CHAPTER 5

The impact of time on quality of motor control of the paretic upper limb after stroke

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Chapter 5

ABSTRACT

Objective. To establish the time course of recovery regarding smoothness of upper limb movements in the first 6 months after stroke.

Design. Cohort study with 3D kinematic measurements in week 1, 2, 3, 4, 5, 8, 12 and 26 after stroke.

Setting. On-site 3D kinematic measurements in stroke units, rehabilitation centers, nursing homes and patients’ homes.

Participants. Forty-four patients (19 women, 25 men; mean age: 58 ± 12 years) with a first-ever unilateral ischemic stroke and incomplete upper limb paresis (27 left sided, 17 right sided) were included.

Main Outcome Measures. In each measurement, an electromagnetic motion tracker acquired hand and finger trajectories during a reach-to-grasp task. Movement duration was determined and smoothness of hand transport and grasp aperture were quantified by normalized jerk. Using random coefficient analysis the effect of progress of time on smoothness of hand transport and grasp aperture was investigated.

Results. During the first 5 weeks after stroke, there was a significant contribution of progress of time to reductions in movement duration and normalized jerk of hand transport and grasp aperture (p < 0.01).

Conclusions. The present longitudinal 3D kinematic study showed that smoothness of paretic upper limb movements improves in the first 8 weeks after stroke. This improvement suggests that motor control normalizes in the first 8 weeks after stroke and can be mostly explained by spontaneous neurological recovery that occurs typically in the first weeks after stroke. Future 3D kinematic studies should investigate whether therapies starting early after stroke can improve the quality of motor control beyond spontaneous neurological recovery.
INTRODUCTION

Time poststroke is one of the most neglected features in explaining recovery of the paretic upper limb after stroke.\textsuperscript{1,2} Based on clinical assessment scales, several longitudinal studies have shown that most improvements in motor function and capacity occur during the first 10 weeks after stroke.\textsuperscript{1,3,4} These early time-dependent improvements are assumed to reflect processes of spontaneous neurological recovery such as recovery of penumbral tissue\textsuperscript{5}, alleviation of diaschisis\textsuperscript{6} and reorganization of the dendritic spine architecture of cortical and cortico-spinal neurons.\textsuperscript{7} Since it is unclear whether spontaneous neurological recovery leads to normalization of the quality of motor control in the first weeks after stroke, there is a need for intensively repeated 3D kinematic measurements, preferably conducted during functional movements such as reaching and grasping.\textsuperscript{8}

Several 3D kinematic studies have shown that the quality of motor control after stroke is deficient, as reflected by a significant reduction in the smoothness of upper limb movements.\textsuperscript{9–11} The mechanism underlying this reduced smoothness is unknown, but may involve segmentation of reaching movements caused by poor interjoint and intermuscular coordination.\textsuperscript{12,13} However, longitudinal studies investigating the time course of smoothness during an early stage after stroke are almost lacking in the literature.

The first aim of the present study was to investigate the time course of recovery in terms of the smoothness of upper limb movements in the first 6 months after stroke. The second aim was to assess how progress of time contributes to normalization of the smoothness of upper limb movements. We hypothesized that smoothness would normalize in a natural logistic pattern of recovery, as was found in previous studies using standard clinical assessment scales. Secondly, we hypothesized that the longitudinal change in smoothness would be time-dependent and only significant in the first 10 weeks after stroke, when spontaneous neurological recovery occurs.
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METHODS

Participants
Forty-four patients (19 women, 25 men) were included in the present study, which was part of the EXPLICIT-stroke programme. All included patients met the following criteria: (1) having experienced a first-ever ischemic stroke involving the territory of the medial or anterior cerebral artery as revealed by computerized axial tomography or magnetic resonance imaging scan; (2) no intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) or alteplase, since thrombolysis influences the spontaneous neuronal processes in the brain and may therefore affect the time course of smoothness after stroke; (3) aged between 18 and 80 years; (4) able to sit independently without trunk support for at least 30s; (5) showing motor deficits in the arm and/or hand, but nevertheless being able to grasp objects within the first 3 weeks after stroke; (6) no severe deficits of cognition, as indicated by a score of 23 or higher on the Mini Mental State Examination (MMSE); (7) no severe deficits of communication, as indicated by a score of 4 or higher on the Utrecht Communication Observation (UCO); (8) no complicating medical history such as cardiac, pulmonary, or orthopaedic disorders; and (9) having provided written informed consent.

