Proportional Recovery From Lower Limb Motor Impairment After Stroke

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Background and Purpose—In people with preserved corticospinal tract (CST) function after stroke, upper limb impairment resolves by ≈70% within 3 months. This is known as the proportional recovery rule. Patients without CST function do not fit this rule and have worse upper limb outcomes. This study investigated resolution of motor impairment in the lower limb (LL).

Methods—Patients with stroke and LL weakness were assessed 3 days and 3 months after stroke with the LL Fugl–Meyer. CST integrity was determined in a subset of patients using transcranial magnetic stimulation to test for LL motor-evoked potentials and magnetic resonance imaging to measure CST lesion load. Linear regression analyses were conducted to predict resolution of motor impairment (ΔFugl–Meyer) including factors initial impairment, motor-evoked potential status, CST lesion load, and LL therapy dose.

Results—Thirty-two patients completed 3-month follow-up and recovered 74% (95% confidence interval, 60%–88%) of initial LL motor impairment. Initial impairment was the only significant predictor of resolution of motor impairment. There was no identifiable cluster of patients who did not fit the proportional recovery rule. Measures of CST integrity did not predict proportional LL recovery.

Conclusions—LL impairment resolves by ≈70% within 3 months after stroke. The absence of a nonfitter group may be because of differences in the neuroanatomical organization of descending motor tracts to the upper limb and LL. Proportional recovery of the LL is not influenced by therapy dose providing further evidence that it reflects a fundamental biological process. **(*Stroke*. 2017;48:00-00. DOI: 10.1161/STROKEAHA.116.016478.)**

Key Words: motor ■ lower extremity ■ stroke ■ upper extremity

The resolution of impairment and recovery of function are both important components of motor recovery after stroke.[1] Greater residual impairment requires more compensation to recover function. Most patients resolve ≈70% of their initial upper limb (UL) impairment within 3 to 6 months after stroke, which has been called the proportional recovery rule.[2–7] Proportional recovery occurs regardless of stroke type (hemorrhage or ischemic),[8] previous stroke,[8] or therapy dose.[4,8] Patients with functionally[4,8] and structurally[6,7] intact descending motor pathways from the ipsilesional primary motor cortex follow the rule, whereas for those without recovery tends to be poor. Proportional recovery of aphasia has also been observed, indicating that it may occur across different domains.[9] These findings suggest proportional recovery reflects a fundamental biological process.[4–6,10,11]

No studies investigating proportional recovery of lower limb (LL) impairment have been previously reported. The aim of this study was to investigate resolution of impairment in the LL and to determine whether CST integrity was required for proportional recovery.

Materials and Methods

Patients aged ≥18 years with new LL weakness (<100 on LL Motricity Index) after ischemic or hemorrhagic stroke were eligible for the study. Previous stroke and treatment with stroke thrombolysis and endovascular clot retrieval were allowed. Patients with cerebellar stroke, contraindications to transcranial magnetic stimulation (TMS) or magnetic resonance imaging (MRI), or inability to consent to research participation were excluded. Written informed consent was gained from each participant, and the study was approved by the regional ethics committee.

Baseline demographic and clinical information were recorded for each participant including age, sex, stroke severity (National Institutes of Health Stroke Scale), and LL strength (Motricity Index). The LL component of the Fugl–Meyer (FM) scale was administered 3 days and 3 months after stroke. LL physical therapy dose was recorded in minutes during inpatient rehabilitation. Assessors were blinded to all aspects of patient care. Resolution of motor impairment was calculated as the difference between FM scores at baseline and 3 months (ΔFM). Initial motor impairment (FM_{ii}) was calculated as maximum LL FM score (34) minus baseline FM score.

The integrity of the descending motor pathways was determined in a subset of patients using transcranial magnetic stimulation on days 5 to 7 and MRI on days 7 to 10 post-stroke. These time points are consistent with previous studies[4,6–8] and intended to reduce false-negatives for motor-evoked potential (MEP) status and the effects of

Received December 22, 2016; final revision received January 26, 2017; accepted February 1, 2017.

