

# Recovery and Prediction of Dynamic Precision Grip Force Control After Stroke

Gaia Valentina Pennati, Jeanette Plantin, Loïc Carment, Pauline Roca,

Jean-Claude Baron, Elena Pavlova, Jörgen Borg, Påvel G Lindberg

# ► To cite this version:

Gaia Valentina Pennati, Jeanette Plantin, Loïc Carment, Pauline Roca, Jean-Claude Baron, et al.. Recovery and Prediction of Dynamic Precision Grip Force Control After Stroke. Stroke, 2020, 10.1161/STROKEAHA.119.026205 . inserm-02483088

# HAL Id: inserm-02483088 https://inserm.hal.science/inserm-02483088v1

Submitted on 18 Feb 2020  $\,$ 

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## Title

Recovery and prediction of dynamic precision grip force control after stroke

## Authors

Gaia Valentina Pennati, MD<sup>1</sup>, Jeanette Plantin, MSc<sup>1</sup>, Loïc Carment, PhD<sup>2</sup>, Pauline Roca<sup>3</sup>,

PhD, Jean-Claude Baron<sup>3</sup>, MD, PhD, Elena Pavlova, PhD<sup>1</sup>, Jörgen Borg, MD, PhD<sup>1</sup>, Påvel G Lindberg, PhD<sup>1, 2</sup>

<sup>1</sup>Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Division of Rehabilitation Medicine, Stockholm, Sweden

<sup>2</sup>Institut de Psychiatrie et Neurosciences de Paris, Inserm U1266, Paris, France

<sup>3</sup>Institut de Psychiatrie et Neurosciences de Paris, Inserm U1266, Hôpital Sainte-Anne, Université Paris Descartes, Paris, France

# **Corresponding author**

Gaia Valentina Pennati, Division of Rehabilitation Medicine, Danderyd Hospital, SE-18288 Stockholm, Sweden

Tel.: +46722779072; E-mail: gaia.valentina.pennati@ki.se

## **Cover Title**

Precision grip recovery after stroke

# Total number of tables and figures

Tables 2; Figures 3

# Keywords

Stroke/Complication; Recovery of function; Predictions and Projections; Brain Imaging; Corticospinal Tract

# Search terms

Cerebrovascular Disease/Stroke; Rehabilitation; Prognosis; Quality and Outcomes; Magnetic

Resonance Imaging

# **Word Count**

5484

STROKE/2019/026205 R3

#### Abstract

Background and Purpose: Dexterous object manipulation, requiring generation and control of finger forces, is often impaired after stroke. This study aimed to describe recovery of precision grip force control after stroke, and to determine clinical and imaging predictors of 6 month performance.

Methods: 80 first ever stroke patients with varying degrees of upper limb weakness were evaluated at 3 weeks, 3 and 6 months after stroke. Twenty-three healthy individuals of comparable age were also studied. The Strength-dexterity test was used to quantify index finger and thumb forces during compression of springs of varying length in a precision grip. The coordination between finger forces (CorrForce), along with Dexterity-score and Repeatability-score were calculated. Anatomical MRI was used to calculate weighted corticospinal tract lesion load (wCST-LL).

Results: CorrForce, Dexterity-score and Repeatability-score in the affected hand were dramatically lower at each time point compared to the less-affected hand and the control group, even in patients with mild motor impairment according to Fugl-Meyer assessment. Improved performance over time occurred in CorrForce and Dexterity-score but not in Repeatability-score. The Fugl-Meyer hand subscale, sensory function and wCST-LL best predicted CorrForce and Dexterity-score status at 6 months ( $R^2$  .56 and .87, respectively). wCST-LL explained most of the variance in CorrForce ( $R^2$  .34) and Dexterity-score ( $R^2$  .50) at 6 months. Absence of recovery in CorrForce was predicted by wCST-LL> 4 cc and in Dexterity-score by wCST-LL> 6 cc.

Conclusions: Findings highlight persisting deficits in the ability to grasp and control finger forces after stroke. Sensory and motor hand impairments together with wCST-LL can predict performance at 6 months and degree of CST lesion alone predicts lack of post stroke precision grip recovery.

Clinical Trial Registration–URL: http://www.clinicaltrials.gov. Unique identifier: NCT02878304.

