Changing Motor Synergies in Chronic Stroke

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INTRODUCTION

Stroke is the third-ranking cause of death and the first-ranking cause of long-term disability in the United States (AHA 2006). Graying of the population will increase the prevalence of stroke and has prompted the development of robotic tools for delivering movement therapy (Krebs et al. 1998; Lum et al. 2003). However, they focused on analysis of patients at a specific stage of recovery. However, they focused on analysis of patients at a specific stage of recovery. They considered a form of impairment and the ability to “extinguish” synergistic movements is regarded as a goal of therapy. For the upper extremity, these stereotyped movement patterns are often described as the flexion synergy (characterized by simultaneous shoulder abduction and elbow flexion) and the extension synergy (characterized by simultaneous shoulder adduction and elbow extension) (Trombly and Radomski 2002).

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METHODS

Subjects

One hundred seventeen community-dwelling volunteers (average age 58.8 ± 1.2 SE) who had a single stroke ≥6 mo before enrollment verified by brain imaging, 2) sufficient cognitive and language abilities to understand and follow instructions (Mini-Mental Status Score of ≥22 or interview for aphasic subjects), and 3) stroke-related impairments in muscle strength of the affected shoulder and elbow between grades 1/5 and ≤3/5 on the Motor Power (MP) scale (Gregson et al. 2000; O’Brien 1986) (neither hemiplegic nor fully recovered motor function in the muscles of the shoulder and elbow). Subjects were excluded from the study if they had a fixed contraction deformity in the affected limb and also if they demonstrated improvement over three measurements made during the 4-wk observation period before treatment. None of the subjects was engaged in conventional occupational or physical therapy programs or received pharmacological management of spasticity and tone (i.e., Botox) during the experimental trial. All subjects volunteered for the study and gave their informed consent. The experimental protocol was approved by the Committee on the Use of Human Experimental Subjects of the Massachusetts Institute of Technology and the Institutional Review Boards at Burke Rehabilitation Hospital, Spaulding Rehabilitation Hospital, and University of Maryland (Baltimore VAMC).

Apparatus

MIT-MANUS and its commercial version InMotion2 (Interactive Motion Technologies, Cambridge, MA) were used to collect data in this study. MIT-MANUS, designed at the Massachusetts Institute of Technology, is a robot intended for promoting neurological recovery (Hogan et al. 1992, 1995; Krebs et al. 1998). During all movements analyzed and presented in this paper, the robot was unpowered and acted as a low-friction passive measurement device that restricted subjects’ hand motion to the horizontal plane. The positions of two resolvers (MIT-MANUS) or encoders (InMotion2) located at the two joints of the robot were acquired digitally (sampling frequency $f_s = 200$ Hz, 16 bits quantization). The robot end-effector positions in the horizontal plane ($x$ and $y$ coordinates; see Fig. 1) were derived from these recordings and from forward kinematic equations of the robot arm.

Experimental protocol

All subjects participated in an 18-session robotic treatment protocol. Trials commenced after the baseline assessments on the F-M (Duncan et al. 1983; Fugl-Meyer et al. 1975) and MP (O’Brien 1986) showed that motor impairments were stable across three evaluation sessions spaced 2 wk apart.

During each therapy session, subjects were directed to make a number of point-to-point movements, ending as near as possible to the target location, while sitting in a chair. The torso was restrained by a five-point seatbelt to minimize torso movements, the elbow was supported by a low-friction pad, and the forearm and hand were supported by a specially made arm trough that attached to the robot handle. During these sessions the robot was powered. If the subject was unable to move or hit the target, the robot assisted his/her hand toward the targets as needed (Hogan et al. 2006; Krebs et al. 2003). A center target and eight targets equally spaced around a circle were displayed on a monitor, and visual feedback regarding the current position of the robot endpoint (subjects’ hand position) was provided. The center of the workspace was located in front of the subject at the body midline with the shoulder elevation at 45° with the elbow slightly flexed. Subjects moved from the center to each target and back, starting at “North” and proceeding clockwise. Each target was 14 cm from the center. Each therapy session lasted for 1 h.