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***Stroke* is available at http://stroke.ahajournals.org** **DOI: 10.1161/STROKEAHA.116.016478**

edema on MRI measures. For TMS, a flat figure-8 coil was placed over the scalp, oriented to generate a medial-lateral current flow in the LL motor cortex. MEPs were recorded from the paretic tibialis anterior muscle. If no MEPs were elicited at rest, patients were instructed to activate the paretic leg or the contralateral leg if unable to activate the paretic side.[12] Participants were considered MEP+ if an MEP of any amplitude was consistently observed with the leg either active or at rest.

T1-weighted MRI was used to calculate CST lesion load. A template CST was constructed from diffusion-weighted images acquired from 85 patients with stroke, between the contralesional primary motor cortex and inferior border of the pons. Lesion masks were hand drawn on individual patients' T1 images by 1 researcher and independently verified by 2 others. Lesion load was calculated as the percentage of CST template voxels overlapped by the stroke lesion mask.[8]

Bivariate correlations were used to examine relationships between resolution of impairment (ΔFM) and initial motor impairment (FM_{ii}), MEP status (present or absent), lesion load, age, sex, previous stroke, stroke type (ischemic or hemorrhage), comorbidities (Charlson Comorbidity index), LL therapy dose (minutes), and LL therapy intensity (minutes per day). Variables with $P<0.1$ were entered into multivariable linear regression with ΔFM as the dependent variable and the intercept set to the origin. Further regression analyses were completed with the subsets of patients who underwent TMS and MRI.

Results

Of the 41 patients recruited, 32 completed the 3-month assessment (Table 1). Four patients died, 2 were withdrawn because of the development of new medical issues, and 3 were lost to follow-up. MEP status was determined for 22 patients, and lesion load was calculated for 23 patients. Most patients were nonambulatory at baseline (59%), half scored >7 on the National Institutes of Health Stroke Scale, and 5 patients had no affected LL movement at baseline (Motricity Index score of zero).

FM_{ii} and therapy dose were entered into linear regression analysis of the full data set with resolution of impairment (ΔFM) as the dependent variable. FM_{ii}, therapy dose, and either MEP status or lesion load were entered into regression analyses for the TMS and MRI subsets, respectively. Age, sex, stroke type, previous stroke, comorbidities, and therapy intensity were excluded as they did not correlate with ΔFM ($P>0.1$).

FM_{ii} predicted recovery from impairment (Table 2), as patients resolved 74% (95% confidence interval, 60%–88%) of initial impairment. Patients whose ΔFM differed from predicted ΔFM by ≥4 points were classified as outliers, but there was no identifiable cluster of nonfitters (Figure). Therapy dose and lesion load were not predictors of ΔFM (Table 2). In the subset with TMS data, ΔFM was 3 points lower in patients without MEPs ($P=0.06$).

Discussion

This is the first report of proportional recovery from LL motor impairment after stroke. Patients recover ≈70% of their available improvement as demonstrated previously in the UL[2–7] and in speech (Figure).[9] This study showed that people with previous stroke and intracerebral hemorrhage can also recover proportionally as reported in the UL[8] (Figure) although a larger sample is required to explore this finding for the LL. In keeping with reports for the UL,[4,8] therapy dose was not a predictor of recovery from LL motor impairment,

Table 1. Participant Characteristics

Demographic characteristics (n=32)	
Age, y	
Median age (range)	71 (39–96)
Sex	
Female	17 (53%)
Stroke risk factors	
Smoker	4 (13%)
Ex-smoker	7 (22%)
Diabetes mellitus	11 (34%)
Hypertension	20 (63%)
Dyslipidemia	13 (41%)
Atrial fibrillation	9 (28%)
Previous cardiac history	9 (28%)
Comorbidities	
Charlson Comorbidity index median (range)	1 (1–3)
Stroke characteristics	
First stroke	
Yes	28 (87%)
Stroke type (Oxfordshire classification)	
Total anterior circulation infarct	3 (9%)
Partial anterior circulation infarct	14 (44%)
Lacunar infarct	9 (28%)
Posterior circulation infarct (excluding cerebellar)	2 (6%)
Intracerebral hemorrhage	4 (13%)
Hemisphere	
Right	15 (47%)
Alteplase	
Yes	5 (16%)
Endovascular clot retrieval	
Yes	1 (3%)
Stroke severity	
NIHSS median (range)	7 (0–18)
Clinical LL measures	
FAC score	
Nonambulatory (FAC=0)	19 (59%)
Dependent ambulation FAC (1, 2, 3)	12 (38%)
Independent ambulation (FAC≥4)	1 (3%)
Lower limb impairment	
Fugl–Meyer score out of 34, median score (range)	
3 d	19 (7–33)
3 mo	32 (19–34)
Motricity Index, median (range)	53.5 (0–92)
LL therapy dose median hours (range)	11 (0–43)
LL MEP present (subset n=22)	14 (64%)
Lesion load (subset n=23)	
% overlap median (range)	15 (0–52)