## Introduction

Impaired fine motor control of fingers is common after stroke, reducing the ability to grasp and manipulate objects and negatively impacting daily activities and quality of life.<sup>1</sup> Accurate evaluation of precision grip (i.e., the ability to grasp an object between the tactile pads of the thumb and fingertips) is therefore likely to be important for prognosis and for the development of targeted upper limb interventions. Post stroke precision grip deficits, when grasping stable objects, have been well characterized and include impaired dosing of force (to the object being manipulated) and loss of coordination of grip and lift (upward) forces.<sup>2,3</sup> However, few studies have described dynamic finger force control (i.e., the ability to appropriately generate dynamically scaled and directed force by the digits while grasping unstable objects), which is frequently affected after stroke<sup>4</sup>, or its longitudinally recovery<sup>5, 6</sup>, leaving many aspects unclear. The first aim of the present longitudinal study of 80 individuals with first ever stroke was to describe the recovery of dexterous manipulation as assessed by the Strength-dexterity test. This test allows to quantify the dynamic interaction between fingertip forces and measures the ability to stabilize an unstable object in a precision grip<sup>7</sup>. In addition, the coordination between finger forces (CorrForce), the ability to dynamically adapt applied finger forces (Dexterityscore) and the reproducibility of performance (Repeatability-score) were also investigated. Since force generation is usually more compromised distally after stroke<sup>8</sup> and differs in time course of recovery from individuated finger control<sup>9, 10</sup>, we hypothesized that precision grip force control measures would show a proportionally greater impairment compared to maximal power or pinch grip force and to upper limb motor impairment measured with the Fugl-Meyer assessment. The present study's second aim was to identify best predictors of both 6-month status and longitudinal recovery in precision grip force control after stroke. Based on previous reports, we hypothesized the strongest predictor would be the degree of lesion to the corticospinal tract (CST)<sup>9, 11, 12</sup>, but also that the best prediction model would additionally include measures of hand sensory<sup>12, 13</sup> and motor impairment<sup>14</sup>.

# Methods

The data supporting this study findings are available from the corresponding author upon reasonable request.

## Study design and participants

Eighty post stroke subjects (57 male; age 52.7 $\pm$ 9.4 years) admitted as inpatients to the Department of Rehabilitation Medicine at Danderyd Hospital, Stockholm, Sweden with a firstever CT or MRI-verified stroke and upper limb muscle weakness (score $\leq$  4/5 on Manual Muscle Testing) were included. Exclusion criteria included history of any other neurological or rheumatologic disorders of the hand, cerebellar lesions, contraindications to MRI scan, and severe cognitive dysfunction. Twenty-three healthy adult individuals of comparable age (11 male; age 46.9 $\pm$ 13.1 years) and with no history of neurological disease constituted a control group. Assessments in stroke patients were conducted bilaterally at 2-6 weeks (mean time 3 weeks, T1), three (T2) and 6 months (T3) after injury, and with the dominant hand in the healthy individuals.

Written informed consent was obtained from all participants. The study was approved by the Regional Ethical Review Board in Stockholm (DNR: 2011/1510-31/3). All procedures complied with the Declaration of Helsinki.

#### Clinical measures

Fugl-Meyer assessment of the upper extremity (FMA-UE) was used to measure upper limb motor function (excluding the three reflex-items, yielding a maximum of 60 points).<sup>15</sup> Motor impairment levels were defined as: severe= 0-12, severe-moderate= 13-30, moderate-mild= 31-47 and mild= 48-60.<sup>16</sup> Gross manual dexterity was assessed with the Box & Block Test

(BBT) and compared to normative data (please see <u>http://stroke.ahajournals.org</u>), maximum voluntary contraction (MVC) in power grip with the Jamar isometric dynamometer (Digital Hand Dynamometer, Saeham, South Korea) and in key-pinch with the Jamar pinch gauge (Pinch Gauge, B&L Engineering, USA). Tactile sensation of finger tips was examined with the Semmes-Weinstein Monofilament (North Coast Medical, Inc., USA) (from 0= absent sensation, to 5= normal sensation). Two-point (2p) discrimination was measured at the thumb and index finger tips with the Dellon-McKinnon Disk-Criminator (0= total absence of sensation, 1= perceived stimuli at a distance  $\geq 12 \text{ mm}$ ,  $2=\geq 7 \text{ mm}$  and 3=<7 mm, considered normal sensation).

#### Strength-dexterity test and performance measures

The Strength-dexterity test allows quantification of the dynamic regulation of fingertip forces during a pinch task.<sup>17</sup> The method measures the ability to compress and control a variety of springs (N= 8) which are unstable and prone to buckling and with diverse length (free length from 1.80 cm of spring 8 to 4.60 cm of spring 1), and therefore with different demands on strength and dexterity (spring 8= easiest, spring 1= most difficult to compress).

Dynamic index finger and thumb forces were recorded using two force sensors (unit: gramforce, gf)<sup>17</sup>, and analyzed off-line using Matlab R2017B (MathWorks, Natick, MA, USA). Coordination of index finger and thumb forces was investigated by calculating a correlation coefficient between force signals (CorrForce).

