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Learning, Not Adaptation, Characterizes Stroke Motor Recovery: Evidence From Kinematic Changes Induced by Robot-Assisted Therapy in Trained and Untrained Task in the Same Workspace

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Abstract

Both the American Heart Association and the VA/DoD endorse upper-extremity robot-mediated rehabilitation therapy for stroke care. However, we do not know yet how to optimize therapy for a particular patient's needs. Here, we explore whether we must train patients for each functional task that they must perform during their activities of daily living or alternatively capacitate patients to perform a class of tasks and have therapists assist them later in translating the observed gains into activities of daily living. The former implies that motor adaptation is a better model for motor recovery. The latter implies that motor learning (which allows for generalization) is a better model for motor recovery. We quantified trained and untrained movements performed by 158 recovering stroke patients via 13 metrics, including movement smoothness and submovements.

Improvements were observed both in trained and untrained movements suggesting that generalization occurred. Our findings suggest that, as motor recovery progresses, an internal representation of the task is rebuilt by the brain in a process that better resembles motor learning than motor adaptation. Our findings highlight possible improvements for therapeutic algorithms design, suggesting sparse-activity-set training should suffice over exhaustive sets of task specific training.

Index Terms

Kinematics; motor adaptation; motor learning; rehabilitation robotics; stroke

I. Introduction

STROKE is a leading cause of permanent disability world-wide. Every year over 785 000 persons suffer a stroke in the U.S. and about 70% of stroke survivors lose motor skills of the arm and hand [1]. First proposed in the 1980s, robot-mediated therapy is increasingly becoming part of poststroke rehabilitative care. Our working model behind such therapy is best expressed by Hebbian ideas of nervous system plasticity, mainly that neurons that “fire” together, “wire” together. The human brain is capable of self-organization, or neuroplasticity [2], [3], so that training and rehabilitation offer an opportunity for motor recovery [4], [5]. The scientific rationale for rehabilitation robots for the upper extremity is anchored on this concept of motor plasticity and on evidence that intensive repetition of movement promotes motor recovery following a stroke [6]–[9]. Rehabilitation robots can perform repetitive tasks in a highly consistent and controllable manner, and they continuously record patients’ movement kinematics and dynamics features. Such features can be used to not only quantify therapy outcomes, but also to design a robot control loop which tailors the therapeutic action of the robot to the patient’s motor abilities [10], [11].

Several rehabilitation robots for the upper extremity have been proposed. Examples include MIT-Manus [5], ARM Guide [12], MIME [13] and the more recently developed PLEMO [14], ARMin [15], and MEMOS [16]. Clinical effectiveness greater than sham robot-therapy or a matched amount of traditional occupational therapy was reported in several studies [4], [13], [17], [18], including the recent Veterans Administration (VA) multicenter, randomized, controlled clinical trial reported in the *New England Journal of Medicine*, which enrolled 127 patients six months or more after stroke and showed that robot-mediated therapy improved outcomes over 36 weeks as compared with usual care [19]. These results led to the 2010 “Comprehensive Overview of Nursing and Interdisciplinary Rehabilitation Care of the Stroke Patient: A Scientific Statement from the American Heart Association (AHA)” [20]. This guideline recommended that: “Robot-assisted therapy offers the amount of motor practice needed to relearn motor skills with less therapist assistance. Most robots for motor rehabilitation not only allow for robot assistance in movement initiation and guidance but also provide accurate feedback… Most trials of robot-assisted motor rehabilitation concern the upper extremity (UE), with robotics for the lower extremity (LE) still in its infancy… ” This AHA report suggested that UE robot-assisted therapy has already achieved Class I, Level of Evidence A for stroke care in the outpatient setting and care in chronic care settings. It suggested that UE robot-assisted therapy has achieved Class IIa, Level of Evidence A for stroke care in the inpatient setting. To explain, Class I is defined as: "Benefit ⋙ Risk. Procedure/Treatment SHOULD be performed/administered;" Class IIa is defined as: "Benefit ≫ Risk, IT IS REASONABLE to perform procedure/administer treatment;" and Level of Evidence A is defined as "Multiple populations evaluated: Data derived from multiple randomized clinical trials or meta-analysis." Similar endorsement came later in 2010 from the "VA/DoD Clinical Practice Guideline for the Management of Stroke Rehabilitation [21]."