FAC indicates Functional Ambulation Category; LL, lower limb; MEP, motor-evoked potential; and NIHSS, National Institutes of Health Stroke Scale.

Table 2. Linear Regression Statistics for Predictors of ΔFM

	Predictor	β	β 95% CI	Adj R^2	F	P Value
Complete cohort (n=32)	FM_{ii}	0.74	0.60 to 0.88	0.93	206.28	<0.001
	Therapy dose, min	−0.001	−0.003 to 0.002			0.569
TMS (n=22)	FM_{ii}	0.81	0.63 to 0.99	0.94	106.28	<0.001
	MEP (1=MEP−)	−3.38	−6.97 to 0.202			0.063
	Therapy dose, min	0.000	−0.003 to 0.003			0.96
MRI (n=23)	FM_{ii}	0.71	0.533 to 0.891	0.93	96.50	<0.001
	Lesion load	0.051	−0.056 to 0.158			0.33
	Therapy dose, min	−0.001	−0.005 to 0.002			0.41

CI indicates confidence interval; FM, Fugl–Meyer; FM_{ii}, initial motor impairment; MEP, motor-evoked potential; MRI, magnetic resonance imaging; and TMS, transcranial magnetic stimulation

which supports the theory that proportional recovery reflects a fundamental biological process.[11]

Approximately 30% of patients do not resolve UL impairment proportionally.[2,4–6] If the same were true for LL impairment, 9 patients would have been expected to not fit the rule and exhibit poor recovery. However, there was no identifiable cluster of nonfitters and even more severely impaired patients recovered proportionally. Although it is possible that the 4 patients who died may not have fit the rule (median National Institutes of Health Stroke Scale 11), it seems that almost all patients demonstrate proportional recovery from LL impairment. This may be because of greater redundancy in the form

