>0.923*</td>
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<tr>
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<td>0.710</td>
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<tr>
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<td>0.833^</td>
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<td>-</td>
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<tr>
<td>MRTDvol</td>
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<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>0.732</td>
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<tr>
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<td>N.A.</td>
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<tr>
<td>VA</td>
<td>-</td>
<td>N.A.</td>
<td>0.742</td>
<td>-</td>
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</table>

* significant ($p<0.05$) correlation, ^ trend ($p<0.1$)
Δ: delta, changes between t=0 and F2; MRTDstim, electrically evoked maximal rate of torque development; MVCf, Maximal Voluntary Contraction torque of the knee flexors; PL, paretic lower limb; NL, non-paretic lower limb; FM, Fugl-Meyer assessment; BBS, Berg Balance Scale; RMI, Rivermead Mobility Index; 10 m, 10 m walk test.

Figure 5.3: correlations between ΔMRTDstim of PL and ΔFM (r=0.99, p=0.01, n=4), between Δtriplet of PL and ΔFM (r=0.90, p=0.04, n=5), between Δtriplet of PL and ΔRMI (r=0.92, p=0.03, n=5), between ΔMVCf of NL and ΔBBS (r=0.92, p=0.03, n=5) and between ΔMVCf of PL and Δ10m (r=0.99, p=0.002, n=5).
Chapter 5: Functional recovery and muscle properties after stroke: a longitudinal study

Discussion

A considerable improvement was found in de scores at the tests of functional performance, especially up to F2. In general also the muscle variables improved over time. Changes in muscle variables of the 5 subjects that were measured at t=0, F1 and F2 were shown to correlate with improvements in tests of functional performance during the first 9 months after stroke.

Functional performance

It is remarkable that from the 5 subjects we followed until F2, subject 1 scored the lowest values of all subjects (n=14) that took part in the study at t=0 at all variables of the paretic lower limb (Table 5.3), whereas subject 3 scored the best. The actual improvement in the Timed “get-up-and-go” test (TUG) between t=0 and F2 may be even greater than presented in Table 5.2. Subject 1 was not able to perform the TUG at t=0, but during F1 that subject was able to do the TUG in 81 s. Nevertheless, the score of this subject could not be used, since the improvement could not be calculated due to the missing value at t=0. This same subject 1 scored 9 at the Motricity Index (MI) at t=0 but 0 at F1 and F2. Moreover, subject 3 achieved the maximal score of 100 at MI during all three measurement points and only one subject improved between F1 and F2 at his test. These may be reasons why we found no significant improvement over time for MI in the five subjects who did these 2 follow-ups.

An improvement of 7%, from 45 to 52% of maximum attainable recovery (n=8) at the Fugl-Meyer Lower Extremity test (FM) was found from ~3.5 months (t=0) to half a year (F1) after stroke (n=8) (Figure 5.2). For FAC a significant increase from 68 to 88% was found and for MI 47 to 53% (not significant) (Table 5.2). Kwakkel et al.\textsuperscript{39} similarly observed an improvement from about 62% to 65% (n=101) at the FM, 51 to 59% at the FAC and 58 to 59% at the MI during the first half year after stroke. Both the present results and those of Kwakkel et al.\textsuperscript{39} showed that most improvement took
place within the first 3 months until half year after stroke, as was also found by others\textsuperscript{34,59}.

**Muscle variables**

As would be expected after hemiparetic stroke, PL scored consistently lower than NL on the muscle variables (voluntary extension and flexion torque, triplet torque, voluntary activation and maximal rate of voluntary torque development). Variable results in changes in muscle characteristics were found per subject between t=0 and F2 (Table 5.3). Also in literature there are different results. Carin-Levy et al.\textsuperscript{13} reported, in line with our results, no significant change over time in the strength and muscle mass of both paretic and non-paretic (arm and) leg muscle during the first 6 months after stroke. However, Newham and Hsiao\textsuperscript{43} did observe increased strength throughout the first half year after stroke, while activation failure remained constant. Andrews et al.\textsuperscript{2} showed an increase in both PL and NL knee extensor strength from admission (~2 wk post stroke) to discharge (~4 wk post stroke). So, there are no consistent data indicating that muscle variables improve after stroke.