According to the EXPLICIT-stroke protocol all patients were screened and included in the first week after stroke at the stroke units of 11 hospitals in The Netherlands. Screening was performed by medical doctors, occupational therapists and physical therapists who were employed at the stroke units and were trained to recruit patients according to the EXPLICIT-stroke protocol. Depending on the impairment level and site of inclusion, included patients participated in clinical measurements as well as fMRI, transcranial magnetic stimulation, 3D kinematics and haptic robotics. Inclusion and intake was performed by the researcher who performed all clinical measurements. All 3D kinematic measurements were conducted by one researcher (JVK). The EXPLICIT-stroke protocol (registered with the Netherlands National Trial Register with trial number NTR1424) was approved by the local Ethics Committee. All patients underwent a clinical and 3D kinematic assessment of the upper paretic limb in weeks 1, 2, 3, 4, 5, 8, 12, and 26 after stroke.
Clinical evaluation
During the baseline session, type of stroke was established with the Bamford Classification. The severity of the infarct was assessed with the National Institutes of Health Stroke Scale (NIHSS). Motor impairments were assessed with the upper extremity section of the Fugl-Meyer Motor Assessment (FMA-UE). The ability to perform functional tasks with the paretic upper limb was assessed with the Action Research Arm Test (ARAT). The ability to perform activities of daily living (ADL) was assessed with the Barthel Index (BI).

Kinematic set-up
Kinematic data were recorded with a portable electromagnetic motion tracking device (Polhemus Liberty, Polhemus, Colchester, Vermont). As depicted in Figure 5.1, the electro-magnetic source was placed at the edge of the table next to the participant at the side of paresis. The position and orientation data of the sensors have been shown to be accurate within a distance of 60 cm from the source in multiple environments, such as a motion laboratory, treatment room and home situation. In addition, the reliability of the 3D kinematic parameters obtained with this device is good to excellent. These findings suggest that this device is suitable for use in a multi-center longitudinal study in patients with stroke as they move from the stroke unit to rehabilitation centers, nursing homes and their home situation. As depicted in Figure 5.1, all upper limb movements were measured relative to a global reference frame with its origin at the center of the magnetic source, x-axis directed forward, y-axis directed upward, and z-axis directed rightward. To standardize the 3D kinematic set-up, the same portable electromagnetic motion tracker and portable table with a height of 76 cm were used for all measurements.

Double-sided adhesive tape was used to attach the motion sensors to the thorax and to six segments of the paretic arm of each patient: scapula, upper arm, forearm, hand, thumb, and index finger. The location of the sensors is depicted in Figure 5.1. This study focused on the forearm, hand, and finger sensors. A pointer device (ST8 stylus, Polhemus, Colchester, Vermont) was used for anatomical calibration before each measurement to locate the basis of the third metacarpal bone (BMIII) relative to the hand sensor, as the reference position of the hand. The locations of the tips...
of the thumb and index finger were digitized with respect to their associated finger sensors. The sampling frequency during the motion recordings was 240 Hz.

Figure 5.1  

A) Determination of the maximal reaching distance (MRD). B) Illustration of the task execution. During the task execution, the subject starts in the initial position (left panel). Subject reaches for the block (small black square) at the block position (middle panel) and places the block at the end position (right panel). The small rectangles on the subject (left panel) indicate the positions of the sensors. The large black square at the side of the subject indicates the position of the electromagnetic source. The dashed line represents the maximum reaching distance of the arm.