However, much remains to be done to afford optimal therapy tailoring treatment to the particular patient's needs. In fact, we anticipate that characterizing the specific effects of different interventions, developing methodologies for therapy design, and developing models for neuro recovery which would afford personalized treatment represent the main thrust of this decade [22], [23]. For example, the extent to which robot-mediated training generalizes is rarely assessed, although generalization in new situations beyond the trained ones is a key feature that should be tested when developing new rehabilitation interventions [24]. Likewise, there are few quantitative models of the process of motor recovery following a stroke. Hence most advances occur on a trial-and-error basis.

Motor learning and motor adaptation are two of the potential models for motor recovery from stroke that researchers have recently started to encode in the design of robotic treatments. Several research groups are exploring performance-based control algorithms (see, for example, [10], [25], [26]) that incorporate concepts of motor learning, including efforts to monitor continuous and conscious engagement of the patient in the robotic training programs. Results are promising as some of these algorithms have been shown to yield higher outcomes than robotic training programs designed to mimic conventional neurorehabilitation treatments such as strength or sensorimotor training [22]. Others are investigating additional aspects of motor learning and the viability of reverse-engineering motor adaptation processes so as to design appropriate force fields that eventually result in desired after effects [27], [28]. Whether motor recovery following a stroke is better characterized as a process similar to motor adaptation or to motor learning is still unclear.

In this study, we explore differences between adaptation and learning to afford better insight and better robotic therapies. While there is considerable debate on the differences between motor learning and motor adaptation, it is becoming increasingly clear that motor adaptation and learning are two different processes [29]. It is generally accepted that motor learning allows limited generalization to occur (presumably based on some form of acquired internal representation) while motor adaptation does not. For example, we define the initial acquisition of the ability to ride a bicycle (which can generalize and facilitate learning to ride a motorcycle) as motor learning but define the initial improvement in performance observed after several decades without riding a bicycle as adaptation. Improvements obtained with motor learning are maintained over time, while after effects resulting from adaptation are short-lived [29]. In Huang and Krakauer's model [29] adaptation is seen as part of motor skill learning for a particular task that adjusts for different environmental conditions. This explanation is consistent with studies on stroke patients that have shown that a tailored adaptation condition can result in improved movement kinematics outside of the robot, but the improvements fade quickly [29], [30]. Whether motor recovery following stroke can be modeled as adaptation or learning remains however unclear, but answering this question has important implications. The adaptation model implies that we must train an exhaustive set of tasks, while the learning model implies that we must understand the limitations of generalization and train through a more sparse set of tasks. This study investigated whether motor learning or motor adaptation is a more suitable model for motor recovery from stroke by analyzing trained and untrained movements of recovering stroke patients with kinematic macro-metrics (including smoothness) and micro-metrics (submovements).

Smoothness has been used to describe movement of unimpaired [31] and stroke subjects [32] and has been quantified with different metrics, including number of speed peaks [33] and jerk, the third derivative of position [31]. Changes in smoothness have been observed in movements performed by unimpaired subjects learning new tasks and in recovering stroke subjects [34]–[38]. Arguably such changes are caused by the blending of discrete submovements [35], [37], [39]. While submovement conjecture remains a topic of research, submovements appear to account for many movement features [34], [40]–[47].

In this study, we analyzed movements performed by 158 stroke survivors undergoing a robot-mediated therapy program. Subjects were trained exclusively on point-to-point reaching movements and were tested on both the trained point-to-point movements and untrained circle drawing movements at different stages of recovery. Our goal was to investigate whether untrained and trained movements were characterized by similar changes in smoothness and submovements. A positive result indicated by a high correlation among changes of the trained and untrained movements would suggest that recovery shares traits with motor learning rather than motor adaptation. Our working hypothesis was that motor learning would lead to a positive transfer of improvements to untrained tasks within a “region” (possibly small) that “surrounded” the trained tasks.