A Dexterity-score was calculated:

$$Dexterity - score = \frac{\sum_{i=0}^{m} Max \, Spr \, (8-i) + Test \, Spr \, (8-m-1)}{\sum_{i=0}^{7} Max \, Spr \, (8-i)}$$

where Max Spr= force required for full compression of that spring, Test Spr= average of maximal sustained compression forces achieved with the test spring,  $\sum_{i=0}^{7} Max Spr (8 - i)$ = sum over the eight springs of the forces required to compress to solid length, m= spring number

 $(-1 \le m < 6)$ . The Dexterity-score indicates the maximal level of instability that the patient's sensorimotor system is able to control, and higher values reflect better performance. The previous formula<sup>17</sup> was modified excluding dead bands of compression force of the test spring (i.e., the regions in the beginning and end of the compression range), to account for the characteristics of this study population in the sub-acute phase after stroke, which was mostly unable to maintain the subsequent longer spring in spite of the ability to produce enough force. A Repeatability-score, evaluating the reproducibility of performance across the ten trials, was computed:

$$Repeatability - score = 1 - \frac{SD Test Spr (8 - m - 1)}{Max Spr (8 - m - 1)}$$

where SD Test Spr= standard deviation of the average of maximal sustained compression forces achieved with the test spring, Max Spr= force required for full compression of that spring, m= spring number ( $-1 \le m < 6$ ). A high Repeatability-score indicated that the subject was able to reproduce similar dynamic force compression across trials.

Patients unable to perform dynamic compressions were assigned values equal to 0 for CorrForce and Dexterity-score, indicating complete loss of precision grip.

For details on assessment procedure, please see Supplemental Material <u>http://stroke.ahajournals.org</u>.

### Magnetic Resonance Imaging

Brain imaging was performed at T1 with an Ingenia 3.0T MR-system (www.usa.philips.com) with an 8HR head coil. High resolution T1-weighted anatomical images were acquired using TFE 3D (3D gradient echo-based sequence): FOV 250x250x181 mm, matrix 228x227, slice thickness 1.2 mm, slice spacing 0.6 mm and number of slices 301 (Echo time= shortest, relaxation time= shortest). T2 FLAIR images were also acquired.

#### Lesion maps

#### STROKE/2019/026205 R3

Before delineating lesion maps, T1-weighted images were normalized to MNI template using SPM12 (www.fil.ion.ucl.ac.uk/spm/software/spm12/). Cost function masking was used to avoid distortion of lesion by normalization procedure<sup>18</sup>, and the images were inspected visually to rule out poor normalization. Lesion maps were manually drawn on all axial slices of normalized T1 anatomical images using MRIcron (http://people.cas.sc.edu/rorden/mricron/index.html/) by researcher (PL) and verified by experienced neurologist (JCB) who were blinded to all clinical data except the lesioned hemisphere. Lesion location was verified on FLAIR images and lesion maps were binarized. Lesion volume (unit: cubic centimeter, cc) was calculated using MRIcron. Lesion maps were used to calculate weighted corticospinal tract lesion load (wCST-LL; unit: cubic centimetre, cc)<sup>19</sup> using previously constructed CST template based on regions of interest in the precentral gyri, posterior limb of internal capsule, cerebral peduncle and anteromedial pons.<sup>20</sup>

### Statistical analysis

Group differences and effect of time were investigated using one way-ANOVA and two-way repeated measures ANOVAs. Bonferroni's post-hoc procedure was computed for mean comparisons. Spearman's rank order correlation test (Spearman's Rho,  $r_s$ ) was used to investigate relations between force control, clinical and MRI measures.

A multivariable linear regression analysis was performed to predict precision grip impairment at 6 months using the most significant clinical and imaging variables identified in the correlation analysis. Hierarchical linear regression models, in which wCST-LL was entered first, were used to ascertain the unique variance accounted for by the clinical variables. Proportional recovery scores in precision grip measures were calculated.<sup>21</sup> The study population was then divided into two groups, with recovery (recovery<sup>pos</sup>, score>0) and absence of recovery (recovery<sup>abs</sup>, score≤ 0), and univariate logistic regression models were performed to test predictors of recovery. The significance level was set at  $p \le .05$ . All statistical analyses were performed using SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp). Predictive models were verified by leave-one-out cross-validation using R, Version 3.6.0 (R Core Team).

## Results

#### Clinical measures

FMA-UE showed moderate-severe upper limb motor impairment in stroke patients, as shown in Table 1. Measures of sensory and motor functions were significantly reduced in the affected hand compared to the less-affected hand. BBT revealed number of patients with impaired gross manual dexterity, including in the less-affected side (n= 41 at T1 and n= 26 at T3).

#### Precision grip force control

Precision grip force profiles are shown in Figure 1. Dynamic compression forces were lower in amplitude and less stable in the affected hand and characterized by poor correlation between index finger and thumb forces (reduced CorrForce). Healthy subjects performed the Strength-dexterity test with an average of sustained compression force of 146.63 gf, and stroke patients at T1 with 109.51 gf with the less-affected hand and 43.7 gf with the affected hand.

There was a statistically significant difference between groups in CorrForce, Dexterity-score and Repeatability-score [GROUP: F(2, 168) = 62.54, p< .001; F(2, 168) = 122.08, p< .001 and F(2, 130) = 7.51, p< .005, respectively]. Post-hoc tests revealed that the three variables were significantly lower in the affected hand compared to the less-affected side and to the healthy control group (p< .001). No significant difference between the less-affected hand and the control group was detected in the measures.