All subjects went through clinical and robot-based evaluations at the admission, midpoint (ninth session), and the end of the treatment protocol. During the clinical evaluations, subjects’ recovery was assessed by clinical scales. In this study only the results of the F-M scale are reported. All other clinical results are reported elsewhere (Daly et al. 2005; Fasoli et al. 2003, 2004; Ferraro et al. 2003; Finley et al. 2005; MacClellan et al. 2005; Stein et al. 2004). During each robot-based evaluation session, subjects were directed to make 20 individual attempts to complete a circle-drawing task, while sitting in a chair with the torso and paretic limb constrained, as described earlier. After being shown a circular disk of 14 cm radius, the subject was asked to draw a similar shape by moving the end-effector of the robot in the horizontal plane in a terminated motion (Krebs et al. 1998). The circle-drawing task, which was not trained during the robot therapy sessions, was chosen because it requires the coordination of both shoulder and elbow joint movements (Lacquaniti et al. 1987; Tseng and Scholz 2005; Verschueren et al. 1999), which is affected after stroke. The starting point and movement direction were controlled, rather than selected by the subjects. Specifically, subjects were asked to draw five circles clockwise and five circles counterclockwise starting at 9 o’clock, and five circles clockwise and five circles counterclockwise starting at 3 o’clock. This design was chosen to counterbalance possible biases in subjects’ performance due to different lesion sides.

Data analysis

Data analysis was performed on the kinematic data collected during the circle-drawing robot-based evaluation sessions as subsequently detailed.

AXES RATIO METRIC. The axes ratio metric characterizes the goodness of a circle. It was derived directly from the kinematic data collected during the circle-drawing tasks. A movement was considered to begin when the speed first became >2% of the peak speed and was considered to end after the speed dropped and remained below the 2% threshold again.

The axes ratio was calculated as the ratio between the minor and major axes of the ellipse best fitting the hand path in Cartesian coordinates. The fitting ellipse was computed as described in Oliveira et al. (1996). Lengths of the major and minor axes of the ellipse were calculated respectively as the first and second largest eigenvalue of the covariance matrix of $x$ and $y$, where $x$ and $y$ represent positions along the $x$- and $y$-axis, respectively. The resulting axes ratio is a number between 0 and 1. As the ratio increases the fitting ellipse tends to approximate a circle.

JOINT ANGLES CORRELATION METRIC. The joint angles correlation metric characterizes the independence of the subject’s shoulder and
elbow joint movements. Modeling the human arm as a two-link mechanism, the shoulder and the elbow joint angles and their correlation were estimated from the measured hand path. The shoulder and elbow joint angles, respectively, were computed using the inverse kinematics equations of the human arm (Yoshikawa 1990).

For a subject with a stroke in the left hemisphere (right arm paresis) the joint angles were given by (see Eq. 1)

\[
\theta_1 = \tan^{-1}(y, x) - \tan^{-1}(k, x^2 + y^2 + l_1^2 - l_2^2) \quad \theta_2 = \tan^{-1}(k, x^2 + y^2 - l_2^2 - l_1^2 + \theta_1)
\]

(1)

where \(k = \sqrt{(x^2 + y^2 + l_1^2 + l_2^2) - 2(x^2 + y^2 + l_1^2 + l_2^2)} \), \(-\pi \leq \tan^{-1} \leq \pi\), \(l_1\) is upper arm length, and \(l_2\) is lower arm length. For a subject with a stroke in the right hemisphere (left arm paresis) the joint angles were given by an equation similar to Eq. 1.

Values of the parameters of the arm model were estimated from the measurements of 50th percentile for U.S. males and females (Difffrient 1974). With respect to Fig. 1, \(l_2\) was calculated as the sum of the forearm length (estimated as 0.254 and 0.234 m for male and female, respectively), the distance from the wrist to the grip line (0.076 and 0.071 m for male and female, respectively), and the handle of the robot (0.03 m radius); \(d_2\) was calculated as the sum of the distance between the subject’s body midline and the border of the table (0.114 and 0.107 m for male and female, respectively, assuming no space between the subject’s body and the table) and the distance from the subject’s body midline with the shoulder elevation at 45° with the elbow slightly flexed. We assumed that the shoulder elevation was constant throughout the horizontal plane was calculated as \(l_1\) cos (45°).

Finally, the correlation between the shoulder angle \(\theta_1\) and the elbow angle \(\theta_2\) was calculated as

\[
C(\theta_1, \theta_2) = \frac{\text{Cov}(\theta_1, \theta_2)}{\sqrt{\text{Cov}(\theta_1, \theta_1)} \cdot \sqrt{\text{Cov}(\theta_2, \theta_2)}}
\]

(2)

where \(C\) is the covariance matrix. We considered only the absolute value of the correlation. Therefore the correlation is a number between 0 and 1. Lower values indicate higher isolation or independence (i.e., smaller coupling) of the shoulder and elbow joint movements.

