Voluntary activation failure contributes more to plantar flexor weakness than antagonist coactivation and muscle atrophy in chronic stroke survivors

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Klein CS, Brooks D, Richardson D, McIlroy WE, Bayley MT. Voluntary activation failure contributes more to plantar flexor weakness than antagonist coactivation and muscle atrophy in chronic stroke survivors. J Appl Physiol 109: 1337–1346, 2010. First published August 19, 2010; doi:10.1152/japplphysiol.00804.2009.—The contributions of nervous system muscle activation and muscle atrophy to poststroke weakness have not been evaluated together in the same subject. Maximal voluntary contraction (MVC) torque, voluntary activation (twitch interpolation), and electromyographic (EMG) amplitude were determined bilaterally in the plantar flexors of seven chronic stroke survivors (40–63 yr, 24–51 mo poststroke). Volumes of the plantar flexor muscles were determined bilaterally with magnetic resonance imaging (MRI). The mean (±SD) contralesional (paretic) MVC torque was less than one-half of the ipsilesional leg: 56.7 ± 57.4 vs. 147 ± 35.5 Nm (P = 0.006). Contralesional voluntary activation was only 48 ± 36.9%, but was near complete in the ipsilesional leg, 97 ± 1.9% (P = 0.01). The contralesional MVC EMG amplitude (normalized to the maximum M-wave peak-to-peak amplitude) of the gastrocnemii and soleus were 36.0 ± 28.5 and 36.0 ± 31.0% of the ipsilesional leg. Tibialis anterior (TA) EMG coactivation was not different between the contralesional (23.2 ± 24.0% of TA MVC EMG) and ipsilesional side (12.3 ± 5.7%) (P = 0.24). However, TA EMG coactivation was excessive (71%) in one subject and accounted for ~8% of her weakness based on the estimated antagonist torque. Relative (%ipsilesional leg) plantar flexor and gastrocnemii volumes were 88 ± 6% (P = 0.004) and 76 ± 15% (P = 0.01), respectively. Interlimb volume differences of the soleus, deep plantar flexors, and peronei were not significant. Preferred walking speed (0.83 ± 0.33 m/s) was related to the contralesional MVC torque (r² = 0.57, P = 0.05, N = 7), but the two subjects with the greatest weakness walked faster than three others. Our findings suggest that plantar flexor weakness in mobile chronic stroke survivors reflects mostly voluntary activation failure, with smaller contributions from antagonist activity and atrophy.

hemiparesis; muscle volume; magnetic resonance imaging; torque; soleus; gastrocnemius

NEUROMUSCULAR WEAKNESS is common in chronic stroke survivors (>1 yr), demonstrated by a lower maximal voluntary contraction (MVC) strength of the contralesional (paretic) than ipsilesional limb (29, 47, 50). Weakness may arise from impairments of the nervous and muscular systems (41). There may be a reduction in descending input to contralesional motoneurons, resulting in a decline in muscle activation (4, 14). Weakness may also reflect muscle atrophy (11, 12, 24, 38, 39, 43), spasticity (29), and excessive antagonist activity (29, 54). Despite the importance of strength for daily functions (36), the contributions of muscle activation and atrophy to poststroke weakness have not been evaluated together in the same subject.

The MVC torque reflects the algebraic sum of torques produced by the agonist and antagonist muscles and thus is affected by their level of activation (6). The capacity for agonist muscle activation can be measured through the application of electrical stimulation to the muscle or motor nerve during a MVC (e.g., twitch interpolation) (3). Activation capacity in healthy adults is ~90% during most MVCs (i.e., <10% activation failure) (10, 37, 52), although this level is often difficult to reach in the plantar flexors (3). Few studies have determined activation capacity in chronic stroke survivors using twitch interpolation, and none evaluated the plantar flexors (33). Activation failure was greater in the contralesional than ipsilesional quadriceps of chronic survivors, but this failure did not explain all of the weakness (33). Newham and Hsiao (37) recorded bilateral quadriceps activation and strength during the first 6 mo following stroke. They reported significant ipsilesional (mean, 25%) and contralesional (40%) activation failure and contralesional weakness (53%) of ipsilesional MVC during the first month poststroke. Over the ensuing 5 mo, contralesional strength improved significantly, but gains in activation were modest and not significant (37).

It is known from electromyographic (EMG) recordings that antagonist muscles are active during a MVC (6). In healthy adults, antagonist EMG amplitude is ~5–25% of the muscle’s maximal (MVC) value when acting as an agonist (e.g., coactivation percentage) (6, 37, 54). Excessive antagonist activity may reduce the MVC torque by restraining the torques generated by the agonist muscles (6). There is some evidence of increased antagonist activity in the contralesional limb of stroke survivors (20, 29, 54), although this is not a universal finding (29, 37). However, an increase in coactivation percentage poststroke may reflect a reduction in the agonist MVC EMG, with little or no increase in absolute antagonist activity (54). In this case, the antagonist torque may be modest and contribute little to weakness. The antagonist torque associated with a given level of antagonist muscle activity can be estimated from the EMG amplitude-torque relationship of the same muscle when acting as an agonist (6).