Procedure

While seated at the table with a height of 76 cm, participants performed a functional reaching task with the paretic arm. Reaching and grasping form two major components in many activities of daily living that are performed with the upper limb. Furthermore, objects are often replaced after they have been grasped, for instance during eating and cleaning. Therefore we used a task that consisted of reaching, grasping and the replacement of an object. Specifically, the task consisted of two parts, (1) a reach-to-grasp movement toward a block, followed by (2) a displacement of the block toward a target location. The reach-to-grasp movement started with the hand in front of the shoulder on the edge of the table, keeping the thumb against the index finger. Participants were asked to grasp and displace a cubic block of 5×5×5 cm and 150g after the experimenter gave a verbal ‘GO’ signal. The block was placed in front of the shoulder at each participant’s individual maximum reaching distance of the non-paretic arm, which was determined as shown in Figure 5.1. The reach-to-grasp movement ended successfully when the block had been grasped and had lost contact with the table. Immediately after this block lift, the reach-to-grasp movement proceeded to the second part of the movement, during which the block had to be displaced toward a target position located at the contralateral side. The task is depicted in Figure 5.1. Participants were instructed to grasp the block
between their thumb and index finger and not to slide their hand over the table but to move it through the air. After the ‘GO’ signal, participants were allowed to move their trunk away from the back of the chair if this was more comfortable, but they had to remain seated and were not allowed to slide or twist over the seat of the chair. Seven trials were recorded in each measurement.

**Data analysis**

The analysis focused on the first part of the experimental paradigm: the reach-to-grasp movement. The start of reach-to-grasp was defined as the moment at which the forearm sensor exceeded 5% of the maximum speed during the forward reach. The end of reach-to-grasp was given as the moment at which the block lost contact with the table and the displacement of the block started. The end of reach-to-grasp was therefore defined as the moment at which the forearm sensor exceeded 5% of the maximum speed during the displacement of the block. The time-series for displacement of the hand and for grip aperture were determined between the start and end of reach-to-grasp and were filtered with a second order Butterworth low-pass filter with a cut-off frequency of 20 Hz. All data analyses were performed using custom made algorithms in Matlab version R2006a (MathWorks, Natick, Massachusetts).

**Kinematic parameters**

Movement duration (MD) was used as an overall parameter to quantify reach-to-grasp performance and was defined as the time between the start and end of reach-to-grasp. The smoothness of hand displacement and grasp aperture was quantified by jerk measures. Mathematically, jerk is defined as the third derivative of a specific position variable. To quantify the amount of jerk in the hand displacement and grasp aperture, the jerk was squared and integrated over the total movement duration:

$$J_{\text{hand}} = \sqrt{\frac{1}{2} \int_{t_{\text{start}}}^{t_{\text{end}}} \text{jerk}_{\text{hand}}^2(t) \, dt}$$  \hspace{1cm} (5.1)
where \( J_{\text{hand}} \) and \( J_{\text{grasp}} \) represent the amount of jerk in the hand displacement and grasp aperture signal. \( t_{\text{start}} \) represents the moment of start of reach-to-grasp, whereas \( t_{\text{end}} \) represents the moment of end of reach-to-grasp. \( \text{jerk}_{\text{hand}}(t) \) represents the third derivative of hand displacement and \( \text{jerk}_{\text{grasp}}(t) \) represents the third derivative of grasp aperture.