The main limitation of our study is the small sample size at F2 and F3. Although all new patients with stroke in the rehabilitation centre were examined by physicians, a large number were ineligible for our study, because they had severe cognitive and/or communicative problems, medical complications, no hemiparesis of the lower extremity or, conversely, were too heavily paralyzed and had a previous stroke. A considerable number of patients were not willing to participate (or in case of follow-ups to continue), mainly due to their changed life after stroke and/or the intensity of the protocol. Around half of the eligible patients completed the entire protocol (4 measurement days) at t=0. The scores of stroke severity of our patients (FAC median and quartiles 4 (2.25-4)) confirmed that we managed to recruit a very wide a range of stroke patients at t=0, but this contributed to the difficulty in statistics, besides the great drop-out of patients during the follow-ups. However, studies with smaller samples sizes than ours have detected significant changes in muscle strength over
time in NL\textsuperscript{27} and PL compared to control\textsuperscript{43}. Thus, it is likely that, if changes in the thigh muscles of our patients had occurred, these must have been small.

**Correlation between muscle variables and functional performance**

The severity of post stroke paresis is related to a person’s ability to perform functional tasks; Others found correlations between lower limb isometric knee extension strength and functional performance, like gait distance\textsuperscript{7} and speed\textsuperscript{7,9,31}, sit-to-stand\textsuperscript{11,31}, transfers\textsuperscript{5}, stair climbing\textsuperscript{8} and balance\textsuperscript{31}. The new aspect in this study is that we wanted to investigate whether changes in functional performance during the first 9 months after stroke related to changes in muscle characteristics.

Most relations were found within subjects between changes in muscle variables of PL and changes in scores at the BBS, a sitting and standing balance measure and the FM, an impairment measure developed to assess physical recovery after stroke\textsuperscript{49}. In our cross-sectional study\textsuperscript{31} strong significant correlations were found between muscle variables of both PL and NL and various tests of functional performance. However, in the present study if we look within subjects, we hardly see any correlations between changes in muscle variables of NL and changes in scores at the functional performance tests over time. This indicates that longitudinal data are essential to gain the required information regarding which (muscle) variables should be trained to induce improvements in functional performance, because cross-sectional data are not exclusive enough.

A question that remains to be answered is what may have caused the improvements in functional recovery? It is suggested that functional gains experienced by stroke patients are primarily attributable to spontaneous recovery (changes over time that occur naturally) of functional performance of which eighty percent occurs within six months after the onset of stroke\textsuperscript{40} while others\textsuperscript{59} state that there is some recovery between 3 weeks and 6 months in almost all acute stroke patients and that at 6 months over 45% of survivors were functionally independent.
Secondary changes as a result of stroke could be expected in skeletal muscle, e.g. changes in myofiber type\textsuperscript{18} or number and size of motor units. The latter is already reported in the second week after stroke onset\textsuperscript{35}. For instance, a change in muscle fiber composition, characterized by selective type II fiber atrophy and predominance of (slow twitch, oxidative) type I fibers has been shown in paretic muscles\textsuperscript{51,21,17,26,22}, which would lead to concomitant changes in contractile speed of the muscle fibers towards those of slow muscles. We can imagine that such a change in fiber type composition can be combated, for instance by training, during the first year after stroke, so that muscle speed characteristics can be restored.

**Conclusions**

The (small) alterations in the muscle variables correlated well with the improvements in scores on tests of functional performance. Although the correlations do not necessarily imply causality, we think (intrinsic) muscle speed and strength are important variables which can potentially be prolific targets to improve during rehabilitation. It is therefore recommended to investigate the effects of strength training of the thigh muscles during at least the first 6 months after stroke. Bohannon concludes in his review\textsuperscript{10} that resistance training programs are effective at increasing strength in patients who have experienced a stroke but there is no clear evidence for the effect of strength training on functional activities after stroke\textsuperscript{42}. Main results of Saunders’ review\textsuperscript{50} include only 4 strength training trials\textsuperscript{44,33,36,60} and lack non-exercise attention controls, long-term training and follow up. Strength measures were reported to improve after resistance training, albeit without clear benefits for functional performance (e.g. gait speed)\textsuperscript{50}. Therefore, in addition, the strength training may be combined with task-specific functional training\textsuperscript{56,32}, because it has “the potential to drive brain reorganization toward more optimal functional performance”\textsuperscript{52}. When muscles are weak, e.g. isometric contractions can be used in the early stages of rehabilitation as a means of improving the muscle’s ability to contract, but once muscle strength reaches a certain threshold, exercises should be biomechanically similar the daily life actions to be trained to transfer increased force-generating ability into improved performance\textsuperscript{52}.

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From such an intervention study on functional recovery it can be elucidated whether increasing strength and speed really improves functional performance.