Plantar flexor weakness following stroke may compromise mobility, since these muscles provide most of the power for forward gait progression (53). It is known that stroke subjects with the weakest ankle plantar flexors tend to walk at the slowest speeds (36). Although plantar flexor weakness and atrophy have not been determined together in the same stroke subject, they have been addressed separately in different studies. The mean contralesional plantar flexor MVC of chronic stroke survivors was reported to be ~70% (50), 50% (29), and 25% (47) of the healthy adult MVC. Odajima et a. (39) found...
that the mean contralesional plantar flexor cross-sectional area (CSA) in well-ambulatory, poor-ambulatory, and wheel-chair-dependent stroke subjects was ~80, 70, and 60% that of healthy adults, respectively. Together, the findings of these studies suggest that some of the plantar flexor weakness is explained by atrophy.

The soleus and gastrocnemii have specialized roles in mobility and together generate ~80% of plantar flexor MVC torque (15, 18). Atrophy is greater in the gastrocnemii than the soleus in human aging and spinal cord injury (8, 35), but whether this is the case following stroke is not known. Gastrocnemii atrophy could limit walking speed, consistent with its relatively large type II fiber content (23). Although MRI is the preferred method for determining the size of adjacent muscles, only one study used it to evaluate muscle morphology poststroke (43). They found that atrophy was greater in the contralesional triceps brachii than biceps brachii (43).

The primary aim of this study was to determine the extent to which voluntary activation failure, antagonist coactivation, and muscle atrophy contribute to plantar flexor weakness in chronic stroke survivors. A secondary aim was to examine the association of these measurements and preferred walking speed. We hypothesized that weakness would reflect both activation failure and atrophy, and that atrophy would be greater in the gastrocnemii than the soleus.

MATERIALS AND METHODS

Subjects

Five men and two women (55.8 ± 3.6 yr) with ischemic or hemorrhagic stroke were recruited from the Toronto Rehabilitation Institute (Table 1). Individuals were included in the study if they had a single stroke at least 2 yr earlier and hemiparesis. Exclusion criteria included persons with musculoskeletal impairments (arthritis, joint injury) or cardiovascular morbidity other than that attributed to stroke, uncontrolled hypertension, and an inability to provide informed consent.

Chedoke-McMaster (19) motor scores of the leg and foot were determined, and they ranged from mild to moderate (Table 1). Subjects 4–6 generally had greater tone, apparent as a more stiff-legged gait, and limited use of the contralesional arm, than the others. Subjects 4 and 7 used a single-point cane when outdoors, and subjects 3 and 6 wore an ankle-foot orthosis.

All subjects could walk independently for extended periods. Four subjects (1, 3, 5, and 6) participated in 20–30 min of aerobic exercise (treadmill, cycle, or elliptical machine) about two times per week at local fitness clubs over the previous 6 mo to 1 yr. None performed any resistance training of the plantar or dorsal flexors. The study was approved by the research ethics committees of the Toronto Rehabilitation Institute and the University of Toronto. Written, informed consent was obtained from the subjects.

Table 1. Characteristics of the study population

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>CMSA, Leg/Foot</th>
<th>Speed, m/s</th>
<th>TSO, mo</th>
<th>Paretic Side</th>
<th>Diagnosis</th>
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<tr>
<td>1</td>
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<td>67</td>
<td>185.4</td>
<td>104.5</td>
<td>5/5</td>
<td>1.35</td>
<td>36</td>
<td>R</td>
<td>Hemorrhage</td>
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<tr>
<td>2</td>
<td>M</td>
<td>63</td>
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<td>81.8</td>
<td>4/4</td>
<td>1.0</td>
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<td>R</td>
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<td>61.4</td>
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<td>37</td>
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<tr>
<td>5</td>
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<td>95.4</td>
<td>3/3</td>
<td>0.58</td>
<td>24</td>
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<td>0.91</td>
<td>48</td>
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<td>Infarction</td>
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</tbody>
</table>

M, male; F, female; CMSA, Chedoke-McMaster Stroke Assessment Score (19); speed, walking speed; TSO, time since onset of stroke; R, right; L, left.

Data Collection

2-min walk. On each of the two visits, and before recording the MVCs, subjects completed a walk test (7). They walked 14 m over a straight course in a premeasured corridor at their preferred pace with their usual walking aids. At the 14-m mark, they turned 180° and walked in the opposite direction over the same course. This walking pattern was repeated until 2 min elapsed. The test administrator walked behind the subject, but provided no encouragement. The distance walked was recorded, and the faster average walking speed of the two visits is reported. The walking speed of the stroke subjects was compared with the speed of 10 healthy control subjects who completed the same test once. They were 6 men (57 ± 6 yr, 178.6 ± 3.5 cm, 88.2 ± 3.5 kg) and 4 women (51 ± 9 yr, 170.6 ± 10.4 cm, 63.6 ± 4.2 kg).

Calf circumference. The circumference of both legs in the region of the largest calf girth was determined with a cloth tape measure.

Setup for MVC torque, EMG, and voluntary activation recordings. The subjects were tested on two visits to the laboratory. To minimize general fatigue, only one leg was tested per visit. The MVC of the contralesional leg was recorded during the first visit. Approximately 1 wk later, the MVC of the ipsilesional leg was recorded. We deemed that a second test session of the same leg was unnecessary to characterize limb differences in strength and activation. Previous studies found no significant differences in contralateral plantar flexor strength between the first testing session and a second session held 2–4 days (13) or 7 days later (44).