CorrForce and Dexterity-score improved over time in stroke patients [TIME: F(2, 224)= 4.4569, p= .01265; F(2, 224)= 12.417, p< .001, respectively]. (Figure 2) Dexterity-score significantly improved between each time point (T1 vs T2 and T2 vs T3) in the affected-hand

whereas CorrForce showed a more gradual increase, with a significant difference between T1 vs T3 only (p<.005). Despite the improvement over time, both values remained significantly lower compared to the less-affected side at T3 (p<.001). Moreover, of the 33 patients with mild degree of residual impairment in FMA-UE at T3, four (12%) continued having pathological values in CorrForce and eleven (33%) in Dexterity-score (i.e.,< mean – 2SD of healthy subjects). (Figure 3) Repeatability-score in the affected-hand did not change significantly over time after stroke.

#### Relation between clinical scales and precision grip force control in the affected hand

Age and dominant hand being affected by the stroke (in 41.3% of patients) did not significantly correlate with any force control variables. Both CorrForce and Dexterity-score correlated significantly with motor and sensory impairment measures at each time point (corrected for multiple comparisons). At T1, CorrForce correlated strongly with FMA-UE and FMA-Hand ( $r_s$ = .80 and  $r_s$ = .86, p< .01), and with other clinical assessments of motor and sensory impairments. Similarly, Dexterity-score at T1 strongly correlated with FMA-UE and FM-Hand ( $r_s$ = .86 and  $r_s$ = .91, p< .01), and other motor and sensory impairments (please see http://stroke.ahajournals.org).

#### Relation between brain lesion and precision grip force control in the affected hand

Lesion volume (mean= 116.88±147.79 cc) correlated negatively and weakly with FMA-Hand ( $r_s$ = -.30, p< .01) and precision grip control measures ( $r_s$ < -.30, p< .05) at T1. At T3, lesion volume correlated just moderately with CorrForce ( $r_s$ = -.37, p< .01) and did not significantly with Dexterity-score. The wCST-LL (mean= 3.83±3.51 cc) showed enhanced negative correlation with CorrForce ( $r_s$ = -.56, p< .01) and Dexterity-score ( $r_s$ = -.58, p< .01). These relationships were even stronger at T3: CorrForce ( $r_s$ = -.62, p< .01) and Dexterity-score ( $r_s$ = -.72, p< .01).

#### Prediction of precision grip force control recovery at 6 months

Significant regression equations were found for predicting precision grip force control status at T3 (please see <u>http://stroke.ahajournals.org</u>). FMA-Hand, 2p Discrimination test and wCST-LL emerged as highly significant predictors for both CorrForce (F(3,54)=22.625, p<.005 with an R<sup>2</sup> of .557) and Dexterity-score (F(3,54)=125.186, p<.005 with an R<sup>2</sup> of .874). The cross-validated coefficients of determination (R<sup>2</sup>) for CorrForce and Dexterity-score were .482 and .854, respectively. Hierarchical models (Table 2) indicated that wCST-LL alone explained most of CorrForce (R<sup>2</sup>= .344) and Dexterity-score (R<sup>2</sup>= .502) at 6 months. It also showed that FMA-Hand and 2p Discrimination together accounted for a significant additional portion of the variance in CorrForce (R<sup>2</sup>= .213) and Dexterity-score (R<sup>2</sup>= .373).

## Prediction of probability of positive recovery in precision grip force control

Thirty-three (52%) patients improved to some extent in CorrForce from T1 to T3 and thirtynine (64%) patients in Dexterity-score. Univariate logistic regression models revealed that wCST-LL was the most significant predictor for both recovery<sup>pos</sup> in CorrForce and Dexterityscore ( $X^2$ = 6.530, df= 1 and p= .011, and  $X^2$ = 11.307, df= 1 and p= .001, respectively). The predictive model for recovery in CorrForce explained 14.5% (Nagelkerke R<sup>2</sup>) of the variance in CorrForce recovery and correctly classified 61.4% of cases. The predictive model for recovery in Dexterity-score explained 25.0% of the variance in recovery and gave an overall correct prediction rate of 78.9%. The predictive accuracy of the model for recovery in CorrForce was 61.4% and for the model for recovery in Dexterity-score was 78.9% (please see http://stroke.ahajournals.org). Higher wCST-LL was associated with a reduced likelihood of recovering CorrForce and Dexterity-score (odds ratio .793, 95% CI: .657 - .959, p= .017, and odds ratio .724, 95% CI: .589 - .891, p= .002, respectively). Thus, every 1-cc increase in wCST-LL decreased the odds of having recovery<sup>pos</sup> in CorrForce by about 21%, and by about 28% in Dexterity-score. The critical value in wCST-LL from the logistic regression that predicted positive recovery in CorrForce was 4.42 cc and was 6.14 cc for recovery in Dexterity-score. Of all the patients with wCST-LL values greater than 4.42 cc, 60% presented no positive change in CorrForce while 77% of the patients with a lesion broader than 6.14 cc had no recovery in Dexterity-score.