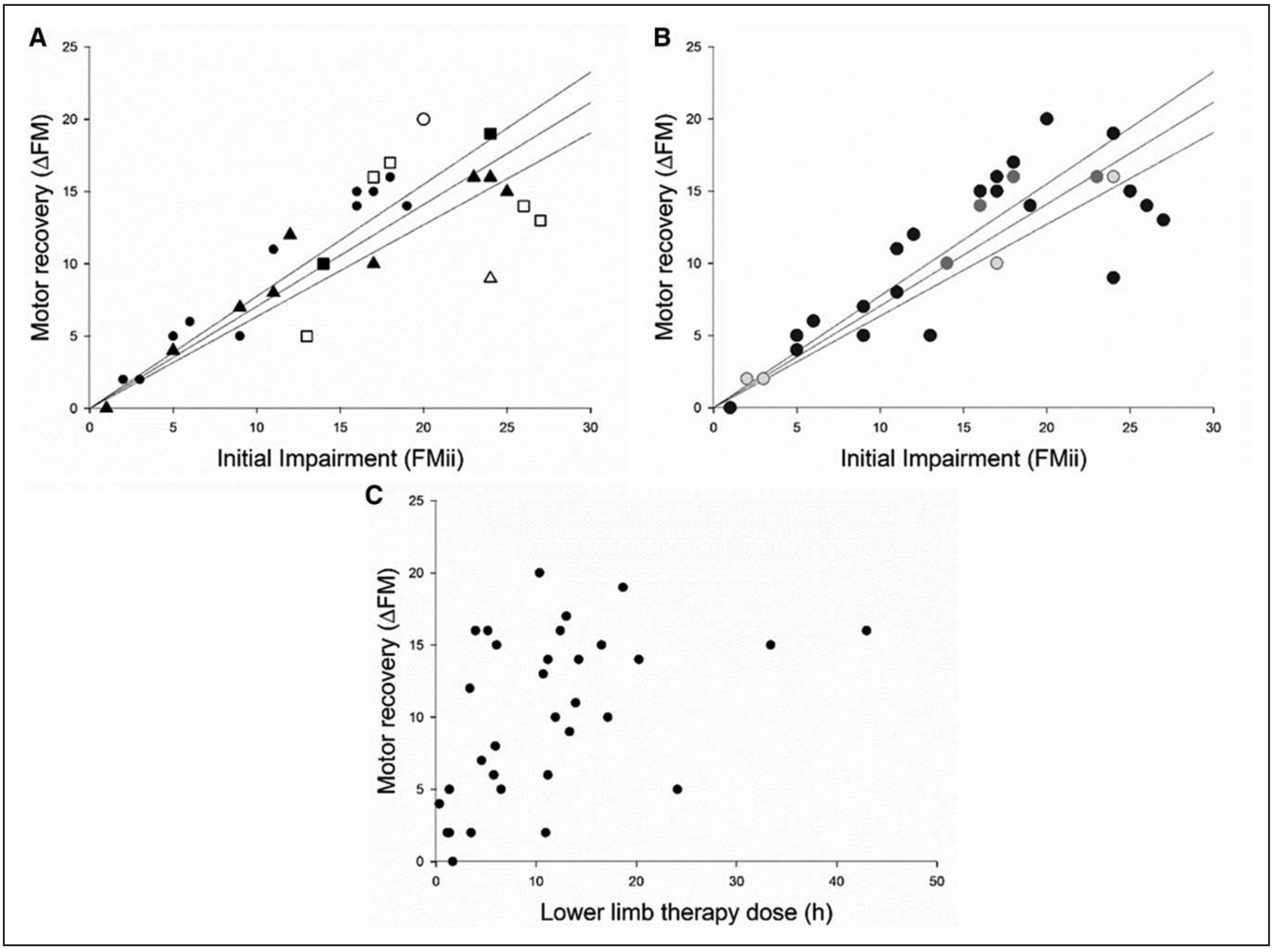

Figure. A, Resolution of lower limb motor impairment (Δ Fugl–Meyer [FM]) is proportional to initial impairment (FM_{ii}) regardless of motor-evoked potential (MEP) status. Circle, MEP+; square, MEP−; triangle, no TMS data; open symbols=outlier ≥4 points outside predicted ΔFM. **B**, Resolution of impairment is also proportional in patients with hemorrhagic stroke and previous stroke. Black, first ischemic stroke; dark gray, hemorrhagic stroke; light gray, previous stroke. **C**, Resolution of impairment is not proportional to lower limb therapy dose. Regression lines have 95% confidence intervals.

of alternate descending pathways to the LL, such as the reticulospinal tract and projections from the contralesional cortex.[13] The potential contribution of uncrossed descending pathways did not increase the proportion of recovery above 70%.

As there was no cluster of nonfitters, measures of CST integrity were not useful for identifying which patients would recover proportionally. Patients without LL MEPs still recovered proportionally although there was a trend toward less recovery. This may be related to the technical challenges of stimulating LL motor cortex with TMS, resulting in false-negatives. Other limitations were that MEP status and lesion load were collected only for a subset of patients, and LL sensory loss was not recorded. The findings in this report are preliminary, and larger samples are needed to explore the relationships between CST integrity and LL proportional recovery.

Summary

LL impairment resolves by ≈70% within 3 months after stroke. The absence of an identifiable group of nonfitters indicates that proportional recovery from LL impairment is achievable for most patients, in contrast to the UL where a functional CST is required. This may mean that measures of CST integrity are not needed to predict proportional resolution of LL impairment. Measuring proportional recovery may be a useful tool in future trials for determining whether interventions in the subacute stage are interacting with the neurobiological mechanisms of recovery.

Sources of Funding

This study was supported by The Health Research Council of New Zealand (11/270) and the Julius Brendel Trust.

Disclosures

None.

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JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association | American Stroke Association

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Stroke. published online March 24, 2017;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628