Subjects sat in a custom-built chair with their leg positioned in a torque-measuring dynamometer. The dynamometer was custom-made based on the blueprint of a device described previously (31). The angle of the knee and hip joints were 90°. The knee was stabilized from above with a U-shaped clamp. The foot was secured on the steel plate of the device with two Velcro straps: one across the instep, and the other 1 cm proximal to the great toe. The ankle joint was dorsiflexed 10° from the neutral (0°) position, which is the angle associated with peak or near peak (~95%) MVC torque (45). Bilateral MVCs were carried out at the neutral position in two subjects (subjects 2 and 6) because their contralesional ankle could not be dorsiflexed beyond neutral. During the recordings, the opposite leg was not restrained, and the foot rested on a stool. Despite the shorter gastrocnemii length in the flexed than the extended knee position, the magnitude of plantar flexor weakness following stroke has been found to be independent of knee joint angle (i.e., 90 vs. 180°) (48).

Disposable silver-silver chloride EMG electrodes (Bortec Biomedical, Calgary, Alberta) were used to record the MVC EMG and compound action potentials (M-waves). The electrodes were placed in a bipolar configuration (2 cm center-to-center spacing) over the distal third of the tibialis anterior (TA), lateral gastrocnemius (LG) medial gastrocnemius (MG), and midline of the soleus (2 cm below the distal end of the MG). A ground electrode (1-cm disk) was placed at the midlevel of the medial surface of the tibia.

The raw EMG signals were amplified (~500) and filtered between 30 Hz and 1 kHz (Astro-Medical, model P511, West Warwick, RI). Torque was sensed by a load cell (LCD-500, Omega Engineering,
Stamford, CT) located below the ankle joint and then amplified (×400) and filtered (DC-100 Hz). The device was calibrated by measuring the DC voltage when known weights were attached to the foot plate. Torque and EMG signals were converted to digital format by a 12-bit converter (1401 Plus, Cambridge Electronic Design, Cambridge, UK) at sampling rates of 500 and 2,000 Hz, respectively, and analyzed offline using Spike 2 software (Spike 2, version 5.13, Cambridge Electronic Design).

M-wave protocol. Single pulses (50- or 100-μs duration) were applied over the tibial nerve in the popliteal fossa using a constant-current stimulator (DS7A, Digitimer, Herthfordshire, UK) and bar electrode (Medtronic, Skovlunde, Denmark) (3). Initially, the position of the bar electrode was adjusted so that mild-intensity pulses (~25–100 mA) evoked an M-wave in the soleus, LG, and MG. Single pulses were then applied every 5 s at progressively greater current intensity (5-mA increments) until the soleus M-wave peak-to-peak amplitude reached a maximum (Mmax), as displayed on an oscilloscope. That is, M-wave peak-to-peak amplitude did not increase, despite five increments in current intensity. This procedure also evoked Mmax in the LG and MG in five of the seven subjects, as confirmed by checking the recorded M-waves. However, the LG or MG M-wave did not reach Mmax with the above process in two subjects (e.g., reached ~85% of the Mmax). In these subjects, additional step increments in current were applied over and above that needed to evoke the soleus Mmax to achieve the gastrocnemii Mmax.

MVC and voluntary activation protocol. A few brief (2–3 s) practice contractions of the plantar flexors were completed during which subjects were instructed to exert about one-half of their maximal effort. Three to four MVCs were then recorded, each lasting ~4–5 s followed by a 2-min rest. Subjects were strongly encouraged to give their best effort, and feedback of the torque trace was provided. Single supramaximal pulses (50- or 100-μs duration) were applied over the tibial nerve during and after each MVC to determine the voluntary activation (3, 16). The investigator triggered the stimulation manually ~2–4 s after MVC onset, when the torque trace plateaued, and again ~1 s after the torque returned to the baseline. Stimulus current was 120% of the current that evoked Mmax in the soleus, LG, and MG.

Dorsiflexor MVC and submaximal torque protocol. After recording the plantar flexor MVCs, three to four dorsiflexor MVCs (and associated activation and EMG measures) were recorded. In addition, subjects completed a series of 3- to 4-s submaximal dorsiflexor contractions at progressively greater torque, with each contraction separated by ~30 s of rest. These targeted torques (displayed on the oscilloscope) started at ~10% MVC and increased by steps of 5–10% MVC until a torque of ~50–70% MVC was achieved. This procedure was done to characterize the TA root-mean-square (RMS) EMG-dorsiflexor torque relationship, from which antagonist torque associated with the plantar flexor MVC was estimated (6). Only data pertaining to TA coactivation are reported in the results.

MRI acquisition. Images of the leg were acquired up to 1 mo after recording the MVCs. Subjects were supine in a 3T whole body scanner with the lower leg in a quad head coil (Signa Excite HDx, General Electric). The leg was extended (knee angle of 180°) and elevated slightly with padding under the knee and ankle to avoid compressing the plantar flexors. The ankle was stabilized in ~20° of plantar flexion, as measured with a goniometer. The opposite leg was placed outside the coil and was supported with padding. Serial T1-weighted spin-echo sequences were acquired from each leg separately. The order in which the contralesional and ipsilesional leg was scanned was balanced across subjects. Scout images of the lower leg were acquired in the coronal and sagittal planes. On the monitor display, a grid of ~40–50 axial slices was aligned perpendicular to the tibial shaft in the coronal and sagittal planes, between the knee and ankle joints. Images were acquired in an interleaved fashion using the following parameters: repetition time 850 ms, echo time 18 ms, field of view 200 mm, matrix 256 × 256, slice thickness 10 mm, interslice gap 0 mm, number of acquisitions 2.