References


50. Saunders DH, Greig CA, Young A, Mead GE. Physical fitness training for stroke patients (Cochrane Review). The Cochrane Library 2004(1).

Chapter 5: Functional recovery and muscle properties after stroke: a longitudinal study
Chapter 6

Changes in muscle characteristics and jump height following 3 weeks of unilateral lower limb suspension

Astrid M. Horstman
Jo C. de Ruiter
Noortje T.L. van Duijnhoven
Maria T.E. Hopman
Arnold de Haan

Submitted
Summary

We investigated whether, as a result of limb unloading, changes in maximal voluntary and electrically evoked torque and rate of torque development during single joint isometric muscle contractions were related to changes in jump performance involving dynamic muscle contractions and several joints. Six healthy male subjects (21 ± 1 years) underwent 3 weeks of unilateral lower limb suspension (ULLS) of the right limb. Plantar flexor and knee extensor maximal voluntary contraction (MVC) torque and maximal rate of torque development (MRTD), voluntary activation and maximal triplet torque (thigh; 3 pulses at 300 Hz) were measured next to squat jump height before and after ULLS.

MVC of plantar flexors (MVCpf) and knee extensors (MVCke) and triplet torque decreased by 12% (p=0.012), 21% (p=0.001) and 11%, (p=0.016), respectively. Voluntary activation did not change (p=0.192). Absolute MRTD during voluntary contractions decreased for plantar flexors (by 17%, p=0.027) but not for knee extensors (p=0.154). Absolute triplet MRTD decreased by 17% (p=0.048). The reduction in MRTD could be fully attributed to reduction in maximal torque. Jump height with the previously unloaded leg decreased significantly by 28%.

No significant relations were found between any of the muscle variables and jump height (r<0.48), but decreases in torque were (triplet, r=0.83, p=0.04) or tended to be (MVCke r=0.71, p=0.11) related to the decreases in jump height. Thus, reductions in isometric muscle torque following three weeks of limb unloading were significantly related to decreases in the more complex jump task, although torque in itself (without intervention) was not related to jump performance.
Introduction

Unloading, for instance during prolonged bed rest or during space flight, is known to decrease muscle cross-sectional area (CSA)\(^1,37,41\) and strength\(^17,5,30,8,34\). Gravitational muscles, like the knee extensors and the plantar flexors, are exposed to altered patterns of activity as a result of unloading and therefore their contractile properties change\(^46,18\). Also a reduced neural drive capacity may be expected after unloading\(^16,25,38\), which could further decrease the ability to generate maximal voluntary torque\(^19,13\) and fast torque development\(^34,44,8\). Although the consequences of muscle unloading for contractile properties of individual muscle groups is well documented\(^15,6\), the consequences for more complex whole body functioning are less well studied. In the present study we aimed to relate changes in static muscle contractile properties and voluntary activation of single muscle groups, to the maximum performance of dynamic multi-joint squat jump performance.

The capacity to activate a muscle as fast as possible is important during daily life, since the time allowed to build up muscle torque is limited\(^22\) during balance corrections, e.g. after tripping, and fast powerful tasks such as jumping. Maximal rate of isometric torque development (MRTD) has been related to fall prevention\(^36\) and jump performance\(^12\). MRTD \textit{in vivo} is dependent on properties of the muscle tendon complex and on neural activation. It is indicated that contractions in which torque needs to be developed as forcefully and rapidly as possible require higher levels of neural activation compared with maximal contractions of several seconds or longer\(^11,16,8,27,4\).

Jump height is thought to be a more relevant measure of leg-extension power than isolated force responses. It is shown that very good jumpers are stronger than bad jumpers\(^47,26\), but for the quadriceps muscles, correlations between maximal voluntary knee extension torque and jump height have only been found in heterogeneous subject groups that, for example, included both men and women\(^20\). Most studies did not find relationships between isometric torque and jump performance\(^2,20,21,52\). Also
correlations between muscle contractile speed during fast voluntary contractions and jump performance were found to be poor\(^{31,35,50}\) or absent\(^{31,3,14,33,12}\) in cross sectional studies. In longitudinal studies, which are not obscured by inter individual differences such as in body composition and jumping technique, positive effects of muscle strength training on complex whole body performance such as jumping have been reported\(^{7,28,23}\). Therefore, it is expected that interventions which would negatively affect contractile properties of individual muscle groups would have a detrimental effect on more complex dynamic tasks such as jumping. We used unilateral lower limb suspension (ULLS), a model promoting disuse with intact joint mobility, relatively low costs and only moderate encroachment on daily physical activities. To our knowledge, the present study is the first to relate changes in maximal torque and MRTD, due to unloading, during single-joint isometric knee extensor and plantar flexor torque development, to changes in a more natural whole body movement like jumping. We hypothesized that without an intervention the relations between contractile properties of individual muscle groups (knee extensors and plantar flexors) and jump performance would be weak or absent, but that decreases in maximal torque and MRTD following unilateral lower limb suspension would be related to decreases in jump performance.

