Force control of quadriceps muscle is bilaterally impaired in subacute stroke

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Chow JW, Stokic DS. Force control of quadriceps muscle is bilaterally impaired in subacute stroke. J Appl Physiol 111: 1290–1295, 2011. First published September 1, 2011; doi:10.1152/japplphysiol.00462.2011.—We tested the hypothesis that force variability and error during maintenance of submaximal isometric knee extension are greater in subacute stroke patients than in controls and are related to motor impairments. Contralateral (more-affected) and ipsilateral (less-affected) legs of 33 stroke patients with sufficiently high motor abilities (62 ± 13 yr, 16 ± 2 days postinjury) and the dominant leg of 20 controls (62 ± 10 yr) were tested in sitting position. After peak knee extension torque [maximum voluntary contraction (MVC)] was established, subjects maintained 10, 20, 30, and 50% of MVC as steady and accurate as possible for 10 s by matching voluntary force to the target level displayed on a monitor. Coefficient of variation (CV) and root-mean-square error (RMSE) were used to quantify force variability and error, respectively. The MVC was significantly smaller in the more-affected than less-affected leg, and both were significantly lower in controls. The CV was significantly larger in the more-affected than less-affected leg at 20 and 50% MVC, whereas both were significantly larger compared with controls across all force levels. Both more-affected and less-affected legs of patients showed significantly greater RMSE than controls at 30 and 50% MVC. The CV and RMSE were not related to the Fugl-Meyer motor score or to the Rivermead Mobility Index. The CV negatively correlated with MVC in controls but only in the less-affected leg of patients. It is concluded that isometric knee extension strength and force control are bilaterally impaired soon after stroke but more so in the more-affected leg. Future studies should examine possible mechanisms and the evolution of these changes.

force steadiness; force variability; force accuracy; knee extension strength; hemiparesis

NEGATIVE EFFECTS OF STROKE on motor function are well documented, including reduced strength and slower rate of torque generation (8), deficits in postural control during quiet standing (22), abnormal muscle activation patterns during gait (35), impaired manual tracking (9), and grip force control (5). Strength testing after stroke typically involves measurement of force (torque, power) during maximal voluntary effort. This is in stark contrast to the actual use of muscles in daily activities, which requires production of submaximal and finely graded forces.

Force control generally refers to the ability to produce accurate and steady muscle output under static or dynamic conditions. Characteristics of force control have been extensively studied in the elderly (16, 25). When asked to maintain a submaximal isometric force, especially at a low level [i.e., ≤10% of maximum voluntary contraction (MVC)], older healthy subjects show greater force variability than young adults in various muscles (63). Force (targeting) error is also greater in elderly compared with young adults (29, 32). However, no difference in force variability between young and elderly has been found during a constant-force task (28, 61). In neurological patients, reduced force steadiness and accuracy have been reported in essential tremor (4), Parkinson’s disease (45), and children with cerebral palsy (2, 54) or developmental coordination disorder (55).

Despite prolific research in motor disorders and rehabilitation after stroke, the effect of stroke on force control has not received much attention until recently. Lodha and colleagues (37) reported increased variability [coefficient of variation (CV)] and regularity (approximate entropy) in isometric wrist/finger extension force in nine stroke subjects 4 mo to 12 yr post-onset. They also found that force variability and regularity at moderate force levels were more increased among patients with lower Fugl-Meyer motor scores in the affected upper extremity. Because the variability in motor output depends, in part, on the muscle tested (25), it is unknown whether findings in the upper extremity can be extended to the lower extremity or whether time after stroke plays any role. Furthermore, the apparent disturbance in motor control on the ipsilesional side after stroke (34, 36, 58, 66) suggests that force control may also be impaired, which previously had not been assessed.

Disturbed motor control after stroke results in various sensorimotor impairments (50, 64), including altered motor unit firing rates (27, 48), abnormal muscle coactivation patterns (21, 35), and abnormal muscle synergies (20, 24). These factors may affect the ability to maintain steady and accurate force output after stroke. Moreover, Rosenfalck and Andreasen (48) suggested that poor utilization of muscle feedback may also be responsible for larger force variability in people after stroke compared with normal subjects.