Data Analysis

M-waves and twitch torque. Three parameters of the Mmax potential were determined (Fig. 1A): 1) latency, the time from the onset of the stimulus to the onset of the potential; 2) duration, the time between

![Fig. 1. M-wave peak-to-peak maximum amplitude (Mmax) and maximal voluntary contraction (MVC) recordings in subject 4. A: Mmax potentials of the contralesional (solid trace) and ipsilesional (dotted trace) soleus, lateral gastrocnemius (LG), and medial gastrocnemius (MG) via tibial nerve stimulation (post-MVC-evoked responses), and tibial anterior (TA) via common peroneal nerve stimulation. The arrows indicate the beginning and end of the contralesional MG Mmax. Note the MG amplitude calibration bar corresponds to 2 mV in the contralesional limb and 4 mV in the ipsilesional limb. B: plantar flexor MVC torque in the contralesional (top trace) and ipsilesional (bottom trace) leg. Below the torque traces are the associated bilateral raw electromyographic (EMG) signals of the soleus, LG, MG, and TA. The large spikes (truncated) in the EMG records correspond to the evoked M-waves.](http://jap.physiology.org/DownloadedFrom/)
the onset of the potential and the end of the second phase of the potential (in some cases three or four phases), defined by isoelectric crossings; 3) peak-to-peak amplitude, the absolute sum of the largest positive and negative peaks of the potential. The peak twitch torque was the difference between baseline and maximum torque.

**MVC torque and voluntary activation.** The peak MVC torque over the 500-ms period before the interpolated twitch was determined for each trial. The interpolated torque was the difference between the torque at the onset of the stimulus (e.g., the event marker) and the evoked peak torque. Voluntary activation was calculated according to the following: \[ \frac{1}{2} \left( \frac{T_t}{T_s} \right) \times 100\% \], where \( T_s \) was the interpolated torque evoked by the stimulus during the MVC, and \( T_t \) was the peak torque of the postcontraction twitch (16).

**MVC EMG.** The RMS EMG of the soleus, LG, MG, and TA were determined over a 500-ms period of each MVC trial, just before the interpolated twitch, and encompassed the peak torque. Comparisons of absolute EMG between the contralesional and ipsilesional limb may be confounded by peripheral-related factors, including electrode placement and skin impedance (5, 45). To minimize these peripheral effects, the MVC RMS EMG of the soleus, LG, and MG, and TA were normalized to their respective Mmax bilaterally (e.g., MVC RMS EMG/M-wave amplitude). The normalized MVC RMS EMG of the LG and MG were averaged together and are presented as gastrocnemii EMG in the results.

**Antagonist coactivation.** The TA RMS EMG over a 500-ms period of the plantar flexor MVC was determined bilaterally. This TA activity was expressed as a percentage of the maximal TA RMS EMG recorded during a dorsiflexor MVC (e.g., coactivation percentage). The TA RMS EMG-dorsiflexor torque data corresponding to the submaximal contractions were plotted and analyzed with linear regression. Antagonist torque (Nm) associated with the plantar flexor MVC was estimated by substituting the absolute TA coactivation EMG (mV) into the linear regression equation (see Fig. 3).

**Muscle volume.** The images were converted from original DICOM format into TIFF files. The same investigator analyzed the images on a computer using available software (ImageJ, version 1.38, National Institutes of Health, Bethesda, MD). The border of each muscle or muscle group was manually traced for all axial slices from origin to insertion, and the associated CSAs were determined (25). Visible muscle compartments were determined over a 500-ms period of each MVC trial, just before the interpolated twitch was determined for all subjects. Correlations between contralesional MVC or muscle volume and walking speed are based on all seven subjects. Hereafter, MVC RMS EMG and TA RMS EMG are referred to as MVC EMG and TA EMG, respectively. Also, the terms relative MVC torque, relative MVC EMG, and relative volume refer to the contralesional value as a percentage of the ipsilesional value. Differences were considered significant when \( P < 0.05 \), and data are presented as means ± SD.

## RESULTS

**Bilateral M-wave, MVC torque, and EMG recordings of one subject (subject 4) are shown in Fig. 1.** The LG and MG Mmax were smaller in the contralesional (continuous trace) than ipsilesional leg (dotted trace), whereas the difference in soleus Mmax was negligible (Fig. 1A). Note the greater ipsilesional than contralesional MVC torque (Fig. 1B, top two traces). Also note the relatively large interpolated twitch corresponding to a contralesional activation of only 43% and sparse EMG. Absolute TA EMG activity was less in the contralesional than ipsilesional limb (Fig. 1B, bottom two traces). However, the calculated TA coactivation percentage was larger in the contralesional (11%) than ipsilesional leg (6%), indicative of the small relative TA MVC EMG (16%).

### M-Waves and Twitch Torque

The differences between the contralesional and ipsilesional gastrocnemii Mmax latency (4.8 ± 0.5 vs. 4.7 ± 0.6 ms), duration (15.5 ± 5.0 vs. 12.6 ± 2.9 ms), and amplitude (5.0 ± 1.0 vs. 7.9 ± 4.0 mV) were not significant. Corresponding data for soleus Mmax were also not different between limbs: 6.4 ± 1.4 vs. 6.6 ± 1.3 ms, 18.9 ± 8.3 vs. 14.1 ± 2.8 ms, and 3.9 ± 0.9 vs. 5.3 ± 4.0 mV. Across subjects, the gastrocnemii and soleus Mmax amplitude and duration were not significantly correlated to their respective volume, nor to MVC torque or absolute MVC EMG. These findings suggest that contralesional MVC EMG deficits have more to do with altered neural drive than peripheral influences (e.g., muscle conduction velocity, muscle size) (5). Despite voluntary weakness, twitch torque was greater in the contralesional (25.8 ± 6.1 Nm) than the ipsilesional leg (20.3 ± 4.5 Nm) \( (P = 0.04, N = 7) \).