**Methods**

**Subjects**

Ten healthy young men with a minimum age of 18 years (22 ± 2 years, 1.88 ± 0.06 m and 77 ± 8 kg) volunteered in this study. Exclusion criteria were >5 h of physical activity per week; hypertension; contraindication for maximal exercise or electrical stimulation; recent bone fracture; heart failure; muscle, skin, metabolic and bone diseases; functional limitations in upper or lower limbs; use of drugs with hemodynamic effects and any medical or surgical history that could influence the study outcome.

The project carried the approval of the Medical Ethics Committee of the Radboud
University Nijmegen Medical Centre. All subjects signed an informed consent before participation. One week prior to the baseline measurements, subjects were familiarized with all testing procedures. Unfortunately, two subjects withdrew because of poor tolerance of electrical stimulation and another two for personal reasons unrelated to the study. Therefore, 6 subjects (21 ± 1 years, 1.87 ± 0.06 m and 79 ± 9 kg) completed the 3 weeks of ULSS.

**ULLS**

The ULLS model used in this study was described by Berg *et al.*\(^5\) and Seynnes *et al.*\(^40\). In brief, the subjects were wearing a left shoe with a 7.5 cm thick sole and performed all daily activities on crutches. The right leg was unloaded by means of a shoulder strap running around the foot and the ankle (Figure 6.1), which was worn during all locomotor activities. The length of the strap was adjusted to prevent the foot touching the floor and to maintain the ankle angle at 90° (instead of a more plantar flexion position), so that no additional loss of muscle mass occurred as a result of short muscle length\(^45,49\). Subjects were instructed not to load the suspended limb (e.g. not touching the ground, no driving etc). They were constrained to wear support stockings in order to limit the risk of deep venous thrombosis. Compliance with the suspension was monitored through regularly (personal, by telephone or via email) communication with the subjects and they kept a diary.

![Figure 6.1: model of unilateral lower limb suspension. The left shoe with thick sole and the shoulder strap running around foot and ankle to unload the right foot.](image-url)
Experimental design

Maximal voluntary isometric knee extensions and plantar flexions and fast voluntary contractions of both muscle groups were performed. Moreover, electrically evoked contractions (supramaximal triplets, see below) were used for the knee extensors to establish voluntary activation and maximal rate of torque development during maximal electrical activation. Squat jump height on one leg (both left and right) and on two legs was determined. The experiments were performed on the same day, starting with the jumps, followed by measurements of the contractile properties of the plantar flexors and that of the knee extensors, with at least 1.5 hours of rest in between these three tests. After the measurements at baseline (pre), the subjects started walking on crutches and 3 weeks later, this period ended with the performance of the same measurements done prior to the ULLS (post).

Torque measurements

Knee extensors: Maximal voluntary isometric forces of the knee extensors of the right limb were measured on a custom built dynamometer (VU University Amsterdam, The Netherlands) at a knee angle of 120° (180° corresponds with fully extended knee), at which angle usually the highest torque is produced\textsuperscript{11}. Subjects were tightened with a hip and trunk belt to avoid changes in hip and knee angle during isometric contractions. The lower leg was strapped tightly to a force transducer (KAP, E/200 Hz, Bienfait B.V., Haarlem, The Netherlands, range: 0-2 kN) just above the ankle by means of a cuff. The knee angle of 120° was determined with a handheld goniometer (model G300, Whitehall Manufacturing, California, USA) using the greater trochanter, the lateral epicondyle of the femur and the lateral malleolus of the fibula as references\textsuperscript{24}, while the subject produced a voluntary contraction at about 50% of the maximal voluntary contraction torque (MVC) (dynamometer) or when he was standing in the start position prior to the jump test. The distance between the lateral femur epicondyle and the force transducer in the dynamometer was taken as the external moment arm which was multiplied with the measured forces to obtain torques.
Plantar flexors: Maximal voluntary isometric forces of the plantar flexors were measured using another custom made dynamometer (VU University Amsterdam, The Netherlands). Subjects were seated, hip and knee angle were 90° and ankle angle was 15° dorsal flexion position. In this position, also the gastrocnemius muscles and not only the soleus muscles have a substantial contribution to the triceps surae torque\textsuperscript{39,32}. Subjects were tightened with a hip and trunk belt and their right foot was strapped into a standard shoe with a sturdy flat sole that was in turn tightly strapped to a force transducer (K.A.S., A.S.T., Wolnzach, Germany, range: 0-10 kN). The leg was fixed tightly by a top restraining bar that was secured on the thigh, just proximal to the knee joint to minimize the movement of the leg and to avoid changes in knee and ankle angles during force generation. The distance between the middle of the medial malleolus and a fixed point at the shoe (at the height of the ball of the foot) was measured representing the external moment arm used to calculate plantar flexion torque.