The primary objective of this study was to examine the ability of patients who recently sustained a stroke to maintain steady and accurate force output during submaximal isometric knee extension compared with healthy controls. The secondary objective was to explore the relationship between force variability and motor impairments after stroke. The following three hypotheses were tested. Based on the results of Lodha et al. (37), we hypothesized that the force variability and error while maintaining a constant knee extension output would be greater in the contralateral (more-affected) limb of stroke subjects compared with the dominant side of controls. Since motor control on the ipsilesional (less-affected) side also seems to be disturbed after stroke (34, 36, 58, 66), our second hypothesis was that the force control in the less-affected limb would be better than in the more-affected limb but worse than in controls. Assuming that the force control is related to neurological impairment after stroke (37), our third hypothesis was that the force variability would negatively correlate with knee extension strength and the overall motor function early after stroke. The preliminary results have been presented in abstract form (13).
METHODS

Subjects. Thirty-three patients (13 women, 61 ± 11 yr; 20 men, 64 ± 15 yr) were recruited from the population receiving first in-patient rehabilitation after stroke. The inclusion criteria were first documented stroke, able to follow simple instructions, and ability to walk independently for 7 min with or without assistive devices. Patients were excluded if they had visual (hemianopia) or perceptual (neglect) deficits, knee pain, or received artificial knee replacement. They were tested 16 ± 4 days (range 8–25 days) poststroke, usually a few days before discharge from the inpatient rehabilitation. The age-matched control sample included 6 women (62 ± 11 yr) and 14 men (62 ± 9 yr) who reported no orthopedic or neurological disorders at the time of testing. The age difference between the two groups was not significant (unpaired t-test, \( P = 0.694 \)). Each subject attended one data collection session and signed the informed consent approved by the Institutional Review Board of the Methodist Rehabilitation Center.

Stroke subjects were assessed by a physical therapist using the lower extremity motor section of the Fugl-Meyer scale (26) and Rivermead Mobility Index (19, 30) before commencing force trials. Both scales are commonly used in a rehabilitation setting for clinical assessment of motor deficits after stroke. These scores could not be obtained in four patients because the therapist was not available.

Experimental setup. An isokinetic dynamometer (Biodex System 3, Biodex Medical Systems, New York) was used for assessing isometric strength and force control. The torque sensor of the dynamometer was directly connected to a custom-built amplifier (model AD627, Analog Devices, Norwood, MA; gain = 500, CMRR > 90 dB, input impedance = 20 \times 10^6 Ohms, nonlinearity = 25 parts/million, bandwidth = 1 kHz), which provided high-resolution voltage output with minimum noise at the overall gain of 1,000 (overall sensitivity 57.5 mV/N·m). The torque signal was exported to a portable analog-to-digital converter (model DI-720, 14-bit resolution, DATAQ Instruments, Akron, OH) and displayed on a 17-in. LCD monitor in real time using WINDAQ/Pro software (DATAQ Instruments). The converter-exported torque signal was also connected to a custom-built amplifier (model AD627, Analog Devices, Norwood, MA; gain = 500, CMRR > 90 dB, input impedance = 20 \times 10^6 Ohms, nonlinearity = 25 parts/million, bandwidth = 1 kHz), which displayed voltage output from the amplifier. The monitor was mounted on a swing arm for easy adjustment and positioned 40–50 cm directly in front of the subject’s head. The torque signal was also exported to an EvaRT data acquisition system (Motion Analysis, Santa Rosa, CA) sampled at a 1,200-Hz rate and 12-bit resolution.

Experimental protocol. The force control testing protocol was the same for all subjects. Both legs were tested in patients in random order, and only in the dominant leg in controls. Each subject was tested in a comfortable seated position with both hips at ~85° of flexion. The axis of the dynamometer was aligned with the lateral epicondyle of the femur. The subject was secured in the chair with two padded diagonal chest straps, a padded strap across the pelvis, and a strap over the tested thigh. The Biodex resistance pad was positioned over the shin ~10 cm above the lateral malleolus. The foot of the non-tested leg rested on a support bar.

The subject was first asked to perform five repetitions of maximum isokinetic knee extension-flexion at 210°/s and 60°/s as a warm-up. In the remaining trials, the subject performed isometric knee extension at a 90° angle. The experimental protocol started with three trials of isometric MVC, 3–4 s each (the MVC force is proportional to the peak knee extension torque because of the constant moment arm). In each MVC trial, the operator marked the baseline level and the maximum deflection of the torque signal on a blank paper taped to the monitor. The maximum deflection and the vertical scale of the display (V/division) were used to calculate the height of deflection from baseline to 10, 20, 30, and 50% of MVC (pre-MVC force) so that the 50% deflection occupied at least half of the screen height. The paper with target forces marked along the right edge covered the entire screen except for 3–4 cm along the right edge, which allowed matching a live torque signal with the target (12). The 40% MVC level was not tested to minimize the possibility of fatigue (physical and mental) and shorten the duration of the testing session, particularly relevant for stroke subjects who were tested bilaterally. Moreover, lower rather than higher force levels were of interest because force control deficits in the elderly are more pronounced at lower levels (63).