**MVC Torque and Voluntary Activation**

Contralesional MVC torque averaged only 38% (range, 0–90%) of the ipsilesional MVC: 56.7 ± 57.4 vs. 147 ± 35.7 Nm \( (P = 0.006, N = 7) \). Contralesional voluntary activation was 48.5 ± 36.9% (0–92%), much less than the ipsilesional leg: 96.8 ± 1.9% (94–99%) \( (P = 0.001, N = 7) \). No contralesional MVC EMG or torque was evident in subject 7 during attempted plantar (dorsal) flexion, although EMG activity was present when walking. For this subject, MVC torque, MVC EMG, and activation were assigned a value of zero.

**MVC EMG**

The gastrocnemii MVC EMG-to-Mmax ratio was less in the contralesional than ipsilesional side: 0.012 ± 0.01 and 0.042 ± 0.018, respectively \( (P = 0.02, N = 7) \). The corresponding values for the soleus were 0.016 ± 0.013 and 0.042 ± 0.016, respectively \( (P = 0.02, N = 7) \). The relative gastrocnemii and
soles MVC EMG averaged 36.0 ± 28.5 and 36.0 ± 31.0%, respectively.

**Antagonist Coactivation**

Coactivation percentage tended to be larger in the contralesional (23.2 ± 24.0%, range 5–71%) than ipsilesional leg (12.3 ± 5.7%, range 6–21%), but the difference was not significant (P = 0.24, N = 6). The larger contralesional mean reflected the much larger contralesional than ipsilesional values in subject 3, evident during all three MVCs: 71, 61, and 59 vs. 21, 21, and 20%. The augmented contralesional coactivation percentage in this subject reflected a larger absolute coactivation EMG combined with a smaller contribution from atrophy. Across six subjects (excluding subject 7), relative MVC torque was positively associated with voluntary activation \( (r^2 = 0.88, P = 0.006) \) and relative MVC EMG \( (r^2 = 0.84, P = 0.01) \), but not with relative plantar flexor \( (r^2 = 0.24; P = 0.3) \) or gastrocnemii \( (r^2 = 0.18; P = 0.4) \) volumes (Fig. 2B).

We estimated the antagonist torque bilaterally using the TA EMG-dorsiflexor torque linear regression equation (6). The TA EMG increased linearly with increasing dorsiflexor torque in both limbs of all subjects, with coefficients of determination \( (r^2) \) above 0.9 in all cases. For subject 3, the linear regression equations for the contralesional and ipsilesional limb were

\[
\begin{align*}
\text{y} & = 0.010 + 0.07 (r^2 = 0.96) \\
\text{y} & = 0.016x + 0.002 (r^2 = 0.97)
\end{align*}
\]

respectively (Fig. 3). Antagonist torque was estimated by substituting the absolute coactivation EMG \( (y) \) of the contralesional \( (0.23 \text{ mV}) \) and ipsilesional leg \( (0.15 \text{ mV}) \) into the respective equations and solving for \( x \). For subject 3, the estimated antagonist torque was larger in the contralesional (16 Nm) than ipsilesional leg (9 Nm). Accounting for the antagonist torque bilaterally by adding them to the plantar flexor

**Central vs. Peripheral Contributions to Weakness**

The largest recorded relative MVC torque and the associated activation and relative MVC EMG (average of gastrocnemii and soleus), as well as relative total plantar flexor volume, are shown for each subject in Fig. 2B. These data suggest that most of the weakness can be attributed to voluntary activation failure with a smaller contribution from atrophy. Across six subjects (excluding subject 7), relative MVC torque was positively associated with voluntary activation \( (r^2 = 0.88, P = 0.006) \) and relative MVC EMG \( (r^2 = 0.84, P = 0.01) \), but not with relative plantar flexor \( (r^2 = 0.24; P = 0.3) \) or gastrocnemii \( (r^2 = 0.18; P = 0.4) \) volumes (Fig. 2B).

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**Variability of Voluntary Activation, Relative MVC EMG, and Relative MVC Torque**

Individual data corresponding to the four recorded contralesional MVCs in subject 1 and all three recorded contralesional MVCs in each of subjects 2–6 are presented to show the variance of the data (Fig. 2A). Shown left to right for each subject are voluntary activation, relative MVC EMG (average of gastrocnemii and soleus), and relative MVC torque. Differences between contralesional MVC trials were modest. The mean contralesional SD and range (N = 6), compiled from the individual subject SD for all trials for activation, relative MVC EMG, and relative MVC torque were 3.7% (0.5–10%), 4.2% (0.1–13%), and 3.2% (0.7–6%), respectively.

Fig. 2. A: individual contralesional voluntary activation (▲), relative (%ipsilesional side) MVC EMG (●), and relative MVC torque (○) for all plantar flexor MVC trials in subjects 1–7. The MVC EMG is the average of the gastrocnemii and soleus after normalization to each muscle’s Mmax. B: the largest recorded relative MVC torque and associated voluntary activation and relative MVC EMG in each subject. Also shown is the relative total plantar flexor volume (■).

Fig. 3. Relationship between TA root-mean-square EMG and dorsiflexor torque of the contralesional (▲) and ipsilesional leg (●) in subject 3. The best fit line through these measures, but excluding the MVC (rightmost data points), is shown. The dorsiflexor antagonist torque (Nm) at the recorded level of TA EMG coactivation (mV), estimated from the regression equation, is displayed (dotted lines and arrows) for the contralesional (16 Nm at 0.23 mV) and ipsilesional leg (9 Nm at 0.15 mV).