II. Methods

A. Subjects

One-hundred and fifty-eight individuals, 42 inpatients (sub-acute stroke) and 116 outpatients (chronic stroke), were enrolled. Subjects’ demographic data is summarized in Table I.

Inclusion criteria for inpatients were: 1) first single focal unilateral lesion with diagnosis verified by brain imaging to the cortical and subcortical territories (excluding thalamic lesions); 2) 2 ± 2 weeks after stroke onset at the start of the study; 3) cognitive function sufficient to understand the experiments and follow instructions; and 4) upper limb hemiparesis as measured by standard instruments (specifically, Fugl–Meyer Assessment (FM) below 38 out of 66 [48]).

Inclusion criteria for outpatients were: 1) diagnosis of a single, unilateral stroke at least six months prior to enrollment verified by brain imaging to the cortical and subcortical territories; 2) sufficient cognitive and language abilities to understand and follow instructions (Mini-Mental Status Score of 22 and higher or interview for aphasic subjects);

and 3) stroke-related impairments in muscle strength of the affected shoulder and elbow between 7 and 38 on the FM scale (neither hemiplegic nor fully recovered motor function in the muscles of the shoulder and elbow). Outpatients were excluded from the study if they had a fixed contraction deformity in the affected limb.

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).

B. Experimental Apparatus

MIT-Manus and its commercial version InMotion2 (Interactive Motion Technologies, Inc., Watertown, MA) were used in this study. MIT Manus is a robot intended for promoting neurological recovery and designed at the Massachusetts Institute of Technology. Five robots were used in this study, all with similar mechanical (inertia, friction, and bandwidth) characteristics [5], [49], [50].

C. Protocol

Subjects went through an 18-session robotic treatment. During each therapy session, they were directed to make 1024 point-to-point reaching movements, ending as near as possible to the target location, while sitting in a chair. 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° and the elbow slightly flexed. Subjects moved from the center to each target, stopped, then returned to the center, starting at "12 o'clock" and proceeding clockwise. Each target was 14 cm from the center. During these sessions the robot was powered. If the subject was unable to move or hit the target, the robot guided her/his hand toward the targets as needed, described elsewhere [5], [10], [22]. Each therapy session lasted for 1 h. Inpatients received standard inpatient rehabilitation care in addition to robot-mediated therapy. None of the outpatients were engaged in conventional occupational or physical therapy programs or received pharmacological management of spasticity and tone (i.e., Botox) during the experimental trial. The FM Test of Upper Extremity Function ([48] upper limb, max 66) was used for the assessment of motor impairment. Outpatients started the robotic treatment after the clinical scales showed that motor impairments were stable across three evaluation sessions spaced two weeks apart (this gradual engagement into the trial and determination that the patient is actually stable is critical to reduce variability, and the approach was coined as "phase-in" phase [51]). Outpatients that demonstrated significant changes during these measurements were excluded from the study. Subjects went through robot-based evaluations at admission, mid-point (ninth session), and end of the treatment protocol. During these evaluation sessions, the robot was unpowered, namely it provided no assistance and acted as a low friction passive measurement device that restricted subjects' hand motion to a horizontal plane. During each session, while sitting in a chair as described above, they were directed to make 80 point-to-point reaching movements similar to the training protocol (40 outbound and 40 return movements). They were also asked to perform twenty individual attempts to complete a circle-drawing task. This task, which was not trained, was performed in the same workspace as the trained movements and it required the continuous coordination of the shoulder and elbow movements. 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 a horizontal plane in a terminated motion [5]. The starting point and movement direction were instructed. Specifically, subjects were asked to draw five circles clockwise and five circles counter-clockwise starting at 9 o'clock, five circles clockwise and five circles counter-clockwise starting at 3 o'clock.

All participants completed the robotic treatment and went through the evaluation sessions, except three inpatients and four outpatients that missed the interim robot-mediated evaluation sessions (for these patients only the initial and final evaluation sessions data were included).