As Hogan and Sternad\(^{20}\) point out, this jerk measure depends on movement length squared divided by the fifth power of movement duration, \( L^2 / MD^5 \), even when the shape of the hand trajectory or grasp aperture curve is invariant. This dependency on movement length and movement duration is not desired and therefore \( J_{\text{hand}} \) and \( J_{\text{grasp}} \) need to be normalized, which is obtained by the following equations:\(^{10,20}\)

\[
N_{J_{\text{hand}}} = \frac{1}{2} \int_{t_{\text{start}}}^{t_{\text{end}}} \text{jerk}_{\text{hand}}^2(t) dt / MD^5/L_{\text{grasp}}^2
\]

\[
N_{J_{\text{grasp}}} = \frac{1}{2} \int_{t_{\text{start}}}^{t_{\text{end}}} \text{jerk}_{\text{grasp}}^2(t) dt / MD^5/L_{\text{grasp}}^2
\]

where \( N_{J_{\text{hand}}} \) and \( N_{J_{\text{grasp}}} \) represent the normalized jerk for hand displacement and grasp aperture, respectively. \( MD \) represents movement duration. \( L_{\text{hand}} \) represents the shortest distance between the start and end positions of the hand and \( L_{\text{grasp}} \) represents the difference in grasp aperture between the start and end of reach-to-grasp. The subsequent statistical analyses were performed on the normalized jerk measures, i.e. \( N_{J_{\text{hand}}} \) and \( N_{J_{\text{grasp}}} \).

**Statistics**

Using random coefficient analysis (SPSS, Version 20.0, IBM Corporation, Armonk, New York), we modelled the longitudinal recovery profiles for \( MD \), \( N_{J_{\text{hand}}} \) and \( N_{J_{\text{grasp}}} \). To check whether our data met the assumptions for normality we plotted...
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the frequency distribution of the parameters and compared these plots visually with a normal distribution. We assessed how each parameter changed as a function of time poststroke using the following multivariable regression model that corrected for the covariates age and baseline value:

\[ Y_{ij} = (\beta_0 + b_{0i}) + (\beta_1 + b_{1ij}) \times X_{ij} + \beta_2 x_i + \epsilon_{ij} \]  
\[ (5.5) \]

where \( Y_{ij} \) is a 3D kinematic parameter for subject \( i \) at time-point \( j \). \( \beta_0 \) is a fixed intercept and \( b_{0i} \) is a random intercept for subject \( i \). \( \beta_j \) is a fixed regression coefficient for time-point \( j \) and \( b_{1ij} \) is a random regression coefficient for subject \( i \) and time-point \( j \). \( X_{ij} \) is a dummy variable for subject \( i \) and time-point \( j \). The last time-point (i.e. 26 weeks after stroke) was used as the reference time-point. \( \beta_x \) is a fixed regression coefficient corresponding to covariate \( x \). \( COV_x_i \) is the value of covariate \( x \) for subject \( i \). The covariates were: (1) age at baseline, since older people may move more slowly than younger people, and (2) the baseline value of the kinematic parameter (\( Y_{i, \text{baseline}} \)), in order to correct for between subject variance. Both covariates were mean-centered to obtain \( \beta_x \) coefficients that correspond to the mean age and baseline scores. \( \epsilon_{ij} \) specifies the residual value for subject \( i \) at time-point \( j \).

The restricted maximum likelihood method (REML) was used in combination with a first order homogeneous autoregressive covariance structure to fit our model, as shown in Equation 5.5, onto the data. This covariance structure assumes that correlation between time-points decreases with increasing intervals between time-points, which is generally the case in longitudinal studies. For each kinematic parameter, the time-window for change was defined as the series of time-points with a significant \( \beta_1 \) coefficient. The significance of each regression coefficient \( \hat{\beta} \) was tested using the \( t \)-statistic which was given as \( \beta \) divided by its standard error. The degrees of freedom were computed using the Satterthwaite’s approximation. Level of significance was set two-sided at \( p < 0.01 \).