#### Discussion

Recovering stroke patients had major difficulties in ability to grasp and control the springs, to coordinate finger forces and to perform reproducibly across trials. Although patients improved over time, many remained impaired in the precision grip force control at 6 months after stroke even in case of good overall upper limb and hand sensorimotor status as measured with clinical measures. Sensorimotor impairments early after stroke and CST lesion load predicted precision grip force control at 6 months and CST lesion load alone was a significant predictor of whether patients would be likely to recover force control during first 6 months post-stroke.

#### Precision grip recovery

Precision grip performance recovered relatively poorly over time in the affected hand, with 24% of patients unable to perform the Strength-dexterity test at T3. CorrForce and Dexterity-score measures improved, but values remained pathological in 39% and 67% of the patients, respectively (far from healthy control performance, Figure 2). In addition, recovery in Repeatability-score was not significant at group level. Decreased performance was even evident in patients with maximal FMA-Hand score (n= 16 at T1 and n= 31 at T3). Individual observations (Figure 3) indicate clinically relevant motor recovery at T3 as measured by FMA-UE despite remaining impairment in fine grip force control and fine manipulative tasks. The slower recovery in correlation of finger forces (compared to Dexterity-score) and the reduced prediction of this measure, support previous reports showing that recovery of strength occurs faster and mainly within the first 3 months after stroke compared to other aspects, such as the ability to manipulate objects and independence of finger movements.<sup>9, 13, 20</sup>

A compromised ability to control dynamic grip forces was also identified in the less-affected hand, in accordance with previous studies<sup>22</sup> and possibly due to disruption of ipsilesional projections of the CST, disinhibition of the non-lesioned hemisphere or disturbance of bilateral frontoparietal-cerebellar networks.

#### Mechanism underlying impaired precision grip force control

Main predictors of poor precision grip force control at 6 months were hand motor impairment, sensory impairment and CST lesion load. The hierarchical regression analysis confirmed our hypothesis that the wCST-LL was the most significant predictor<sup>11</sup> and that sensory function and hand motor impairments explained additional variance of grip force control, extending knowledge on predictors of functional outcomes post-stroke.<sup>23-28</sup>

The degree of lesion to the CST was a key predictor of precision grip force control at 6 months after stroke, reflecting the essential role of CST for fine motor control, especially for precision grip performance and finger individuation.<sup>9, 12, 29</sup> CST lesion load was the only significant predictor of positive change in precision grip control from 3 weeks to 6 months post-stroke.<sup>30, 31</sup> This suggests that neurobiological processes involving residual CST integrity are critical for recovery of fine motor control of fingers after stroke. This is also supported by studies showing motor improvements in stroke patients recovering motor evoked potentials.<sup>20, 32</sup> Quantitatively, however, the moderate predictive value of CST lesion load for recovery of precision grip force control points also to the likely contribution of other neural substrates and multiple pathways in support of the recovery process<sup>33</sup>, such as cortico-cortical connections<sup>34, 35</sup>, cortico-basal ganglia loops and other descending motor pathways such as the reticulospinal tract.<sup>9</sup> The FMA-Hand scores, in the predictive model with lesion load and sensory function, may be considered a surrogate measure of these other contributory factors.

Findings also confirms the importance of early sensory status after stroke for recovery of precision grip force control.<sup>6, 36</sup> A high percentage of patients presented alterations in tactile

sensation and/or in proprioception in the affected hand at three weeks after stroke. This was highly related with poor performance on the Strength-dexterity test at each time point. In manipulation of deformable or unstable objects, such as a compressed spring, somatosensory and visual feedbacks are critical for controlling the direction of fingertip force vectors.<sup>37</sup> Impaired sensory function due to aging or stroke likely explains some of the decline in dexterous manipulation<sup>38, 39</sup> and has recently been shown to predict gains from robotic therapy in the chronic phase post-stroke.<sup>40</sup>

#### Limitations

The timing of the first evaluation varied some between patients (2-6 weeks after stroke) but the variability was low for this kind of longitudinally study and did not affect predictive models. It is recalled that a wCST-LL of 1.0 cc in the centrum semiovale has a different impact compared to a 1.0 cc lesion at the level of internal capsule, due to a higher concentration of CST fibers in the latter. Transcranial magnetic stimulation would have been useful to evaluate presence of a motor evoked potential, shown to be valuable for the prediction of hand impairment according to the Action Research Arm Test.<sup>26</sup> Since reliability of the Strength-dexterity test has not been assessed in stroke patients, further studies are desirable. It is important to note that the study sample was a relatively young stroke group (mean age 52.70 years), which makes it difficult to generalize the results to the entire stroke population.