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MVC torques increased the relative (%ipsilesional leg) plantar flexor MVC torque by 8% (from 56 to 64%). Hence, ~8% of her recorded weakness may be attributed to antagonist restraint. For all subjects combined, the antagonist torque was not different between the contralesional (4.5 ± 6.2 Nm, range 0.1–16 Nm) and ipsilesional leg (7.0 ± 3.2 Nm, range 1–9 Nm) (P = 0.24, N = 6). Accounting for the antagonist torque bilaterally in all subjects did not increase the relative MVC torque significantly (mean increase, 1.1 ± 4.4%, range, −3–8%, N = 6).

**Muscle Volume**

The mean contralesional total plantar flexor volume (cm³) was 88 ± 6% (range 80–96%) of the ipsilesional side: 1.019 ± 297 vs. 1.154 ± 319 cm³ (P = 0.004, Fig. 2B). Side-to-side volume differences varied widely across subjects in the gastrocnemii, deep plantar flexors, and peronei, but minimally in the soleus (Figs. 4 and 5). The mean contralesional gastrocnemii volume was only 76 ± 15% of the ipsilesional leg: 253 ± 91 vs. 334 ± 104 cm³ (P = 0.01). The soleus, deep plantar flexor, and peronei volumes were not significantly different between the contralesional and ipsilesional leg: 442 ± 117 vs. 454 ± 126; 205 ± 75 vs. 238 ± 68; and 119 ± 42 vs. 126 ± 56 cm³, respectively.

**Plantar Flexor Muscle and Fat Anatomic CSA**

The maximal anatomic CSA of the contralesional plantar flexors averaged 89 ± 10% (range, 78–107%) of the ipsilesional leg: 49.5 ± 13.5 vs. 55.6 ± 14.2 cm² (P = 0.01). The plantar flexor fat CSA was higher in the contralesional than ipsilesional leg, but the difference was not significant: 1.6 ± 0.5 vs. 1.2 ± 0.8 cm² (P = 0.06). The relative fat CSA was greater in the contralesional than ipsilesional leg: 3.4 ± 1.6 vs. 2.0 ± 1.3% of the plantar flexor CSA (P = 0.03). The absolute and relative (% of leg CSA) subcutaneous fat CSA were not different between the contralesional (15.3 ± 7.9 cm² and 16.0 ± 8.5%) and ipsilesional side (13.9 ± 8.5 cm² and 13.6 ± 8.0%) (both P > 0.2).

**Calf Circumference**

The contralesional calf circumference, measured at the largest girth with a tape measure, was 3.0, 1.5, and 2.0 cm smaller than the ipsilesional limb in subjects 2, 4, and 6, respectively.

In the remaining four subjects, the contralesional circumference was <1.0 cm smaller or larger than the ipsilesional limb. The mean circumference was not different between the contralesional and ipsilesional limb: 36.6 ± 3.7 cm (30.1–41.0 cm) vs. 37.6 ± 4.2 cm (30.5–42.0 cm) (P = 0.12, N = 7).

**2-min Walk**

The stroke subjects walked an average of 95.7 ± 37.7 m (58.7–162.8 m) over the 2 min, and the mean walking speed was 0.83 ± 0.33 m/s (0.5–1.4 m/s, N = 7, Table 1). Corresponding values for the 10 controls were of 139.1 ± 16.3 m (126–165.6 m) and 1.16 ± 0.14 m/s. Walking speed was slower in the stroke survivors than the controls (P = 0.008, unpaired t-test).

Walking speed and MVC torque (Nm) were correlated in the contralesional (r² = 0.57, P = 0.05), but not the ipsilesional, limb (r² = 0.04, P = 0.6) (N = 7). The correlations between walking speed and relative MVC EMG of the gastrocnemii (r² = 0.5, P = 0.07), soleus (r² = 0.33, P = 0.18), and both muscles combined (r² = 0.42, P = 0.11) were not significant (N = 7). If data for subject 7 are excluded because of zero MVC values, the correlations between walking speed and contralesional MVC (Nm) (r² = 0.8, P = 0.01), and relative MVC EMG of the gastrocnemii (r² = 0.86, P = 0.006), soleus (r² = 0.55, P = 0.09), and both muscles combined (r² = 0.72, P = 0.03) all increase (N = 6). The correlation between walking speed and activation was not significant with (r² = 0.1, P = 0.4), or without (r² = 0.3, P = 0.2) subject 7 included. There were no associations between walking speed and contralesional coactivation percentage (r² = 0.1; P = 0.5, N = 7), or relative volumes (%ipsilesional side) of the gastrocnemii (r² = 0.05; P = 0.6, N = 7) and other plantar flexor muscles.

![Fig. 4. Axial magnetic resonance images of the ipsilesional (A) and contralesional (B) leg of subject 6, taken 8 cm distal to the fibular head. Note the MG, LG, and tibialis posterior (TP, a deep plantar flexor) are smaller in the contralesional than ipsilesional leg, whereas the soleus (S) is affected little. DF; dorsiflexors.](http://jap.physiology.org/Downloadedfrom)
DISCUSSION

To the best of our knowledge, this is the first study to address the contributions of voluntary activation failure, antagonist activity, and atrophy to weakness in the same stroke subject. The plantar flexors were weaker in the contralesional than ipsilesional leg, consistent with earlier reports (1, 29, 47, 48, 50). Our main finding is that the weakness across subjects is caused by activation failure. Also, we show that antagonist activity and atrophy may contribute to weakness in some persons, but to a much lesser extent than activation failure. Changes in specific tension (14), muscle architecture (17), and force transference may also cause weakness, but data on these factors following stroke is limited.