RESULTS

Table 5.1 shows the baseline characteristics of the 44 patients included (i.e., 19 females/25 males). The mean (± SD) age was 58 (± 12) years. All patients were able
to reach and grasp objects and were measured once a week during the first 5 weeks after stroke and subsequently in weeks 8, 12 and 26 after stroke. In total, 293 of the 352 kinematic measurements were conducted. Figure 5.2 shows hand trajectories and the grasp aperture profiles at week 1, week 5 and week 26 after stroke of one patient. This example shows that most change in the smoothness of hand trajectories and grasp aperture occurs between week 1 and week 5 after stroke.

<table>
<thead>
<tr>
<th>Table 5.1: Participant characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristic</strong></td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Missing measurements at each time-point</td>
</tr>
<tr>
<td>Week 1</td>
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<tr>
<td>Week 2</td>
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<tr>
<td>Week 3</td>
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<tr>
<td>Week 4</td>
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<td>Week 5</td>
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<td>Week 8</td>
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<tr>
<td>Week 12</td>
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<tr>
<td>Week 26</td>
</tr>
<tr>
<td>Gender, F/M</td>
</tr>
<tr>
<td>Mean age (SD), years</td>
</tr>
<tr>
<td>Paretic body side, L/R</td>
</tr>
<tr>
<td>Type of stroke (Bamford)</td>
</tr>
<tr>
<td>LACI</td>
</tr>
<tr>
<td>PACI</td>
</tr>
<tr>
<td>TACI</td>
</tr>
<tr>
<td>NIHSS total score *</td>
</tr>
<tr>
<td>Cognitive disturbance</td>
</tr>
<tr>
<td>Disorientation (NIHSS, item 1), no/yes</td>
</tr>
<tr>
<td>Inattention (NIHSS, item 11), no/yes</td>
</tr>
<tr>
<td>Impairments of vision</td>
</tr>
<tr>
<td>Hemianopia (NIHSS, item 3), no/yes</td>
</tr>
<tr>
<td>Deviation conjugée (NIHSS, item 2), no/yes</td>
</tr>
<tr>
<td>FMA upper limb (0 - 66) *</td>
</tr>
<tr>
<td>ARAT total score (0 - 57) *</td>
</tr>
<tr>
<td>BI total score (0 - 20) *</td>
</tr>
</tbody>
</table>

ARAT, Action Research Arm Test; BI, Barthel Index; F, Female; FMA, Fugl-Meyer Motor Assessment; L, Left; LACI, Lacunar Anterior Cerebral Infarction; M, Male; N, Number of subjects; NIHSS, National Institutes of Health Stroke Scale; PACI, Partial Anterior Cerebral Infarction; R, Right; SD, Standard Deviation; TACI, Total Anterior Cerebral Infarction. * Median value (interquartile range)
Frequency distributions of each kinematic parameter showed that $MD$ was normally distributed whereas $NJ_{hand}$ and $NJ_{grasp}$ were not. Therefore, $NJ_{hand}$ and $NJ_{grasp}$ were log-transformed to meet the assumptions for normality. Table 5.2 shows the regression coefficients for each kinematic parameter and each time-point after stroke. The regression coefficients for each time point after stroke indicate the mean difference in the kinematic parameter between that time-point and week 26. The regression coefficients for the covariates yield a correction factor for the difference between the actual and mean age and baseline value. Figure 5.3 depicts the longitudinal change in the regression coefficients. For $MD$, the regression coefficients for time poststroke decreased as a function of time poststroke. Up to week 5 after stroke, $MD$ was significantly larger than $MD$ at week 26 after stroke. The regression coefficients for $\log(NJ_{hand})$ and $\log(NJ_{grasp})$ paralleled this decrease in $MD$ as a function of time poststroke. In addition, up to week 5 after stroke, $\log(NJ_{hand})$ and $\log(NJ_{grasp})$ were significantly larger than $\log(NJ_{hand})$ and $\log(NJ_{grasp})$ at week 26 after stroke.
The regression coefficients for the covariates age and baseline were not significant for all kinematic parameters.