# Conclusions

The current study provides evidence of impaired precision grip in the affected hand over the first 6 months after stroke, even in patients with no or mild-upper limb motor impairment. Early sensory and motor hand impairments and CST lesion load can predict late precision grip deficits. wCST-LL was also related to longitudinal recovery in precision grip control. Finally, the study highlights the need to measure precision grip performance post-stroke with dedicated

assessment, as with the Strength-dexterity test, to detect impairments otherwise unrecognized that might impact the recovery of a useful hand after stroke.

#### Acknowledgements

We express our appreciation to the patients who participated in this study and their families. We thank the medical team of the Division of Rehabilitation Medicine, Danderyd Hospital that contributed to recruitment of patients and provided communication materials.

# **Sources of Funding**

This study was supported by Grant from Lars Hedlund (Karolinska Institutet Dnr 2-1582/2016), Promobilia Foundation, STROKE-Riksförbundet and NEURO Sweden.

#### Disclosures

PGL is a shareholder in the company Aggero MedTech AB manufacturing a measurement instrument for spasticity and has patented a method for measurement of manual dexterity (EP2659835A1). He declares no conflict of interest with the present work.

#### References

- Ekstrand E, Rylander L, Lexell J, Brogardh C. Perceived ability to perform daily hand activities after stroke and associated factors: A cross-sectional study. BMC neurology. 2016;16:208
- Allgower K, Hermsdorfer J. Fine motor skills predict performance in the jebsen taylor hand function test after stroke. Clin. Neurophysiol. 2017;128:1858-1871
- 3. Nowak DA. The impact of stroke on the performance of grasping: Usefulness of kinetic and kinematic motion analysis. Neurosci. Biobehav. Rev. 2008;32:1439-1450
- Seo NJ, Rymer WZ, Kamper DG. Altered digit force direction during pinch grip following stroke. Exp Brain Res. 2010;202:891-901

- Kurihara J, Lee B, Hara D, Noguchi N, Yamazaki T. Increased center of pressure trajectory of the finger during precision grip task in stroke patients. Exp Brain Res. 2019;237:327-333
- 6. Pavlova EL, Borg J. Impact of tactile sensation on dexterity: A cross-sectional study of patients with impaired hand function after stroke. J. Mot. Behav. 2018;50:134-143
- Valero-Cuevas FJ, Smaby N, Venkadesan M, Peterson M, Wright T. The strengthdexterity test as a measure of dynamic pinch performance. Journal of biomechanics. 2003;36:265-270
- Colebatch JG, Gandevia SC. The distribution of muscular weakness in upper motor neuron lesions affecting the arm. Brain : a journal of neurology. 1989;112 ( Pt 3):749-763
- Xu J, Ejaz N, Hertler B, Branscheidt M, Widmer M, Faria AV, et al. Separable systems for recovery of finger strength and control after stroke. J. Neurophysiol. 2017;118:1151-1163
- Lang CE, Wagner JM, Edwards DF, Sahrmann SA, Dromerick AW. Recovery of grasp versus reach in people with hemiparesis poststroke. Neurorehabil Neural Repair. 2006;20:444-454
- Feng W, Wang J, Chhatbar PY, Doughty C, Landsittel D, Lioutas VA, et al. Corticospinal tract lesion load: An imaging biomarker for stroke motor outcomes. Annals of neurology. 2015;78:860-870
- Wolbrecht ET, Rowe JB, Chan V, Ingemanson ML, Cramer SC, Reinkensmeyer DJ.
   Finger strength, individuation, and their interaction: Relationship to hand function and corticospinal tract injury after stroke. Clin. Neurophysiol. 2018;129:797-808
- 13. Semrau JA, Herter TM, Scott SH, Dukelow SP. Examining differences in patterns of sensory and motor recovery after stroke with robotics. Stroke. 2015;46:3459-3469

- Hoffmann G, Conrad MO, Qiu D, Kamper DG. Contributions of voluntary activation deficits to hand weakness after stroke. Topics in stroke rehabilitation. 2016;23:384-392
- 15. Woodbury ML, Velozo CA, Richards LG, Duncan PW, Studenski S, Lai SM. Dimensionality and construct validity of the fugl-meyer assessment of the upper extremity. Arch Phys Med Rehabil. 2007;88:715-723
- 16. Woytowicz EJ, Rietschel JC, Goodman RN, Conroy SS, Sorkin JD, Whitall J, et al. Determining levels of upper extremity movement impairment by applying a cluster analysis to the fugl-meyer assessment of the upper extremity in chronic stroke. Arch Phys Med Rehabil. 2017;98:456-462
- Dayanidhi S, Hedberg A, Valero-Cuevas FJ, Forssberg H. Developmental improvements in dynamic control of fingertip forces last throughout childhood and into adolescence. J Neurophysiol. 2013;110:1583-1592
- 18. Brett M, Leff AP, Rorden C, Ashburner J. Spatial normalization of brain images with focal lesions using cost function masking. NeuroImage. 2001;14:486-500
- 19. Zhu LL, Lindenberg R, Alexander MP, Schlaug G. Lesion load of the corticospinal tract predicts motor impairment in chronic stroke. Stroke. 2010;41:910-915
- 20. Birchenall J, Teremetz M, Roca P, Lamy JC, Oppenheim C, Maier MA, et al. Individual recovery profiles of manual dexterity, and relation to corticospinal lesion load and excitability after stroke -a longitudinal pilot study. Neurophysiologie clinique = Clinical neurophysiology. 2019;49:149-164
- 21. Prabhakaran S, Zarahn E, Riley C, Speizer A, Chong JY, Lazar RM, et al. Interindividual variability in the capacity for motor recovery after ischemic stroke. Neurorehabil Neural Repair. 2008;22:64-71