ORIENTATION METRIC. The best-fitting line to the hand paths collected during the circle-drawing experiments was calculated. The slope of this line (metric in Cartesian space) reveals the direction along which most data are distributed.

AXES RATIO IN JOINT SPACE METRIC. Ellipses were fitted to the curves obtained by plotting \(\theta_1\) versus \(\theta_2\) using a procedure similar to that described earlier. The ellipse major and minor axes were calculated as well as their ratio. Note that the lengths of the axes of this ellipse are related to the ranges spanned by the joints during movements.

STATISTICAL ANALYSIS. We tested whether 1) the fitted ellipse at discharge approximated a circle better than at admission and 2) the joint angle correlation decreased from admission to discharge.

If, during the course of the therapy, subjects became better able to draw circles the axes ratio should increase. If movements of the shoulder and the elbow joints became more independent during the course of therapy the joint angles correlation should decrease.

We also tested whether from admission to discharge there was a change in the 1) major and minor axes of the fitted ellipse, 2) axes ratio in the joint space, and 3) slope of the best-fitting line. In the next paragraph we describe how different patterns of changes would support a process of augmentation or extinction of the initial abnormal synergies.

For each subject, data of initial and discharge evaluations were compared using two-tailed \(t\)-test (all the data collected during each evaluation session were used for the analysis). Additionally, to analyze overall trends of changes, data obtained by averaging the 20 circle attempts for each subject at admission, interim, and discharge were compared using repeated-measures ANOVA.

MOTOR SYNERGIES. As there appear to be several definitions of motor synergies (which seem to carry different implications, e.g., synergies are considered to be “good” among neuroscientists, but “bad” among clinical neuro-rehabilitators), there also appears to be no agreement on how synergies should be measured. In this paper, we used the metrics described earlier to measure motor synergies and investigate how they changed during recovery.

Figure 2 shows how changes in our metrics reflect changes in the abnormal flexor and extensor synergies that are usually “monitored” by clinical neuro-rehabilitators to assess patients’ recovery. Drawing elliptical shapes entails combining elbow flexion and shoulder (horizontal) abduction movements and elbow extension and shoulder (horizontal) adduction movements that are components of the flexor and extensor synergy, respectively. One of the goals of this paper was to describe changes in synergies during stroke recovery and, specifically, to test whether they follow a pattern of augmentation or extinction. Figure 2 also shows how the analysis of changes in our metrics can help gain insight into this issue.

Figure 2A shows idealized elliptical paths approximating a circle to various degrees, drawn counterclockwise. Figure 2B shows the corresponding joint angles versus time (but to emphasize path rather than trajectory, the horizontal axis is in arbitrary units). The narrowest (blue) ellipse approximates paths observed early in recovery (see Fig. 3, bottom left for an example of actual hand path observed).

The gray lines superimposed in Fig. 2B show straight-line approximations to the pattern of coordination of joint angles resembling an idealized instance of the components of the “flexor synergy.” The corresponding hand path is shown in Fig. 2A by the gray curve drawn from left to right. Note that this coordinative pattern of joint angles yields an approximate direction in hand space. A curved pattern of coordination consistent with the aforementioned components of the flexor synergy is shown by the heavy blue lines in Fig. 2B. The corresponding hand path, shown by the heavy blue line in Fig. 2A, differs in detail from the gray curve but shows the same approximate directionality. Thus a preference for specific directions in hand space provides evidence of an underlying pathological synergy.

A progression from the initial (blue) elliptical shape to perfect execution (shown red) may occur in an infinite number of ways. The hand paths corresponding to three possible exemplars are shown in Fig. 2, C, D, and E.

In Fig. 2C the elliptical shape becomes progressively “fatter” (the axes ratio increases) but its orientation is preserved and its major axis remains constant. This panel illustrates how the initial pathological synergies might be preserved throughout recovery. Compare Fig. 2C with Fig. 2, A and B: when going from the blue ellipse to the red circle the initial flexor synergy is not suppressed but progressively augmented. Three of the corresponding paths in joint space are shown color-coded in Fig. 2F, where again the approximate preservation of orientation may be discerned. Note that changes happen by “stretching” the blue path (i.e., the initial joint coordination) along specific directions while maintaining specific constraints (points A and B).