**Figure 5.3** Change in MD and smoothness of hand transport ($\log(N_{j\text{hand}})$) and grasp aperture ($\log(N_{j\text{grasp}})$) as a function of time poststroke. The contribution of time poststroke was significant for all 3-dimensional kinematic parameters until week 8 after stroke (gray).
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Table 5.2: Regression coefficients for recovery of MD and log-transformed values of normalized jerk of hand displacement and grasp aperture

<table>
<thead>
<tr>
<th></th>
<th>MD (s)</th>
<th>Log(NJ&lt;sub&gt;hand&lt;/sub&gt;)</th>
<th>Log(NJ&lt;sub&gt;grasp&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.17 ± .10 (&lt; .001) *</td>
<td>2.004 ± .063 (&lt; .001) *</td>
<td>3.668 ± .069 (&lt; .001) *</td>
</tr>
<tr>
<td>Week 1</td>
<td>1.63 ± .14 (&lt; .001) *</td>
<td>1.074 ± .077 (&lt; .001) *</td>
<td>0.894 ± .087 (&lt; .001) *</td>
</tr>
<tr>
<td>Week 2</td>
<td>1.08 ± .12 (&lt; .001) *</td>
<td>0.754 ± .068 (&lt; .001) *</td>
<td>0.612 ± .076 (&lt; .001) *</td>
</tr>
<tr>
<td>Week 3</td>
<td>0.55 ± .12 (&lt; .001) *</td>
<td>0.396 ± .063 (&lt; .001) *</td>
<td>0.294 ± .071 (&lt; .001) *</td>
</tr>
<tr>
<td>Week 4</td>
<td>0.41 ± .12 (.001) *</td>
<td>0.323 ± .062 (&lt; .001) *</td>
<td>0.201 ± .071 (.005) *</td>
</tr>
<tr>
<td>Week 5</td>
<td>0.32 ± .11 (.004) *</td>
<td>0.253 ± .057 (&lt; .001) *</td>
<td>0.181 ± .066 (.007) *</td>
</tr>
<tr>
<td>Week 8</td>
<td>0.10 ± .11 (.373)</td>
<td>0.084 ± .055 (.129)</td>
<td>-0.030 ± .064 (.643)</td>
</tr>
<tr>
<td>Week 12</td>
<td>0.04 ± .11 (.679)</td>
<td>0.062 ± .046 (.176)</td>
<td>0.005 ± .053 (.931)</td>
</tr>
<tr>
<td>Week 26</td>
<td>0.0 ± 0 †</td>
<td>0 ± 0 †</td>
<td>0 ± 0 †</td>
</tr>
<tr>
<td>Age</td>
<td>0.001 ± .01 (.850)</td>
<td>0.001 ± .005 (.765)</td>
<td>0.001 ± .005 (.878)</td>
</tr>
<tr>
<td>Baseline score</td>
<td>0.12 ± .05 (.040)</td>
<td>0.10 ± .098 (.331)</td>
<td>0.161 ± .095 (.099)</td>
</tr>
</tbody>
</table>

NOTE: Values are mean ± SE (P).
* P < 0.01; † This parameter is set to zero because it is redundant.

DISCUSSION

To the best of our knowledge, the present study is the first to show, by means of an intensively repeated 3D kinematic measures design, that the time-courses of smoothness of reaching and grasping follow a natural logistic pattern of recovery after stroke. Importantly, the progress of time contributed significantly to improvements in smoothness until week 8 after stroke. This finding suggests that improvement in quality of motor control, like improvement in motor synergism,\(^3,4,21\) is time-dependent and parallels spontaneous neurological recovery.\(^22\) This finding is in agreement with those of earlier studies based on clinical assessment scales, which showed that the effect of progress of time, as a reflection of spontaneous neurological recovery, is restricted to the first 6 to 10 weeks after stroke.\(^1\) In addition, it is in line with a recent study showing that smoothness of hand trajectory is a responsive measure for capturing improvements in upper limb quality of motor control early after stroke.\(^23\)