- Semrau JA, Herter TM, Kenzie JM, Findlater SE, Scott SH, Dukelow SP. Robotic characterization of ipsilesional motor function in subacute stroke. Neurorehabil. Neural Repair. 2017;31:571-582
- Stinear CM, Barber PA, Petoe M, Anwar S, Byblow WD. The prep algorithm predicts potential for upper limb recovery after stroke. Brain : a journal of neurology. 2012;135:2527-2535
- 24. Stinear CM, Byblow WD, Ward SH. An update on predicting motor recovery after stroke. Annals of physical and rehabilitation medicine. 2014;57:489-498
- 25. Nijland RH, van Wegen EE, Harmeling-van der Wel BC, Kwakkel G. Presence of finger extension and shoulder abduction within 72 hours after stroke predicts functional recovery: Early prediction of functional outcome after stroke: The epos cohort study. Stroke. 2010;41:745-750
- 26. Stinear CM, Byblow WD, Ackerley SJ, Smith MC, Borges VM, Barber PA. Prep2: A biomarker-based algorithm for predicting upper limb function after stroke. Annals of clinical and translational neurology. 2017;4:811-820
- 27. Kim B, Winstein C. Can neurological biomarkers of brain impairment be used to predict poststroke motor recovery? A systematic review. Neurorehabil Neural Repair. 2017;31:3-24
- 28. Boyd LA, Hayward KS, Ward NS, Stinear CM, Rosso C, Fisher RJ, et al. Biomarkers of stroke recovery: Consensus-based core recommendations from the stroke recovery and rehabilitation roundtable. International Journal of Stroke. 2017;12:480-493
- Lemon RN. Descending pathways in motor control. Annual review of neuroscience.
   2008;31:195-218
- 30. Riley JD, Le V, Der-Yeghiaian L, See J, Newton JM, Ward NS, et al. Anatomy of stroke injury predicts gains from therapy. Stroke. 2011;42:421-426

- 31. Burke Quinlan E, Dodakian L, See J, McKenzie A, Le V, Wojnowicz M, et al. Neural function, injury, and stroke subtype predict treatment gains after stroke. Annals of neurology. 2015;77:132-145
- 32. Byblow WD, Stinear CM, Barber PA, Petoe MA, Ackerley SJ. Proportional recovery after stroke depends on corticomotor integrity. Annals of neurology. 2015;78:848-859
- Rondina JM, Park CH, Ward NS. Brain regions important for recovery after severe post-stroke upper limb paresis. Journal of neurology, neurosurgery, and psychiatry. 2017;88:737-743
- 34. Schulz R, Koch P, Zimerman M, Wessel M, Bonstrup M, Thomalla G, et al.
  Parietofrontal motor pathways and their association with motor function after stroke.
  Brain : a journal of neurology. 2015;138:1949-1960
- 35. Rinne P, Hassan M, Fernandes C, Han E, Hennessy E, Waldman A, et al. Motor dexterity and strength depend upon integrity of the attention-control system.
  Proceedings of the National Academy of Sciences of the United States of America.
  2018;115:E536-e545
- 36. Meyer S, De Bruyn N, Krumlinde-Sundholm L, Peeters A, Feys H, Thijs V, et al. Associations between sensorimotor impairments in the upper limb at 1 week and 6 months after stroke. J. Neurol. Phys. Ther. 2016;40:186-195
- 37. Johansson RS, Flanagan JR. Coding and use of tactile signals from the fingertips in object manipulation tasks. Nature reviews. Neuroscience. 2009;10:345-359
- 38. Dayanidhi S, Valero-Cuevas FJ. Dexterous manipulation is poorer at older ages and is dissociated from decline of hand strength. The journals of gerontology. Series A, Biological sciences and medical sciences. 2014;69:1139-1145
- Lindberg P, Ody C, Feydy A, Maier MA. Precision in isometric precision grip force is reduced in middle-aged adults. Exp Brain Res. 2009;193:213-224

Ingemanson ML, Rowe JR, Chan V, Wolbrecht ET, Reinkensmeyer DJ, Cramer SC.
 Somatosensory system integrity explains differences in treatment response after stroke.
 Neurology. 2019;92:e1098-e1108



**Figure 1.** Dynamic compression force profiles acquired in a patient with the less-affected hand and affected hand at 3 weeks, 3 and 6 months after stroke. Springs of increasing length and higher strength and dexterity requirement were compressed at each time point (spring 8= easiest; spring 1= hardest). Force data from the thumb (red line) and index finger (yellow) and the average compression force (blue) are shown. Less well stabilized profile with a lower amplitude and prolonged release duration time characterized the compression force in the

affected hand. The difference in CorrForce is noticeable between the two hands early after stroke (0.70 versus 0.09).