Experimental procedures

Familiarization session
The measurements of the familiarization session were performed with the right leg one week before the baseline measurements. Dynamometer adjustments and shoe sizes were noted. After a warming-up, maximal voluntary contractions and fast voluntary contractions were practised. Thereafter, subjects were familiarized with electrical stimulation for the quadriceps muscle, by increasing current during triplets (train of three 200 μs-pulses at 300 Hz) at a relaxed muscle. Finally, supramaximal triplets were superimposed on a maximal voluntary isometric contraction.

Muscle torque
On the pre and post ULLS tests days the subjects were asked to generate maximal isometric knee extensions and plantar flexions for 3-4 s to determine MVC. Two to maximally four attempts were allowed, separated by 2 min of rest. MVC was taken as the highest value of these attempts, which did not exceed preceding attempts by
>10%. Real-time force production was visible on a computer screen. Subjects were vigorously encouraged to exceed their maximal value, which was also displayed.

**Voluntary activation**

Volitional tests rely heavily on the subject’s motivation and the ability to maximally recruit his muscles and are often not an accurate reflection of the maximal torque generating capacity of the muscle. Electrically evoked contractions are independent of the subject’s effort. Therefore, a modified super-imposed stimulation technique was used in which electrically evoked triplets were used to establish the subjects’ capacity to voluntarily activate their knee extensor muscles. After explanation of the procedure, the skin of the thigh of the subject was shaved and a pair of self-adhesive surface electrodes (13 x 8 cm, Schwa-Medico, The Netherlands) was placed over the proximal and distal part of the anterior thigh. The knee extensors were electrically stimulated using a computer-controlled constant current stimulator (Digitimer DSH7, Digitimer Ltd., Welwyn Garden City, UK). First, stimulation current, applied to the relaxed muscle, was increased until torque measured in response to a triplet levelled off. The current was then increased by a further 20 mA to ensure supramaximal stimulation (resting triplet). It was assumed that at this point all muscle fibers of the knee extensors were activated. These high frequency stimulations (maximal triplet torque) result in maximal muscle activation with peak torques of about 30% MVC. Triplet stimulation was preferred to twitches because triplet torque is less sensitive to, for instance, length-dependent changes in calcium sensitivity and post-tetanic potentiation and improves the signal-to-noise ratio. Finally, subjects underwent measurements consisting of a triplet superimposed on the plateau of the force signal of the MVC.

**Contraction speed**

MRTD was assessed as indicator of contractile speed using voluntary contractions. For this purpose, fast voluntary isometric contractions were performed. Subjects were asked to perform knee extensions and plantar flexions as fast as possible without a countermovement or pretension (both indicating anticipation of the subject and
influencing the MRTD) just before movement execution\textsuperscript{11}. The command was: 3, 2, 1, GO! Subjects performed these fast contractions until they had two attempts, with a maximum of 5 attempts to avoid fatigue. After each attempt, subjects received feedback and were encouraged to exceed previous values.

For the knee extensors, maximal rates of torque development were also established during electrically evoked contractions, independent of voluntary activation, using the supramaximal triplets.

\textbf{Jump height}

The jump protocol of De Ruiter et al.\textsuperscript{12} was used in the present study. In brief, after a warming up of 12 squat jumps with increasing height, squat jumps were performed with both hands gripped together behind the back to avoid arm support for standardization. The subjects were instructed to hold their trunk as upright as possible. Squat jumps were started from 120° knee angle (the same angle as during the isometric knee extension measurements), which was set manually with a hand-held goniometer using the same anatomical landmarks as used during the isometric knee extensions. During the 1-leg jumps, the other leg was hold a bit forward, so that it was unable to support the jump. Jump height was measured with a tape measure, which slid between two small messing plates between the feet in the floor when subjects jumped\textsuperscript{10}. If the subject landed more than 2cm forward (backward was impossible due to the horizontal bar) compared to the starting position, the jump was not used for data analysis. The reproducibility of this jump method is high (ICC=0.94)\textsuperscript{10}. The sequence of 2-leg, right and left leg squat jumps was randomly chosen, but was the same per subject during the pre and post ULLS measurements. Between consecutive jumps there were 2 minutes of rest and between the sets (one-leg right, one-leg left and two-leg) 5 minutes. In each of the three sets, 3 good jumps were performed with a maximum of 6 jumps.