Smooth coordination patterns are an important characteristic of skilled motor behaviour.\(^24\) Moreover, computer simulations of reach-to-grasp behaviour suggest that minimum jerk is used as an important guiding principle by humans to select the optimal coordination strategy.\(^11,25\) Therefore, the improvements in smoothness early after stroke suggest that spontaneous neurological recovery leads to optimization
of the strategies to control the various degrees of freedom of the paretic upper limb and, with that, to an improved quality of motor control. These improvements in quality of motor control early after stroke further support the hypothesis that spontaneous neurological recovery leads to restitution of motor function.

Several mechanisms may be responsible for the observed improvements in smoothness of reach-to-grasp coordination. A previous study by our group has shown that the ability to make dissociated shoulder and elbow movements during reach-to-grasp increases in the first 5 weeks after stroke. This improvement in the control over the degrees of freedom in the paretic upper limb may lead to more optimal quality of motor control, reflected by the improved smoothness of upper limb coordination patterns. The observed reductions in smoothness early after stroke may also reflect deficiencies in motor unit recruitment. These deficiencies include reduced discharge rates and spontaneous firing of motor units in the paretic upper limb and may lead to inaccurate control of the force output of the paretic muscles. Finally, patients with stroke are assumed to rely more on proprioceptive and visual feedback to make ‘on-line’ corrections at the end of the reach-to-grasp movement. Improvements in smoothness may therefore suggest that these on-line corrections decrease during reaching movements. The above biological mechanisms underlying jerk support the hypothesis that the severity of jerk reflects the amount of noise in the voluntary motor control after stroke.

Study limitations
The present study had some limitations. First, we excluded all patients who were unable to reach and grasp within 3 weeks after stroke. The present results can therefore only be generalized to patients with a mild hemiparesis of the paretic upper limb and with a favourable prognosis for recovery of upper limb function. Second, since we used one discrete reaching paradigm, it is not possible to determine whether the present results can be generalized to other functional or rhythmic upper limb tasks. Third, the random effects model that was used in the present study assumes missing values to be missing at random. However, in week 1 and 2 after stroke a number of patients, in particular with a severe motor deficit at stroke onset, were not able to conduct the reach-to-grasp task, which resulted in non-randomly missing values at these time-
points. An identical analysis onto complete cases in the present study (N = 28) yielded also significant regression coefficients for time poststroke up to week 4, 5 and 2 after stroke for $MD$, $\log(N_{\text{hand}})$ and $\log(N_{\text{grasp}})$, respectively. This time-window of the complete cases is shorter compared to the time-window of the whole sample of patients. This latter finding suggests that the period of spontaneous neurological recovery is relatively shorter in cases with milder deficits when compared to cases with more severe strokes. We argue that these complete cases mainly represent stroke patients with only a mild to moderate deficit of the upper paretic limb. Future studies should therefore also include less challenging paradigms, such as reaching tasks without a grasping component, in order to avoid missing values in the first weeks after stroke. Fourth, the present study did not investigate the spontaneous intrinsic cerebral recovery by measuring structural or functional changes the brain. Future studies should investigate what changes in the brain may be responsible for improvements in the quality of motor control. Finally, the present study did not correct for the type or amount of therapy that the patients received, acknowledging that knowledge on the impact of early rehabilitation interventions on restitution of motor control is still lacking in the literature.

Conclusions
The results of the present study showed that, until 8 weeks after stroke, progress of time poststroke contributes significantly to reductions in normalized jerk of hand and finger movements during reach-to-grasp. This finding suggests that spontaneous neurological recovery in the first weeks after stroke in the brain leads to normalization of quality of motor control of the paretic upper limb. Future studies with intensively repeated measures designs should investigate if a very early start of therapies targeting upper limb function is able to modulate the quality of motor control beyond spontaneous neurological recovery.
REFERENCES