D. Kinematic Macro-Metrics Analysis

Following Rohrer *et al.* [39] and Bosecker *et al.* [11], the following metrics were extracted from speed profiles of center-out point-to-point movements (trained movements), which were calculated as summed squares of the first order difference of the X and Y trajectory components smoothed with a 0–4 Hz bandwidth FIR filter: 1) movement mean speed; 2) movement peak speed; and 3) movement duration. Three smoothness metrics were also computed: 1) speed shape, which was calculated as mean speed divided by peak speed; 2) number of peaks, which was calculated as the negative of the number of peaks in the speed profile; and 3) jerk metric, which was calculated by dividing the negative mean jerk magnitude by the peak speed. The first two are dimensionless and increase monotonically with movement smoothness. Note that the negative sign in the number of peaks metrics was introduced for convenience so that an increase in this metric corresponds to an increase in movement smoothness and is consistent with the speed shape metric. Early in recovery subjects' movements speed profiles are very fragmented and display a series of peaks with deep valleys in between, i.e., mean speed is much less then peak speed. At this stage, the speed metric tends to be relatively low, especially if gaps between fragments or submovements (see below) are long. As subjects recover, their movements are less fragmented and display shallower and shorter valleys between submovements: thus speed metric is higher. The third metric has units of $(1/\text{duration})^2$. Although a dimensionless jerk metric can be defined as a metric which changes monotonically with movement smoothness [52], our jerk metric displays a characteristic nonmonotonic change. Rohrer *et al.* [39] showed via simulation that the jerk metric changes as a function of the distance between submovements onsets (T), i.e., it increases with increasing blending over the interval $0.12\ s < T < 0.26$ s and decreases with increasing blending for $T > 0.26$ s. Note that this nonmonotonic behavior depends on the form of the jerk metric chosen. The metrics described above were also extracted from the kinematic data collected during circle drawing movements (untrained movements). We defined the axes ratio metric calculated as the ratio of the minor and major axes of the ellipse best-fitting the data [53]. This metric is a number between 0 and 1 and can be regarded as a measure of coordination between shoulder and elbow movements. Values closer to 1 indicate that the fitting ellipse tends to better approximate a circle, i.e., improved coordination of shoulder and elbow movements. A movement was considered to begin when the speed first became greater than 2% of the peak speed and was considered to end when the speed first decreased to and remained below the 2% threshold again.

E. Kinematic Micro-Metrics (Submovement) Analysis

We used the method described in Rohrer *et al.* [54] to extract submovements from movement speed profiles. Briefly, the extracted submovement functions were support-bounded log-normal (LGNB) curves, defined as

$$B(t)=\frac{D(T_1-T_0)}{\sigma\sqrt{2\pi}(t-T_0)(T_1-t)}\exp\left\{\left(\frac{-1}{2\sigma^2}\right)\left[\ln\left(\frac{t-T_0}{T_1-t}\right)-\mu\right]^2\right\}$$

where D is the displacement resulting from the movement, T_0 is the movement start time, T_1 is the end time, μ controls the skewness (asymmetry), and σ determines the kurtosis ("fatness") of the curve. The five independent parameters that define LGNB submovements allow them to take on a wide range of submovement- like shapes [55]. In this study, submovements were allowed to take on a duration between 167 and 1500 ms. To reduce the problem of long "tails" often associated with markedly asymmetric submovements, we calculated submovement duration as the time interval between T_{0n} and T_{1n}, where T_{0n} and T_{1n} were defined as the time when the submovement went, respectively, above and below 5% of its peak value [56]. Submovements were optimized simultaneously [54]. An increasing number of submovements were fit to each movement until the "fit error" ε fell below a predetermined threshold, where $\varepsilon = \int|F(t) - G(t)|dt/ \int |G(t)|dt|$ with $G(t)$ the movement speed profile, and $F(t)$ the extracted speed profile. In this study ε was set to 2%.