Figure 2D shows a hypothetical alternative progression (extinction of the initial abnormal synergies) in which the initial directionality first disappears in the earlier stages of recovery (the drawn figure becomes circular, albeit small, before becoming enlarged to achieve perfect execution). Insofar as directionality provides evidence of an underlying pathological synergy this progression would be consistent with the initial pathological synergy first being extinguished before complete recovery is achieved. Three of the corresponding paths in joint space are shown color-coded in Fig. 2G.
Figure 2 shows another hypothetical alternative progression (extinction of the initial abnormal synergies). Directionality in hand space is still evident in the earlier stages of recovery, but it differs substantially from the initially observed direction. Insofar as directionality provides evidence of an underlying abnormal synergy and as the original direction is replaced by a new one, this represents another possible way in which the initial pathological synergy may be extinguished before complete recovery is achieved. Three of the corresponding paths in joint space are shown in Fig. 2H.

To assess the extent to which motor synergies, as measured by our metrics, and their changes characterize recovery, as measured by the F-M scale, we computed how our metrics correlated with the F-M scores. To investigate how motor synergies changed during patients’ recovery we studied how our metrics changed over the course of the therapy.

RESULTS

The average F-M score (upper extremity portion: max 66) of subjects that participated in this study was 20.47 ± 10.220.32.247 on October 26, 2016 http://jn.physiology.org/ Downloaded from by 10.220.32.247 on October 26, 2016

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Arms ratio

Figure 4 shows the values of axes ratio at admission and discharge for each subject sorted in an ascending order. The highest changes from admission to discharge corresponded to subjects with the lowest performance at admission: whereas the average change per patient was 0.11, the lowest and highest 50% exhibited an average change per patient of 0.17 and 0.04, respectively. These data demonstrate that according to this metric the subjects who started with the lowest performance improved the most over the course of therapy.

Figure 4 also shows the changes in the axes ratio metric from admission to discharge for each subject. Filled circles represent statistically significant changes over the course of therapy ($P < 0.05$). Subjects’ axes ratio changed significantly in most cases, with a clear trend in the direction of improved circle drawing: the axes ratio tended to increase over the course of therapy. As the ratio approached 1 the circles became rounder and less elliptical. Axes ratio increased across most subjects from admission to discharge ($P < 0.05$). See Table 1 for a summary of mean changes.

The changes in the axes ratio mainly arose from changes in the minor axis: from admission to discharge the major axis did not change significantly, whereas the minor axis increased significantly ($P < 0.05$).

Joint angles correlation

Figure 5 shows the values of joint angle correlation at admission and discharge for each subject sorted in an ascending order. According to this metric the highest changes from admission to discharge corresponded to subjects with the lowest performance at admission: whereas the average change per patient was −0.13, the lowest and highest 50% exhibited an average change per patient of −0.07 and −0.15, respectively. This means that the subjects who were less able to decouple the movements of their joints at admission improved the most over the therapy.

Figure 5 also shows the differences in joint angle correlation from admission to discharge for each subject. Filled circles represent statistical significance ($P < 0.05$). The changes in the joint angles correlation mainly arose from changes in the minor axis: from admission to discharge the major axis did not change significantly, whereas the minor axis increased significantly ($P < 0.05$).

Table 1. Average changes of metrics and F–M synergy portion for initial, interim, and discharge evaluations

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Initial ($n = 117$)</th>
<th>Interim ($n = 113^*$)</th>
<th>Discharge ($n = 117$)</th>
<th>ANOVA Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axes ratio Cartesian space</td>
<td>0.51 ± 0.01</td>
<td>0.57 ± 0.01</td>
<td>0.61 ± 0.01</td>
<td>Initial vs. Interim</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interim vs. Discharge**</td>
</tr>
<tr>
<td>Joint angles correlation</td>
<td>0.60 ± 0.01</td>
<td>0.53 ± 0.01</td>
<td>0.47 ± 0.01</td>
<td>Initial vs. Interim</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interim vs. Discharge**</td>
</tr>
<tr>
<td>Axes ratio joint space</td>
<td>0.33 ± 0.01</td>
<td>0.36 ± 0.01</td>
<td>0.39 ± 0.01</td>
<td>Initial vs. Interim</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interim vs. Discharge**</td>
</tr>
<tr>
<td>F–M synergy portion</td>
<td>10.37 ± 0.58</td>
<td>11.65 ± 0.59</td>
<td>12.58 ± 0.62</td>
<td>Initial vs. Interim</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interim vs. Discharge**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial vs. Discharge**</td>
</tr>
</tbody>
</table>

Values are means ± SE; $n$ is the number of patients. Reported data are nondimensional. *Four patients missed the interim evaluation. **Indicates statistical significance ($P < 0.05$).
the average slope of the best-fitting line to the shapes drawn by right hemiparesis were investigated separately. Denoting A as Orientation,

declined across almost all subjects from admission to discharge at the end of the robotic therapy trial. Joint angle correlation tended to decrease. This finding implies that subjects were better able to decouple shoulder and elbow movements of the paretic arm at admission, A increased, significantly from admission to discharge (P ≤ 0.05). This suggests that a change in the relationship between the ranges of the angles spanned by the shoulder and elbow joints occurred over therapy. See Table 1 for a summary of mean changes.