Voluntary Activation and Strength

Since muscles receive some of their innervation from the ipsilateral motor cortex, the ipsilesional side usually exhibits some weakness or neural deficit after stroke (1, 37). However, ipsilesional activation was close to 100% in our subjects. Furthermore, the mean ipsilesional strength (154 Nm) is comparable to healthy adult strength recorded with a similar device (149 Nm, average of men and women, 40–52 yr) (52). Others reported that mean ipsilesional plantar flexor or quadriceps strength of chronic stroke survivors was not different or ~10% less than that of healthy adults (1, 30). Our results suggest that favoring of the ipsilesional leg at the expense of the contralesional leg may help to preserve activation capacity and strength (30).

In contrast to the maintenance of ipsilesional activation and strength, large deficits occurred in the contralesional leg. The mean contralesional activation, MVC EMG, and MVC torque were all less than one-half of the ipsilesional values. Further evidence that activation failure is a major cause of weakness is shown by the strong association between activation and relative MVC torque ($r^2 = 0.88$, Fig. 2B). Our findings support earlier studies of poststroke activation failure using twitch interpolation (33, 37). In chronic survivors, Miller and colleagues (33) found that those with a lower quadriceps activation ratio (a variant of the measure used here) tended to show greater weakness. Interestingly, mean contralesional quadriceps activation (70%) and relative MVC torque (78%) 6 mo after stroke (37) are greater than the corresponding values in the present study. This difference may indicate that the plantar flexors are more susceptible than the quadriceps to poststroke activation failure and weakness, but this issue requires further study.

The explanation for voluntary activation failure is not well understood (1). A portion of the descending input to the plantar flexor motoneuron pool may be interrupted as a result of the lesion (e.g., partial muscle paralysis) (4). In addition, activation failure may also reflect a reduced ability to recruit and fully activate motor units still under voluntary control (14, 22). Frontera and colleagues (14) found that TA motor unit firing rates during a contralesional dorsiflexor MVC were ~15 Hz in stroke survivors, about one-half of the normal rate. At such low firing rates, motor units may not reach maximal tetanic force. The different severity of activation failure and weakness across the present subjects may reflect numerous influences, including stroke severity, early treatment and rehabilitation, and limb disuse (9, 41, 42).

On average, the contralesional activation was 15% greater than the relative MVC EMG ($P = 0.12$), with larger differences in subjects 2 and 3 (Fig. 2B). This observation suggests that activation via twitch interpolated and the relative MVC EMG may not provide similar estimates of activation impairment in paretic muscles. Part of this disparity could reflect systematic differences that are independent of stroke. In healthy adults, activation was also greater than relative MVC EMG during quadriceps forces between 25 and 75% MVC (26).

Antagonist Coactivation

In addition to activation failure, excessive antagonist activity may also cause weakness (20, 54). However, apart from subject 3, coactivation percentage and the associated antagonist torque were similar in the contralesional and ipsilesional limb and comparable to healthy adults (6). The excessive contralesional coactivation in subject 3 (71%) was found to account for ~8% of her weakness (Fig. 3). Augmented antagonist activity following stroke may reflect greater diffusion of descending neural drive and/or increased motoneuron excitability (20, 29, 54). Our observations support the notion that antagonist activity is not the primary cause of plantar flexor weakness in chronic stroke survivors (29).

There are few previous data of antagonist activity during plantar flexor MVCs in stroke survivors (29, 54). Yesevich (54) also noted that the TA coactivation percentage was greater in the contralesional (33%) than ipsilesional leg (10%) of 30 stroke survivors, but data were not analyzed statistically. The mean absolute TA EMG (mV) during the plantar flexor MVC was equal in both legs (54), whereas we found this activity to be 40–70% less in the contralesional than ipsilesional limb in four of six subjects (even after normalization to the TA Mmax). Levin and Hui-Chan (29) found no limb differences in the concontraction ratio, e.g., TA EMG/TA EMG + soleus MVC EMG, during a plantar flexor MVC in chronic stroke survivors. However, the concontraction ratio was greater in the contralesional than ipsilesional limb during a dorsiflexor MVC, and the ratio was inversely related to the dorsiflexor MVC force (29). Hence, the contribution of antagonist activity (torque) to dorsiflexor weakness may be greater than the contribution to plantar flexor weakness (6, 29), possibly reflecting the larger mass of the plantar flexors (15).

Muscle Volume

Total plantar flexor volume and anatomic CSA were significantly smaller in the contralesional than ipsilesional limb. Atrophy was most pronounced in subjects 4 (~20%) and 6 (~17%) (Fig. 2B). In healthy adults, a 20% reduction in muscle CSA would be expected to result in a drop in strength of ~20% (15). However, since most fibers may not be recruited during the MVC in our subjects (e.g., subjects 4–7), atrophy likely accounts for <20% of the weakness. Given the variability of activation failure across subjects, it is not surprising that atrophy was unrelated to weakness. The contralesional atrophy and greater fat CSA reported here are consistent with findings in the well-ambulatory stroke survivors studied by Odajima and colleagues (39). They also found that the contralesional total plantar flexor CSA in poor-ambulatory and wheelchair-dependent stroke survivors was smaller than healthy adults by 30 and 40%, respectively. In our subjects,
ipsilesional gastrocnemii volume accounted for ~30% (range, 23–36%) of the total plantar flexor volume, corroborating previous data (15). Hence, a 40% drop in plantar flexor CSA (volume) in immobile stroke survivors (39) likely reflects pronounced gastrocnemii atrophy, as well as atrophy of the other plantar flexors, including the soleus (8). Our muscle CSA measurements excluded visible pockets of fat. If the undetectable amounts of noncontractile tissue are greater in the contralateral than ipsilesional muscle CSA, then we could have underestimated the severity of atrophy.