**Figure 2**. Effect of time on CorrForce (**A**) and Dexterity-score (**B**) in the affected hand (Solid circles) and less-affected hand (Hollow square). Vertical bars denote 95% confidence intervals. CorrForce significantly differed between 3 weeks and 6 months in the affected hand; Dexterity-score significantly improved at 3 months and then at 6 months in the affected hand. No significant differences in precision hand grip were detected over time in the less-affected side.



**Figure 3.** Correlation between Fugl-Meyer assessment of the upper extremity (FMA-UE) and CorrForce (**A**) and Dexterity-score (**B**) measured with the affected hand at 6 months after stroke. Four levels of upper limb motor impairment are displayed according to FMA-UE score: severe= 0-12 (n= 26), severe-moderate= 13-30 (n= 5), moderate-mild= 31-47 (n= 11) and mild= 48-60 (n= 33). The vertical dashed lines indicate the mean–2SD of CorrForce and

Dexterity-score values defined in the healthy subjects. Note the mismatch between recovery in FMA-UE and precision grip scores: patients showing full recovery or mild impairment in upper limb motor function still had reduced CorrForce (n= 4) or Dexterity-score (n= 11) values compared to the healthy control group.

# Table 1. Baseline participants' characteristics

	Patients (N= 80)		Healthy subjects	
	Affected side	Less-affected side	(N=23)	
Age, years, mean±SD	52.70±9.46		46.91±13.12	
Sex (male / female), n (%)	57 (71.3) / 23 (28.7)		11 (47.8) / 12 (52.2)	
Stroke hemisphere (left / right), n (%)	30 (37.5) / 50 (62.5)			
Stroke type (ischemic / haemorrhagic), n (%)	55 (68.8) / 25 (31.3)			
Hand dominance (affected / non-affected), n (%)	33 (41.3) / 45 (56.3)			
NIHSS, mean±SD	7.55±5.50			
wCST-LL, cc, mean±SD	3.83±3.51			
FMA-UE, mean±SD	23.53±23.09			
FMA-Hand, mean±SD	5.59±6.00			
FMA-Proprioception, mean±SD	4.19±3.48			
BBT, mean±SD	15.35±21.48	50.99±14.03		
2p Discrimination test, median (IQR)	0 (0-2)	2 (2-2)		
Monofilament test, median (IQR)	4 (0-8)	9 (8-10)		
Power grip MVC, mean±SD	10.35±13.86	35.3±10.45	41.59±10.63	
Key-pinch MVC, mean±SD	2.72±3.47	8.98±2.37	9.75±1.91	

IQR= Interquartile Range. NIHSS= National Institutes of Health Stroke Scale; wCST-LL= weighted corticospinal tract lesion load; FMA-UE= Fugl-Meyer assessment of the upper

extremity; FMA-Hand= Fugl-Meyer assessment hand subscale; FMA-Proprioception= Fugl-Meyer assessment sensation, position subscale; BBT= Box & Block Test; 2p Discrimination test= Two-point discrimination test; MVC= maximum voluntary contraction.

		$\mathbb{R}^2$	R <sup>2</sup> change	В	Beta	Sig.
CorrForce	Model 1	.344				.000*
	wCST-LL			076	587	.000*
	Model 2	.511	.166			.000*
	wCST-LL			056	429	.000*
	2p Discrimination test			.150	.437	.000*
	Model 3	.557	.046			.000*
	2p Discrimination test			.098	.285	.018*
	FMA-Hand			.023	.349	.021*
	wCST-LL			032	248	.049*
Dexterity-score	Model 1	.502				.000*
	wCST-LL			073	708	.000*
	Model 2	.680	.178			.000*
	wCST-LL			056	544	.000*
	2p Discrimination test			.122	.453	.000*
	Model 3	.874	.195			
	FMA-Hand			.036	.716	.000*
	wCST-LL			018	175	.010*
	2p Discrimination test			.038	.141	.027*

Table 2. Hierarchical Regression Analysis for variables predicting CorrForce andDexterity-score

\*p<.05. wCST-LL= weighted corticospinal tract lesion load; 2p Discrimination test= Twopoint discrimination test; FMA-Hand= Fugl-Meyer assessment hand subscale.