Axes ratio in joint space

The axes ratio in joint space metric changed, and specifically increased, significantly from admission to discharge (P ≤ 0.05). This suggests that a change in the relationship between the ranges of the angles spanned by the shoulder and elbow joints occurred over therapy. See Table 1 for a summary of mean changes.

Robot metrics and recovery

The correlation values between our metrics and the F-M scores are reported in Table 2. Directions of change in the metrics and in the F-M scores were consistent, all indicating that patients’ motor ability improved from admission to discharge. These data suggest that our metrics were good quantitative descriptors of motor synergies, as measured by the F-M synergy portion scores, and were able to account for a significant portion of recovery.

DISCUSSION

Our data show that over the course of an 18-session robot therapy program subjects with chronic motor impairments after stroke, who were recovering as measured by the F-M scale, improved their ability to draw circles and to move their shoulder and elbow independently. The changes we observed in our metrics described the changes in the motor performance of a task, circle drawing, which was not trained during therapy (robot-assisted therapy trained subjects on point-to-point movements). This finding has important implications for generalization of movement training. The patterns displayed by our metrics, which were consistent and correlated with those displayed by the F-M scores, may help elucidate and characterize how abnormal synergies change over recovery.

angle correlation changed significantly for all but a few cases with a clear trend in the direction of improvement: the correlation tended to decrease. This finding implies that subjects were better able to decouple shoulder and elbow movements of the paretic arm at the end of the robotic therapy trial. Joint angle correlation decreased across almost all subjects from admission to discharge (P ≤ 0.05). See Table 1 for a summary of mean changes.

Orientation

Differently from the other metrics, changes in orientation from admission to discharge were small. Subjects with left and right hemiparesis were investigated separately. Denoting A as the average slope of the best-fitting line to the shapes drawn by the subjects and \( R^2 \) as a measure of how successful the fit was in explaining the variation of the data, for the left arm group, composed of 64 patients, we found A = -0.05 (\( R^2 = 0.19 \)) at admission, A = -0.02 (\( R^2 = 0.15 \)) at interim, and A = 0.01 (\( R^2 = 0.12 \)) at discharge; for the right arm group, composed of 53 patients, we found A = 0.05 (\( R^2 = 0.17 \)) at admission, A = 0.02 (\( R^2 = 0.13 \)) at interim, and A = 0.03 (\( R^2 = 0.08 \)) at discharge. For each of the two groups we found no significant differences from admission to interim, from interim to discharge, nor from admission to discharge.\(^1\)

Figure 6 shows histograms of the orientation metric. In each bin the number of subjects displayed only small changes from admission to discharge.

\[^1\] We found a significant difference in the orientation between the left and right arm group at admission (P ≤ 0.05) but not at interim and discharge. The difference may arise from the difference in dynamics between the system composed by the robot and the subjects’ left arm and the system composed by the robot and the subjects’ right arm (Foster 1999; Mussa-Ivaldi et al. 1985). Another possible explanation is related to the different contribution of each cerebral hemisphere to the control of unilateral arm movements (Baggesteiro and Sainburg 2002; Prestopnik et al. 2003; Sainburg and Kalakanis 2000; Sainburg and Wang 2002; Sperry et al. 1969; Wang and Sainburg 2003).

\[^2\] We calculated the F-M synergy portion as the sum of F-M items 3–11 (which measure how well patients are able to move within pathological synergies), items 12, 13, 15, and 16, as well as items 31–33 (which measure how well patients are able to move out of pathological synergies). The items reflected motor abilities in the paretic shoulder and elbow (not forearm, wrist, or hand).
Familiarization of subjects with the task

The changes we observed in the metrics are unlikely to be due simply to increased familiarization of the subjects with the task. The intrasession variability of the robot metrics was significantly smaller than the intersession variability. Specifically, for the axes ratios and the joint angle correlation metrics the SD at admission, interim, and discharge was smaller (P < 0.05) than the SD calculated across all the trials. Also, in a separate study we asked 10 unimpaired subjects to perform circle-drawing tasks, similar to our clinical robot evaluation with 20 circle-drawing attempts, six sessions, two sessions per day over three separate days (maximum time lapse of 3 wk, test 1 to test 6). We found no significant changes between sessions in the metrics (MA Finley, L Dipietro, J Ohlhoff, J Whitall, HI Krebs, and CT Bever, unpublished observations).