Plantar flexor atrophy resulted mostly from atrophy of the gastrocnemii and deep plantar flexors, although limb differences were not significant in the latter (Fig. 5). Gastrocnemii atrophy may be a consequence of disuse atrophy of type II fibers (11, 12). Stroke survivors take 50% fewer steps per day than healthy adults (32). Also, the EMG amplitude of the plantar flexors during walking is less in the contralateral than ipsilesional leg (27). Dietz and colleagues (12) found that type II fiber area was 13–51% smaller in the contralateral than ipsilesional MG in four stroke patients. In addition to fiber atrophy, a reduction in fiber length (loss of sarcomeres in series) may also contribute to the smaller gastrocnemii volume (17). Smaller and shorter gastrocnemius fibers may reduce plantar flexor speed and power proportionally more than strength (18, 51). In contrast to gastrocnemii atrophy, soleus volume was preserved. The different response of the two muscles was unrelated to their relative MVC EMG. Habitual use of the soleus may have been adequate to preserve its volume, but this may not have been the case in the gastrocnemii. In healthy adults, the soleus is active more often than the gastrocnemii (34), consistent with its postural role and higher type I fiber content (23).

We are unaware of any plantar flexor volume data in healthy adults who are of similar age to the present subjects. However, the mean ipsilesional volumes of our subjects seem appropriate for their age compared with published mean volumes of younger and older adults (e.g., accounting for the effect of age on volume) (2, 15, 35). The mean volume of the ipsilesional gastrocnemii for the five men (359 cm³, 51–57 yr) we studied was ~10–25% smaller than the mean volumes of that of 20- to 30-yr-old men (2, 15) and ~5–10% larger than that of 60- to 80-yr-old men (15, 35). The mean volume of the soleus (496 cm³) for the five men are up to 5–10% smaller and larger than that of younger and older men, respectively, a difference that is consistent with less age-related change of this muscle (15, 35). Together with these previous findings, the magnitude of atrophy reported here is likely not overstated.

Functional Implications

The stroke subjects walked slower than the controls, and gait speed and contralateral strength were related (r² = 0.57), similar to previous data (36). In addition, we found that gait speed tended to be related to the relative gastrocnemii MVC EMG (r² = 0.5, P = 0.07), but not with relative soleus MVC EMG, plantar flexor activation, or relative volume. Gait speed–strength associations could mean that persons with severe plantar flexor weakness may not be able to generate (or sustain) the plantar flexor moments necessary to walk at normal adult speeds (36). However, scrutiny of individual data (Fig. 2B) suggests that preferred gait speed may not be limited by weakness. Subject 7 was unable to produce MVC EMG or torque, yet had the third fastest walking speed. Also, subject 6 walked faster than subjects 3–5, even though she had greater weakness and gastrocnemii atrophy.

The gait speed of stroke survivors likely reflects the interaction of impairments, e.g., poor balance, weakness, fatigue, and spasticity (12, 27, 36, 46), and compensations/adaptations (28, 36). We can only speculate as to how subjects 6 and 7 walked relatively fast for their level of weakness. The younger age of subject 6 may partially account for her relatively fast walking speed (21). In addition, contralateral plantar flexor stiffness may be relatively greater in subject 6, judging by her reduced dorsiflexion range of motion. Increased contralateral passive forces associated with stiffer muscles may partially offset the decreased active plantar flexor forces during the push-off phase of gait (28). Compensatory activation of the contralateral hip flexors and/or propulsion by the ipsilesional leg may also be greater in subjects 6 and 7 than the others (36). In a study of 17 stroke subjects, 3 had relatively greater maximum gait speed (1.2–1.4 m/s), despite severe plantar flexor weakness (36). These three generated large contralateral hip flexor moments during gait and produced the greatest hip flexion MVCs of the group. Besides the impact of compensations and adaptations on gait speed, it is acknowledged that tests of muscle strength and gait are not necessarily compatible (42). Indeed, leg EMG activity was evident in subject 7 during walking, but not during the MVC. A relatively larger augmentation of leg muscle activation associated with limb loading could contribute to his relatively preserved walking speed (42).

Our findings provide a rationale for incorporating therapies that increase plantar flexor activation and strength (40). Given the activation failure and gastrocnemii atrophy, a combination of resistance training and task-specific exercises may be necessary for developing functional strength and power (41, 49). Those with severe activation failure may benefit more from progressive locomotor type therapies, since load bearing may activate more motor units than an isolated voluntary contraction (42). However, there are relatively few studies of training-induced improvements in leg muscle activation in stroke survivors (49).

In conclusion, our results suggest that much of the plantar flexor weakness in community-dwelling chronic stroke survivors can be attributed to voluntary activation failure. The findings also suggest that atrophy is greater in the gastrocnemii than the soleus following stroke. Subjects were able to attain functional walking speeds, albeit slower than normal, despite plantar flexor weakness and atrophy.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).
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