F. Statistical Analysis

To analyze overall change trends, data obtained by averaging the trials for each subject at admission and discharge were compared using two-tailed t-tests. A significance level of $p \leq 0.05$ was used for all tests. To study to what extent changes in the kinematics of trained movements generalized to untrained movements, we correlated the corresponding kinematic variables extracted from trained and untrained movements. To protect for type I errors, which could arise from lack of independence of the 13 metrics, we also performed multivariate canonical correlation analysis [57] using the method described in [58]. First we tested the hypothesis that all population canonical correlations were zero; then using Bartlett test we tested a series of null hypotheses that the first k canonical correlations were nonzero and the remaining (13-k) were zero.

III. Results

A. FM Scores

From admission to discharge, the average FM score increased from 10.02 (1.14) to 22.70 (2.28) for inpatients and from 20.47 (standard error 1.15) to 24.35 (standard error 1.27) for outpatients. Hence the changes we observed in the kinematics occurred as patients were recovering, as measured by the FM scale.

B. Changes in Trained Movements

Figs. 1 and 2 report the changes from admission to discharge for the kinematic metrics and submovement parameters extracted from the trained point-to-point movements. Figs. 1 and 2 also summarize the values of the kinematic metrics and submovement parameters at different stages of recovery (i.e., inpatient or outpatient).

Overall for the trained point-to-point movements performed by inpatients, as recovery progressed, movement duration decreased while mean speed and peak speed increased (subjects became able to move faster). The first two smoothness metrics increased but, as in Rohrer *et al.* [39], the jerk metric decreased. Concurrently submovements became fewer, taller (i.e., submovement amplitude increased), longer (i.e., submovement duration increased), and more blended (i.e., submovement interpeak distance decreased and overlap increased), indicating an improved ability of patients to generate bigger “chunks” of movements and concatenate them (Fig. 3). As indicated by submovement skeweness μ and kurtosis σ, over the course of recovery submovements maintained the same amount of asymmetry (μ did not significantly change from admission to discharge) but became “fatter” (σ increased).

The outpatient group displayed changes similar to the inpatient group, but smaller (corresponding to smaller changes in the FM from admission to discharge). For example, the number of peaks metric increased in average from −24 to −10.5 in inpatients and from −16.2 to −9.1 in outpatients. The direction of change is only distinct for the jerk metric that increased from admission to discharge, consistently with the results of the study by Rohrer *et al.* [39].

C. Changes in Untrained Movements

Figs. 4 and 5 report the changes from admission to discharge for the kinematic metrics and submovement parameters extracted from the untrained circle drawing movements. Figs. 4 and 5 also summarize the values of the kinematic metrics and submovement parameters at different stages of recovery (i.e., inpatient or outpatient).

For the untrained circle drawing movements, the axes ratio increased over recovery. This indicated that subjects became progressively better able to draw circles and better coordinate shoulder and elbow movements. In addition, the kinematic macro-metrics (movement duration, mean and peak speed and the three smoothness measures) and micro-metrics (submovement parameters) of these untrained movements exhibited changes similar to those of the corresponding variables extracted from the trained point-to-point movements.

D. Correlation Between Kinematic Changes in Trained and Untrained Movements

Table II reports the values of the correlation among corresponding variables extracted from point-to-point and circle drawing movements. Correlations were significant for 9 out of 13 metrics, with values ranging from 0.83 to 0.93, suggesting that the changes we observed during recovery in trained and untrained movements resulted from the same underlying neural process. Similar results were obtained when correlating patient- by-patient values, with all correlations being significant ($p < 0.01$). Canonical correlation analysis confirmed that 1) association existed between improvements in trained and untrained tasks (the hypothesis that all population canonical correlations was zero was rejected); and 2) the hypothesis of multiple dimension of association between the two sets of measurements was tenable ($k = 9$ and $k = 10$ out of 13 for averaged and patient-by-patient data respectively, being k the smallest number of "important" canonical correlations and associated pairs of canonical variables [58]).