Thus the changes we reported in this study cannot be explained by increased familiarization of the subjects with the task. Rather, we suggest that they reflect a process of changes in motor synergies underlying stroke recovery.

Quantitative description of stroke recovery

This study provided a quantitative, kinematic characterization of the process of stroke recovery. Although the process of recovery from stroke is still far from being understood, recent studies based on invasive methods have started to elucidate how this process occurs in animals (Dancause et al. 2005; Nudo et al. 1996). However, the corresponding knowledge in humans is much poorer because it is mainly based on qualitative observations of motor behavior. A few recent studies reported quantitative data on stroke recovery (Beer et al. 2000; Cirstea and Levin 2000; Cirstea et al. 2003; Dewald and Beer 2001; Dewald et al. 1995, 2001; Finley et al. 2005; Krebs et al. 1999; Lum et al. 2003; Rohrer et al. 2000).

Our findings are consistent with and extend the findings of several previous studies. Similar to Cirstea and colleagues (Cirstea and Levin 2000; Cirstea et al. 2003) we found that stroke patients exhibit abnormal joint coupling. Note that Cirstea and Levin (2000) reported that stroke patients use compensatory trunk synergies for reaching. In our study sub-

TABLE 2. Correlation among metrics and F–M

<table>
<thead>
<tr>
<th>Correlation</th>
<th>Axes Ratio Cartesian Space</th>
<th>Joint Angles Correlation</th>
<th>Axes Ratio Joint Space</th>
</tr>
</thead>
<tbody>
<tr>
<td>F–M synergy portion</td>
<td>Initial 0.61</td>
<td>Initial –0.39</td>
<td>Initial 0.48</td>
</tr>
<tr>
<td></td>
<td>Interim 0.60</td>
<td>Interim –0.43</td>
<td>Interim 0.51</td>
</tr>
<tr>
<td></td>
<td>Discharge 0.57</td>
<td>Discharge –0.39</td>
<td>Discharge 0.44</td>
</tr>
<tr>
<td>F–M total score</td>
<td>Initial 0.55</td>
<td>Initial –0.34</td>
<td>Initial 0.45</td>
</tr>
<tr>
<td></td>
<td>Interim 0.52</td>
<td>Interim –0.32</td>
<td>Interim 0.41</td>
</tr>
<tr>
<td></td>
<td>Discharge 0.48</td>
<td>Discharge –0.29</td>
<td>Discharge 0.32</td>
</tr>
</tbody>
</table>

For each metric a vector containing the values for each patient at admission, interim, and discharge was filled and correlated with a vector containing the corresponding F–M values. Reported data are nondimensional. All correlations are significant (P < 0.05).
jects were strapped with a five-point seatbelt to minimize the effect of torso movements.

Abnormal muscle synergy patterns were found in the upper limb of chronic stroke patients, in both static (Dewald and Beer 2001) and dynamic tasks (Beer et al. 2004; Reinkensmeyer et al. 1999). Whereas previous studies focused on analysis of patients at a specific stage of recovery, this study reported a large-scale analysis of kinematic changes occurring in joint coupling and motor synergies in patients recovering from chronic stroke over the course of a treatment.

Tuning of motor synergies

We suggest that changes in our metrics reflect a process of tuning of motor synergies that underlies stroke recovery.

At admission subject hand paths could be fitted with ellipses with relatively low axes ratios. Thus the presence of a preferred direction (often strongly preferred) appears to be a characteristic of these hand paths. During the course of therapy the axes ratio as well as the minor axis increased, whereas the major axis and the main data orientation did not change significantly. Concurrently, the joint angle correlation decreased and the axes ratio in joint space increased.