\textbf{Data analysis}

Real-time force applied to the force transducer was digitally stored (1 kHz) on computer disc. Force signals were automatically corrected for gravity of the leg:
average force applied by the limb weight to the transducer during the first 50 ms after
start of a recording, with the subject seated in a relaxed manner, was set to zero by
the computer program. All force signals were low-pass filtered (4th order, 150 Hz,
Butterworth). MVC torque (Nm) was defined as the peak force from the force plateau
multiplied by the external moment arm.

MRTD was defined as the steepest slope of torque development during both fast
voluntary contractions (vol)11 of knee extensors and plantar flexors and during the
triplets at 300 Hz (stim) applied to the knee extensors only. The MRTD as such not
only depends on speed properties of the muscle but also on its maximal torque
generating capacity. Therefore, to get a relevant comparison of the contractile speed
of muscles between the different subjects independent of absolute maximal torques,
MRTDvol was normalized to MVC torque and MRTDstim to resting triplet torque.

Voluntary activation is defined as the completeness of skeletal muscle activation
during voluntary contractions and was calculated by means of a modified interpolated
twitch technique24:

\[ \text{Voluntary activation} \, (\%) = [\, 1 - (\text{superimposed triplet/rest triplet})] \times 100.\]

Here the superimposed triplet is the force increment during a maximal contraction at
the time of stimulation and the control triplet is that evoked in the relaxed muscle42.
(Supra maximal) resting triplet torque of the relaxed muscle is used as a measure for
the maximal (intrinsic) torque capacity of the knee extensors, independent of
voluntary activation.

**Statistics**

All results are presented as means ± SD. Paired sample t-tests were used to compare
pre and post ULLS values of MVCs, voluntary activation, triplet torque and jump
height. Pearson’s correlation coefficient was used to establish significance of
correlation between (changes in) muscle variables (MVC of the knee extensors
(MVCke), MVC of the plantar flexors (MVCpf), triplet torque, voluntary activation,
MRTDvol and MRTDstim) and (changes in) 1-leg (right) and 2-leg jump height. In each
statistical analysis, the level of significance was set at p<0.05.

**Results**

**Torque**

Table 6.1 shows the results of the muscle variables before and after limb suspension. The MVC of the plantar flexors significantly decreased by 12.1 ± 5.9% (p=0.01) after ULLS and the MVC of the knee extensors by 20.5 ± 4.6% (p=0.001). Also triplet torque of the knee extensors decreased significantly (by 11.3 ± 8.7%, p=0.02), whereas activation did not show a significant change (p=0.19).

**Maximal rate of torque development**

Absolute MRTD during voluntary contractions decreased by 16.9 ± 11.4% (from 0.92 ± 0.17 kNm·s⁻¹ to 0.76 ± 0.13 kNm·s⁻¹) for the plantar flexors (p=0.03, n=6) and 15.6 ± 32.4% (i.e., from 2.68 ± 0.66 kNm·s⁻¹ to 2.11 ± 0.33 kNm·s⁻¹) for the knee extensors (not significant; p=0.15, n=5, one subject had no valid attempt out of his five attempts post ULLS). Absolute MRTD during electrically evoked contractions in the quadriceps muscles significantly decreased with 17.0 ± 17.7% (i.e., from 2.65 ± 0.75 kNm·s⁻¹ to 2.15 ± 0.52 kNm·s⁻¹) (p=0.048, n=6).

The values for MRTD normalized for maximal torques are also shown in Table 6.1. Normalized voluntary MRTD of the plantar flexors (p=0.683) and knee extensors (p=0.434) nor normalized electrically evoked MRTD of the knee extensors (p=0.296, n=6) changed significantly after ULLS. Three weeks of suspension did not affect the ratio of voluntary over stimulated MRTD in the knee extensor muscles for normalized (1.17 ± 0.46 pre and 1.06 ± 0.47 post; p=0.862) or absolute values (0.38 ± 0.14 pre and 0.39 ± 0.14 post; p=0.39).
**Table 6.1:** Values of the muscle variables pre and post unilateral lower limb suspension.