The force control section of the protocol included a few practice trials for a subject to familiarize with the setup and tasks. The subject was instructed to activate knee extendors so that the displayed torque signal (a horizontal line) matched a designated target force and to maintain the produced force as accurately and steadily as possible for 10 s. Two trials at 10, 20, 30, and 50% of pre-MVC were presented in a random order with a 30- to 60-s rest in between. The data collection started when the produced force became steady and best matched the target force. Thus the rise in force toward the target force was not recorded (Fig. 1). Because increased force variability may in
part be due to muscle fatigue (41), an isometric MVC was repeated at the end to assess for the presence of fatigue. Force levels below 10% of MVC were not tested since they would require stroke subjects to produce very small absolute forces, which are inherently more variable because of the low signal-to-noise ratio (mean force/standard deviation of force) (15, 52, 53).

Data reduction. Torque signal voltage was converted to Newton-meters (N·m) based on the calibration data. MVC torque was smoothed using a sliding average of 600 data points (0.5-s window). For each limb, the largest torque among the three pre-MVC trials was used as the peak knee extension torque. To facilitate strength comparisons between stroke and control subjects, peak torques were also normalized to individual body mass (N·m/kg). Torque data during experimental trials were filtered using a second-order Butterworth low-pass filter (20-Hz cutoff frequency).

The CV and root-mean-square error (RMSE) from target torque were used to quantify force variability and force accuracy, respectively. CV (%) was calculated as the ratio between standard deviation (SD) and mean torque (CV = SD/mean × 100%). RMSE, calculated over the middle 8 s of the trial duration (i.e., time constant = 8 s), represents the absolute difference between the average produced torque and the target torque expressed as a percentage of the target torque (average produced torque – target torque)/target torque × 100%. We opted for normalized measures of force variability and accuracy over absolute values (i.e., variability in SD and error in N·m), which allows comparison across different knee extension strengths. Only the middle 8 s of each 10-s trial were analyzed. For each subject, the trial with a lower CV at each force level was considered the best performance and used for statistical analysis. This conservative approach was considered appropriate so the differences between patients and controls were not inflated.

Statistical analysis. Means and SD were calculated for each strength and force control parameter on the more-affected and less-affected sides in stroke subjects and the dominant side of healthy controls. For testing hypotheses 1 and 2, unpaired t-test was used to determine whether the more-affected and less-affected sides were significantly different from controls, whereas pairwise t-test was used to test for significant differences between the more-affected and less-affected sides. A pairwise t-test was also used to compare MVC peak torques before and after force maintenance task to determine the presence of fatigue. The unequal variance t-test was employed when Levene’s test indicated significant difference in the sample variance (α < 0.05). The results are graphically presented as box-and-whisker plots to compare the distribution of force control data in stroke patients with controls.

Possible significant associations of the force variability parameters on the more-affected side with the more-affected limb strength and clinical scores of motor function were explored using Pearson’s product moment coefficients of correlation (hypothesis 3). Correlation between force variability and strength was also performed in the less-affected limbs and controls for comparison to previous results. A confidence level of P ≤ 0.05 was chosen to indicate statistical significance. No adjustment in alpha level was made for multiple tests because of the exploratory nature of this study.

RESULTS

The Fugl-Meyer motor scores in the more-affected lower limb of stroke subjects (maximum 34) ranged from 7 to 33 (mean ± SD, 25 ± 7). Three patients received the maximum Rivermead Mobility Index of 15, and the lowest score was 4 (11 ± 3).