Figure 3 displays how these changes occur in patients’ data. The left panel of Fig. 3 shows typical data of a subject at admission. The subject draws a shape that is far from being circular (axes ratio = 0.26). Over the course of the movement $\theta_1$ and $\theta_2$ appear similar (joint angle correlation = 0.96). Concurrently, the range spanned by $\theta_2 - \theta_1$ is smaller than that spanned by $\theta_1$. The right panel of Fig. 3 shows discharge data for the subject shown in the left panel. The subject draws a shape that is more similar to a circle (axes ratio = 0.67). Over the course of the movement $\theta_1$ and $\theta_2$ no longer appear similar (joint angle correlation = 0.43). Concurrently, the range spanned by $\theta_2 - \theta_1$ becomes comparable to that spanned by $\theta_1$. From admission to discharge a change occurs in the degree of independence of $\theta_1$ and $\theta_2$, as demonstrated by the altered joint angle correlation (which decreased from 0.96 to 0.43) and in the relationship between $\theta_1$ and $\theta_2$, as demonstrated by the altered axes ratio in joint space (which changed from 0.08 to 0.46).

As shown in Fig. 2, the changes in our metrics reflect changes in the relationship between the shoulder and elbow joint angles and, in particular, in elbow flexion/extension and shoulder horizontal abduction/adduction, which are related to the clinical flexion and extension motor synergies.

The changes we observed between admission, interim, and discharge in the metrics extracted from our experimental data are similar to the changes shown in Fig. 2C. In our data from admission to interim to discharge, overall, the axes ratio metric increased from 0.51 to 0.57 to 0.61, the joint angle correlation decreased from 0.60 to 0.53 to 0.47, and the axes ratio in joint space increased from 0.33 to 0.36 to 0.39. Concurrently, the orientation and the length of the major axis remained constant, whereas the length of the minor axis increased throughout recovery. In Fig. 2C, as the blue ellipse changes into the black ellipse and into the red circle, the axes ratio in Cartesian space increases from 0.14 to 0.57 to 1, the joint angles correlation decreases from 0.94 to 0.58 to 0.16, and the axes ratio in joint space increases from 0.12 to 0.39 to 0.64; moreover, the length of the minor axis increases, whereas the length of the major axis and the main data orientation remain constant.

The changes we observed in our data support the idea that a process of “augmentation” of existing abnormal synergies underlies stroke recovery. As patients recover, the initial abnormal synergies are not suppressed but progressively augmented. The “gains”\(^3\) of other components of movement are gradually changed until recovery is reached (as shown in Fig. 2F the initial joint coordination is stretched until the final joint coordination is reached, and the stretching occurs while maintaining specific constraints). While to the best of our knowledge quantitative characterizations of changes in motor synergies over stroke recovery are not available, directional tuning of synergies has been shown in movements performed by unimpaired subjects: muscle synergies appear to be maximally recruited for movements toward specific directions and gradually decrease for movements away from these directions (D’Avella et al. 2006).

Extinction of abnormal motor synergies

Figure 2, D and E shows possible patterns of recovery where the initial abnormal synergies are extinguished before full recovery is reached. The changes we observed in the metrics derived from our experimental data are not consistent with these patterns. In our data the orientation remained constant, but it did not in the pattern shown in Fig. 2D. In our data the length of the major axis of the fitting ellipse remained constant, but it did not in the pattern shown in Fig. 2E. A process of augmenting existing abnormal motor synergies rather than a process of extinction of old abnormal motor synergies appears to underlie stroke recovery.

Correlation with traditional measures of motor recovery

Recovery from stroke is captured, in part, by improvements in moving the formerly paralyzed or weakened limb and, further, by better coordinating these new or strengthened movements to regain independent joint control. The F-M is a well-established, clinical scale traditionally used to measure recovery.

The changes displayed by the total F-M scores at admission, interim, and discharge were consistent with those displayed by the robot metrics, all indicating an improvement in patients’ motor abilities. Correlation ranged from 0.3 to 0.55 (Table 2), suggesting that these metrics were able to describe, in part, the changes occurring in upper limb motor abilities during recovery. Correlation between our metrics and the F-M synergy portion ranged from 0.4 to 0.6, suggesting that our metrics were able to capture the changes displayed by abnormal motor synergies. The pathological flexor synergy consists of elbow flexion, forearm supination, shoulder abduction, external rotation of the shoulder, and retraction and/or elevation of the shoulder girdle. The pathological extensor synergy consists of elbow extension, forearm pronation, adduction of the arm, internal rotation of the arm, and fixation of the shoulder girdle in a pronated position (Brunnstrom 1970). Thus pathological