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>POST</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVC plantar flexors (n=6)</td>
<td>242 ± 54Nm</td>
<td>211 ± 36Nm*</td>
</tr>
<tr>
<td>MVC knee extensors (n=6)</td>
<td>308 ± 57Nm</td>
<td>246 ± 42Nm*</td>
</tr>
<tr>
<td>Triplet torque knee extensors (n=6)</td>
<td>76 ± 12Nm</td>
<td>68 ± 15Nm*</td>
</tr>
<tr>
<td>Voluntary activation (n=6)</td>
<td>88.3 ± 6.8%</td>
<td>84.7 ± 9.1%</td>
</tr>
<tr>
<td>norm. MRTDvol calf (n=6)</td>
<td>0.45 ±0.08%-ms⁻¹</td>
<td>0.44 ± 0.06%-ms⁻¹</td>
</tr>
<tr>
<td>norm. MRTDvol thigh (n=5)</td>
<td>1.30 ± 0.59%-ms⁻¹</td>
<td>1.20 ± 0.39%-ms⁻¹</td>
</tr>
<tr>
<td>norm. MRTDstim thigh (n=6)</td>
<td>3.48 ± 0.77%-ms⁻¹</td>
<td>3.16 ± 0.33%-ms⁻¹</td>
</tr>
</tbody>
</table>

*MVC,* maximal voluntary torque; *norm.* MRTD, normalized maximal rate of torque development; *vol,* voluntary; *stim,* stimulated. * significantly different from pre ULLS values (p<0.05)

### Jump height

Figure 6.2 shows that two leg jump height decreased significantly (p=0.02) by 20 ± 13%. One leg jump height with the right (suspended) leg decreased significantly (p=0.006) with 28 ± 13%, whereas jump height with the left (non-suspended) leg did not change (p=0.48).

![Figure 6.2: Jump height pre and post unilateral lower limb suspension for 2 leg squat jumps and 1 leg squat jump with right (suspended) and left (non-suspended) leg. * significantly different from pre ULLS.](image)

![Figure 6.3: Per subject pre and post unloading maximal voluntary contraction (MVC) torque and jump height values.](image)
Figure 6.4: Relation between changes (ratio post/pre unloading value) in triplet torque and jump height.

Figure 6.5: Relation between change (post/pre unloading value) in MVC and jump height.

Relations between torque variables and jump height

Figure 6.3 shows that in all subjects both jump height and MVC\textsubscript{ke} were lower post unloading. The relation between reductions in maximal triplet torque and one leg (right) jump height was significant ($r=0.83$, $p=0.04$, Figure 6.4). The relation between the reductions in jump height and MVC\textsubscript{ke} ($r=0.71$, $p=0.11$, Figure 6.5) tended to be significant. These findings suggest that the decreases in force capacity of the knee extensor muscles made an important contribution to the decline in jump performance. No significant correlations were found between changes in MVC\textsubscript{pf} and 1-leg jump height ($r=0.63$, $p=0.18$).

Discussion

As hypothesized from literature findings, no relations were found between any of the muscle variables and jump height before ULLS. As also expected, maximal voluntary torque, absolute maximal rate of torque development during voluntary contractions of plantar flexor muscles and electrically evoked MRTD in the knee extensor muscles significantly decreased after 3 weeks of unloading. However, maximal voluntary
activation of the knee extensors was not affected by ULLS. When normalized for maximal torque, MRTDs did not change after unloading, indicating that the reduction in MRTD could be fully accounted for by the reduction in maximal torque. Two leg jump height and jump height of the suspended leg decreased significantly. Most importantly, the decreases in isometric knee extensor torque were significantly related (involuntary by triplet) or tended to be related (voluntary as MVC\textsubscript{ke}) to the decreases in jump height.

Torque
Our study showed a significant decrease of 12\% in the MVC of the plantar flexors after ULLS and the MVC of the knee extensors decreased with 21\%, which is well in accordance with the 21\% decrease in knee extensor torque found by de Boer \textit{et al.}\textsuperscript{8} after 23 days of ULLS. The decreased maximal voluntary torque with unchanged, maximal voluntary activation, suggests that the loss of muscle mass (decrease in CSA) was the dominating factor. This was confirmed by the decrease in calf circumference and in thigh triplet torque of the suspended leg following ULLS.