As expected, the peak isometric strength was significantly smaller in the more-affected than in the less-affected knee extensors (97 ± 43 vs. 140 ± 56 N·m; P < 0.001). When normalized to the body mass, quadriceps muscles in controls (2.2 ± 0.6 N·m/kg) had significantly greater peak torque than the more-affected (1.1 ± 0.5 N·m/kg; P < 0.001) and less-affected (1.6 ± 0.6 N·m/kg; P = 0.001) limbs of stroke subjects. The peak knee extension torque recorded immediately after the force control task (post-MVC) was on average smaller compared with before (pre-MVC) in each group (more-affected, 95 ± 42 N·m; less-affected, 137 ± 58 N·m; and controls, 170 ± 58 N·m), but the difference was significant only in controls (179 ± 59 vs. 170 ± 58 N·m; P = 0.023).

The CV was significantly smaller in controls compared with either more-affected (P ≤ 0.006) or less-affected (P ≤ 0.023) leg of stroke subjects across all force levels (Fig. 2A). Significantly higher CV was found in the more-affected than less-affected leg in stroke subjects at 20% and 50% force levels. The RMSE was significantly different only at higher force levels (Fig. 2B). Specifically, at 50% force, all groups differed from each other (P ≤ 0.031), with controls having the smallest average RMSE followed by the less-affected and then more-affected leg of patients. The RMSE was also smaller in controls than in the more-affected leg at 30% force (P = 0.012). The box-and-whisker plots indicate that, regardless of the force
level and leg, the majority of stroke subjects had CV above the normative values of controls (Fig. 2A). The deviation from controls was less prominent for RMSE, in particular at lower force levels (Fig. 2B).

The CV in the more-affected leg of stroke patients did not correlate with Fugl-Meyer motor score ($-0.25 \leq r \leq -0.12; P \geq 0.146$), Rivermead Mobility Index ($-0.19 \leq r \leq 0.20; P \geq 0.316$), or the normalized peak knee extension torque ($0.07 \leq r \leq 0.16; P \geq 0.375$). However, significant inverse correlations between CV and normalized peak knee extension torque were found in the less-affected leg of stroke patients and controls (Fig. 3, B and C).

**DISCUSSION**

The purpose of this study was to characterize the degree of force control impairment in knee extensors soon after stroke and to explore the putative relationship between force variability and early recovery of motor function. By testing the three related hypotheses, we obtained the following major findings: 1) the force variability and error during constant knee extension muscle output are greater in the more-affected leg of stroke subjects than in the dominant leg of controls; 2) the force variability and error are less prominent in the less-affected than more-affected leg of stroke subjects but worse compared with controls; and 3) the force variability in the more-affected leg is not associated with peak knee extension strength and early motor deficits. These findings are consistent across different force levels for force variability but are only applicable to higher force levels for force error.

Our first hypothesis that stroke patients show greater force variability and error than controls when attempting to maintain a steady force output was for the most part confirmed. Although CV in the more-affected knee extensors was consistently higher across all examined force levels (10–50% MVC), the accuracy was significantly worse only at 30% and 50% MVC. The computer simulations and experimental results in healthy subjects suggest that force variability is predominantly influenced by variability of discharge rates in active motor units (25). We speculate that force control deficits in subacute stroke could be partly explained by the impaired descending and afferent input to the segmental network controlling discharge patterns of motor units after stroke (7, 23, 27). As a result, the ability to modulate discharge intervals may be compromised (59, 68). It remains unknown whether relative inactivity after stroke is sufficient to contribute to increased force variability, as found in healthy subjects with extended bed rest (51).

Our second hypothesis that force variability and error are smaller in the less-affected than more-affected knee extensors but larger than in controls was also partially supported. Whereas the CV consistently differed across all force levels, only 50% RMSE exhibited the predicted worsening pattern from control to the less-affected leg and then followed by the more-affected leg. The overall results suggest that both legs are impaired early after stroke. The box-and-whisker plots (Fig. 2) clearly indicate high prevalence of bilateral deficits in force control, especially for force steadiness.

Impaired isometric strength and force control in the less-affected knee extensors are consistent with previously reported bilateral changes after stroke (31, 34, 36, 43, 47, 58, 66). Several factors may contribute to impaired motor function of the less-affected limbs, including hemispheric lateralization for the executed tasks and hemispheric asymmetry (36) or evolving maladaptive changes in the intact hemisphere (38). Some peripheral mechanisms may also play a role (1), and the potential contribution of prolonged inactivity early in recovery should be considered (51).