IV. Discussion

A. Mechanisms and Models of Motor Recovery From Stroke

Mechanisms underlying human motor recovery from stroke are poorly understood, arguably due to the lack of descriptive, quantitative data on the recovery process. Robots can be easily equipped with sensors to record position, velocity and force exerted by the patient, thereby allowing researchers to collect unprecedented amounts of quantitative data on the recovery process. This offers a unique opportunity to gain insights into mechanisms underlying recovery and to develop models of recovery, which can in turn be used to design more effective treatments and more efficient training schedules.

We found that trained and untrained movements displayed similar kinematic changes at a macro-level (macro-metrics) and at a micro-level (submovements) level of detail and that such changes were highly correlated. Our results have several implications.

First, they provide support for our working model that submovements blend as a mechanism of motor recovery from stroke. Recovery proceeds by progressively regaining the ability to combine submovements, both in the sub-acute and chronic phase of recovery. Clear changes were found in submovement number (which decreased), peak and duration (which increased) and overlap (which increased), suggesting that over the course of recovery the nervous system became better able to generate "bigger chunks" of movements and combine them. At a macro-level of kinematic detail such improved ability to combine submovements translated into improved movement smoothness, a metric commonly used to quantify movement quality. More importantly, we found that such ability to generate "bigger chunks" of movements and recombine them to produce better quality movements was transferred to contexts different from the ones used for acquiring the ability. During recovery submovements extracted from trained or untrained movements tended to maintain the same shape (no significant changes in skewness and small changes in kurtosis) although small, significant shape changes were observed between trained and untrained movements, supporting the view that submovements are "building blocks" or primitives of movement, whose shape might be optimized for each motor task.

Canonical correlation analysis demonstrated association between improvements in trained and untrained tasks; furthermore Pearson's correlation coefficients between improvements in trained and untrained tasks were significant in 9 out of 13 measures, with values ranging between 0.83 and 0.93, suggesting that the changes we observed in trained and untrained movements resulted from the same underlying neural process underlying motor recovery.

Second, our results suggest that motor recovery from stroke can be better modeled as motor learning than as motor adaptation. This conclusion is consistent with the different time scales that underlie motor adaptation and motor learning: performance changes induced by a learning process are relatively permanent, while those due to adaptation are relatively short-lived and tend to persist only as long as a perturbation is present. The performance improvements we observed were maintained over time, i.e., patients progressively improved over the course of the 18 h training, i.e., 18 × 1024 movements and we know from our previous studies that improvements are retained up to three-years follow-up [59]. This time scale suggests that patients underwent a motor learning as opposed to a motor adaptation process which are easily forgotten: improvements obtained with error-induced after effects resulting from adaptation approaches are short lived, lasting for 30–60 movements (2–4 min) after 600 training movements (40 min) [30]. Our conclusion is also consistent with Huang and Krakauer's hierarchical model [29], where adaptation is a mean used by the CNS to compensate changes in the operating conditions of a motor skill, i.e., at a lower level of control than skill mastering. According to their model, adaptation may evoke improvements apparently similar to those evoked by learning but these will be short-lived; to truly be able to use a skill the learner must acquire the top level control for that skill, which may require more extensive training.

B. Consistency With Previous Studies

In a previous study, Rohrer *et al.* [39], analyzed movements performed by 31 stroke survivors (12 inpatients and 19 outpatients) undergoing robot-mediated therapy with MIT-Manus. Subjects were trained and tested on the same type (point-to-point) of movements. It was reported that movements performed by recovering subjects displayed progressively higher speed, smaller duration, and higher smoothness as measured by the speed shape and the number of peaks metrics. Furthermore, the jerk metric increased in chronic but decreased in sub-acute patients. These changes, including the non-monotonic behavior of the jerk metric, could be accounted for by changes in submovements. Consistent with results reported by Krebs *et al.* [35], submovements in the sub-acute phase of recovery appeared isolated and had a rather stereotyped shape which, given a task, remained relatively constant during recovery. As recovery progressed submovements became fewer, longer, and taller and progressively blended together [39], [54]. The results presented in this paper for 158 stroke patients are consistent with the results of Rohrer *et al.* [39] on trained (point-to-point) movements. They extend Rohrer's findings by showing that changes in movement smoothness and submovement parameters also occur in untrained movements, i.e., there is generalization of training within the same workspace.