\textit{Contraction speed}
Absolute MRTD during fast voluntary contractions in the calf was significantly reduced by 17\% after 3 weeks of ULLS, which is in line with the results of Duchateau \textit{et al.}\textsuperscript{16} who showed that maximal rate of torque development of the calf during voluntary contractions was reduced by 24\% after 5 weeks of bed rest. However, if we normalize the maximal rate of torque development to maximal voluntary torque, we did not observe differences pre and post ULLS, which is also in line with the findings of Duchateau \textit{et al.}\textsuperscript{16} and Mulder \textit{et al.}\textsuperscript{34}. This suggests that the reduction in MRTD can be fully accounted for by the reduction in maximal torque. Moreover, it indicates that muscle fiber contractile speed was not significantly increased, which could have occurred if unloading had led to a shift of fiber types towards fast twitch fibers and potentially increased muscle fiber maximum shortening velocity after unloading would attenuate the reduction in function, reported by others\textsuperscript{29,48,46,43}. However, care has to be taken with interpretation of (lack of) changes in MRTD, since other factors
such as an unloading induced decrease in tendon stiffness, changes in muscle architecture\(^8\) or altered calcium movements and sarcoplasmic reticulum function\(^5\) potentially could have had the opposite effect (decrease) on MRTD.

**Jump height**

As expected, jump height of the non-suspended leg did not change, whereas the jump height of the suspended leg and the two-legged squat performance deteriorated significantly after unloading with 28 and 21% respectively. To our knowledge there are no other studies in which the effects of unloading on jump performance, or other dynamic whole body tasks, in correlation with changes in muscle variables were investigated. As stated before, relations between MVC torque and MRTDs of isolated muscles groups and jump height are often weak or absent without an experimental intervention. Also in the present study, both before and after ULLS this was the case (pre, \(r=0.42\); post, \(r=0.69\)). However, on the individual level the decreases in maximal torque of were accompanied by decreases in jump performance. Despite the small sample size of the present study the relation between reduction in triplet torque and decrease in jump height was significant and the decrease in MVC of the knee extensors tended to be related to the reduction in jump height after ULLS. Response diversity among subjects following unloading with respect to the muscle mass reduction and force decline has been found in other studies and probably is genetically determined. The present findings indicate that the extent of muscle force losses have direct effects for maximal performance of more complex whole body motor tasks such as jumping.

**Conclusions**

This study shows that limb unloading by 3 weeks of unilateral lower limb suspension induced significant reductions in maximal torque of plantar flexor and knee extensor muscles and in maximal rate of torque development of the plantar flexors. Voluntary activation was not affected by 3 weeks of ULLS. Jump height, taken as indicator for whole body performance was also significantly reduced. Whereas cross-sectional studies and our separate pre and post ULLS data indicated only poor relations
between maximal muscle torque (and speed) and jump height, the reduction in triplet 
torque (torque independent of voluntary activation) after ULLS was significantly 
related to the reduction in jump height. Thus, although muscle torque in itself was not 
related to jump performance, ULLS induced changes in torque production during 
static contractions of a single leg muscle group had clear consequences for dynamic 
multi-joint squat jump performance. Furthermore, the present findings indicate that 
when comparing subjects, the different effects of ULLS on the decrease of maximal 
muscle force determine to an important extent the decline in jump performance.

References

1. Alkner BA, Tesch PA. Knee extensor and plantar flexor muscle size and function following 90 days of 
2. Andersen LL, Aagaard P. Influence of maximal muscle strength and intrinsic muscle contractile 
   of resistance exercise during bed rest on skeletal muscle sarcopenia and myosin isoform distribution. J 
6. Berg HE, Tesch PA. Changes in muscle function in response to 10 days of lower limb unloading in 
8. de Boer MD, Maganaris CN, Seynnes OR, Rennie MJ, Narici MV. Time course of muscular, neural and 
   tendinous adaptations to 23 day unilateral lower-limb suspension in young men. J Physiol 2007;583(Pt 
   3):1079-1091.
9. de Haan A. The influence of stimulation frequency on force-velocity characteristics of in situ rat medial 
   gastrocnemius muscle. Exp Physiol 1998;83(1):77-84.
10. de Ruiter CJ, de Korte A, Schreven S, de Haan A. Leg dominance in relation to fast isometric torque 
11. de Ruiter CJ, Kooistra RD, Paalman MI, de Haan A. Initial phase of maximal voluntary and electrically 
    stimulated knee extension torque development at different knee angles. J Appl Physiol 


Chapter 6: Jump height and functional performance after limb suspension