Our results in controls are comparable to several previous investigations on different muscles (3, 10, 11, 14, 17, 62). With respect to the sustained isometric knee extension, CV of 1.6–2.0% across different force levels in our study is similar to 1.8 ± 0.1% at both 10% and 50% MVC obtained by Bazzucchi et al. (10) in older men and women, yet slightly smaller than those reported by Bazzucchi et al. (3) for older women only (2.4 ± 0.9% and 2.2 ± 1.0% at 20% and 50% MVC, respectively). Such negligible differences are likely due to variations in study sample and protocol.

The third hypothesis that the ability to maintain a steady force output is related to muscle strength and motor function after stroke was only partially supported. Although we found no significant associations between CV and strength or motor function in the more-affected leg of stroke patients, modest but significant negative correlations were detected between CV and

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**Fig. 3.** Correlations between normalized strength and force variability for the more-affected (A) and less-affected (B) legs of patients and the dominant leg of controls (C). Symbols after correlation coefficient ($r$) values indicate significant correlations ($* P < 0.05; \dagger P < 0.01; \ddagger P < 0.001$).
strength in the less-affected leg at three of the four force levels. The lack of correlation with the lower extremity Fugl-Meyer motor score is contrary to Lodha et al. (37) who reported negative correlation between Fugl-Meyer upper extremity motor score and force variability in hand/wrist extensors at 5% and 25% levels. Such a discrepancy may be ascribed to time after stroke (chronic vs. subacute here), muscle tested (hand/wrist extensor vs. knee extensor), and recovery pattern (upper vs. lower extremity). Moreover, the upper extremity Fugl-Meyer scale evaluates more refined hand and finger motions (e.g., grasping a pen), which are expected to depend on the ability to maintain fine output of hand/wrist extensors, in contrast to rather gross Fugl-Meyer assessment in the lower extremity.

The lack of significant association between force variability and motor scores suggests that the capacity of more-affected knee extensors to generate steady submaximal forces is not related to gross measures of neurologiical impairment and mobility soon after stroke. This is in contrast to the negative relation between maximal strength and CV found here in the less-affected leg and in healthy subjects, as already reported (6, 56). Such findings warrant further longitudinal studies regarding the link between force steadiness and recovery of strength.

Although we excluded stroke subjects with frank visual (hemianopia) and perceptual (hemineglect) deficits, they still might have some deficit in visual processing (33, 40, 49). Thus future experiments should examine the contribution of visuo-motor processing to force control after stroke, as previously done in healthy subjects (44, 57, 65). Variability in vertical distance from baseline to target location on the screen [visual gain (46)] unlikely played the key role. Prodoehl and Vaillancourt (46) reported that significant changes in force variability and accuracy occurred at visual gain (i.e., visual angle at constant display-eye distance) of 0.05° or smaller, with the effects more pronounced in the elbow than the ankle muscles. Considering screen distance of 50 cm in our study, the visual angle of 0.05° corresponds to a vertical distance of 0.44 mm on the monitor, which is far smaller than the observed force variability in the recorded trials. Also, the effect of fatigue on force variability (41) was excluded in stroke subjects because MVC before and after the force maintenance tasks did not significantly differ. A close examination of the data revealed that post-MVC peak knee extension torque decreased >10% in 4 of 33 patients and increased >10% in 3 patients. For controls, 6 (of 20) showed >10% decrease in post-MVC, and only 1 showed a >10% increase. If fatigue exacerbated force variability among the controls, then the reported differences between patients and controls are underestimated. In any case, this does not seem to substantially change our main findings.

The findings of this study pertain to the subjects with greater motor abilities within the first few weeks after stroke. Our Fugl-Meyer motor score (25 ± 7) and MVC in the more-affected knee extensors (97 ± 47 N-m) obtained on average at 2.5 wk after stroke correspond to those typically found later in the course of recovery (18, 39, 42, 60, 67). The apparent selection bias toward higher level patients was unintentional but was introduced by the requirement for sufficient endurance and ability to fully and safely participate in the protocol as well as to walk a short distance rather independently to examine the relationship between force control and gait parameters in the future. Therefore, our results cannot be generalized to patients with slower recovery early after stroke.

In conclusion, our findings indicate bilateral deficits in isometric knee extension strength and force steadiness within the first month of stroke. Such deficits in force control are apparently unrelated to gross motor impairments. The relation of force steadiness and sensation needs to be more carefully examined as well as whether the location of the lesion or the hemisphere involved plays a role. Future studies should also explore the temporal evolution of force control deficits observed early after stroke and the functional significance of these changes during weight bearing of knee extensors.

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GRANTS

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