\(^3\) We borrow the concept of “gain factor” from engineering. A variable that can be modified by a gain factor can display small modifications from two consecutive values and its value at a certain time is a function of its previous value (gain tuning).
synergies are defined in 3D. Whereas the F-M synergy portion measured patients’ ability to perform predefined movements in 3D space, with the upper limb unsupported against gravity, our metrics quantified changes in elbow flexion/shoulder horizontal abduction and elbow extension/shoulder horizontal adduction, which are components of the flexor and extensor synergies, respectively. Thus by definition our metrics quantified changes in two dimensions and measured them with the upper limb supported against gravity. The differences between the measures performed by the F-M synergy portion and our robot metrics may account for the modest correlation, between 0.4 and 0.6. A ceiling effect of our metrics is another factor that could partially explain such differences. This hypothesis is supported by the fact that in Figs. 4 and 5 the subjects respectively at the higher and lower end of the x-axis (who thus had better starting performance) displayed smaller improvement than subjects at the opposite end of the scale (who started with greater impairment). Alternative measures of ellipse parameters (e.g., Fasse et al. 2000) may reduce possible ceiling effects. The F-M assessment has five evaluation domains (including sensory function, balance, and joint range of motion), but its particular strength is the evaluation of motor impairment in the paretic upper limb (Duncan et al. 1983; Fugl-Meyer et al. 1975; Gladstone et al. 2002). The F-M is well able to detect changes in persons with moderate to severe motor impairments after stroke, partly because of its emphasis on isolated joint movement rather than task-related actions. Reported disadvantages include a potential ceiling effect for higher-functioning patients and its limited number of test items to evaluate distal, fine-motor function (Gladstone et al. 2002). These disadvantages are not relevant to our study: we included persons with stroke who presented moderate to severe motor impairments (not mild strokes), and the circle-drawing task did not require the more specific measure of distal hand function.

Disadvantages of the F-M scale include high interrater variability (Krebs et al. 2002). While the development of quantitative descriptors of stroke recovery is an object of research, we previously used metrics such as movement duration, aiming accuracy, and shoulder strength to characterize training-related changes in motor abilities of stroke patients. Differently from the F-M, these metrics were able to discriminate between the different trainings that had been delivered (H. I. Krebs, B. T. Volpe, J. Stein, C. Bever, L. Dippietro, J. J. Palazzolo, S. E. Fasoli, R. Hughes, D. Lynch, M. A. Finley, J. Ohihoff, W. R. Frontera, N. Hogan, unpublished observations). This finding confirmed that it is important to develop new measures to quantify changes occurring over motor recovery after stroke, especially when the goal is a better understanding of the mechanisms that are targeted by a specific treatment. While the metrics proposed in this paper displayed changes consistent with the F-M, they also expand the battery of metrics we are currently using to develop quantitative models of stroke recovery.

Generalization of movement training

Subjects became better able to draw circles over the course of a robot therapy program. However, during therapy, we trained subjects only in point-to-point movements, not circle drawing. This finding has two main implications. First, it extends our understanding of the effects of robot therapy. Previous work has shown that robot therapy can improve subjects’ reaching performance in the paretic upper limb for which they receive training (Fasoli et al. 2003, 2004; Ferraro et al. 2003; Finley et al. 2005; Stein et al. 2004). Furthermore, the same work has shown that generalization across different limb segments is limited (e.g., shoulder/elbow vs. wrist). Our finding extends such results to the same workspace and limb segments, suggesting that generalization occurs for these conditions in a task for which subjects receive no training. It questions the notion that motor recovery in persons after stroke is always specific to the trained task. It is consistent with previous results in neuroscience on unimpaired subjects that suggested that generalization of motor learning can occur in the same workspace and limb segments (Gandolfo et al. 1996; Malfait et al. 2002). Thus it potentially opens avenues for the design of new protocols for stroke rehabilitation.

Implications for robot-assisted therapy

Whereas the F-M assessment is administered by therapists, the proposed metrics allow automatic measurements of motor synergies for severe to moderate patients. This may have important implications for robot-assisted therapy. Recent developments of such therapies include algorithms for controlling robots to provide patients with customized treatments. For example, the so-called progressive-based performance algorithm records patients’ kinematic data while treatment is being delivered, and uses them to assess patients’ motor abilities; the robot is then controlled to assist patients’ movements based on the measured abilities (Hogan et al. 2006; Krebs et al. 2003). The metrics reported herein can easily be integrated in such types of algorithms (e.g., to change the robot level of assistance to the patients based on the amount of synergies they display), thereby unwrapping new possibilities for designing robot-assisted therapy programs.

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DISCLOSURE

H. I. Krebs and N. Hogan are co-inventors of the Massachusetts Institute of Technology (MIT)–held patent for the robotic device used in this work and hold equity positions in Interactive Motion Technologies, Inc., a company that manufactures this type of technology under license to MIT.

REFERENCES