Our results are consistent with the view that stroke recovery and motor learning have similar traits [22], [24], [60]. In unimpaired subjects motor learning generalizes at the level of the same workspace and limb segments [61], [62] and occurs via changes in movement smoothness and submovements [36], [37]. We found that similar results hold for subjects recovering from stroke and showed that generalization of training in stroke recovery occurs in the same workspace and limb segments: subjects became better able to draw circles (an untrained task) by discharge time as they became better on point-to-point movements (the trained task).

Our results confirm and extend the results of our previous studies on chronic stroke [53], [63]. Dipietro *et al.* [53] analyzed data from 117 chronic stroke patients and showed that subjects trained on point-to-point movements became better able to draw circles although they had not been trained on this task, i.e., subjects' movements showed an increase in the axes ratio metric. A subsequent analysis on 47 chronic stroke patients [63] showed that circle drawing movements became progressively smoother during recovery although subjects had not been trained on circle drawing. The results reported in this study were derived from a data set of 158 subjects, which included 42 sub-acute patients. Differing from [53], [63], this study reported a detailed kinematic analysis of both trained (point-to-point) and untrained (circle drawing) movements at a macro-and micro-level of kinematic detail, and it analyzed correlation among the kinematic variables extracted from trained and untrained data.

C. Quantitative Characterization of Motor Recovery From Stroke

While most descriptions of the process of stroke recovery are highly qualitative, only a few studies reported quantitative, sensor-based data on upper extremity motor performance [33], [64]–[69] and even fewer contained kinematic-based descriptions [11], [39], [53], [54], [70].

This paper reports a kinematic characterization of the process of motor recovery from stroke for 158 subjects at different stages of recovery. A partial analysis of this data set is reported in [39], [53], [63], [71]. We characterized changes in subjects' movement kinematics using two types of metrics, i.e., macro-metrics (including smoothness, duration, speed, and axes ratio) and micro-metrics (submovement parameters). While the former describe coarse features of movement kinematics, the latter allow for a description at a much finer level of detail, potentially providing insight into the mechanisms underlying motor recovery. In both trained and untrained movements, most metrics displayed similar patterns, with sub-acute phase (inpatient) changes greater than chronic-phase (outpatient) changes. For example, the number of peaks metric increased in average from −24 to −10.5 in inpatients and from −16.2 to −9.1 in outpatients. The same patterns were displayed by the FM scale (on average, inpatients FM values increased from 10.02 to 22.70 and outpatients FM values from 20.47 to 24.35), suggesting that the metrics used in this paper could be used as a basis to develop sensor-based evaluation scales [11].

Because they are highly repeatable and can be administered automatically, robot-based scales can potentially overcome the disadvantages of traditional clinical assessment scales which have high inter-rater variability and require time-consuming administration sessions [72], [73]. We are currently using robot-based metrics to develop models to predict clinical scales and characterize the effect of different robot-mediated therapies. Bosecker *et al.* [11] analyzed data from 111 chronic stroke subjects and found that a linear regression model with a set of eight macro-metrics including mean speed, peak speed, speed shape and axes ratio could predict the Motor Status Score (R = 0.71 for training and R = 0.72 for validation). Krebs *et al.* [74] showed that chronic stroke subjects who participated in a robot-mediated therapy program for training movement speed became the speediest performers, indicated by the largest reduction in movement duration and number of submovements, and subjects who were trained on strength improved the most in shoulder strength but the least in shoulder-elbow coordination, indicated by the smallest increase in the axes ratio. Taken together with the results of the Bosecker *et al.* [11] and Krebs *et al.* [74] studies, our results suggest that our kinematic macro-and micro-metrics can be used to develop motor recovery "calibration curves" for quantifying, predicting, and comparing the effect of different types of neurorehabilitation therapies.

D. Implications for Neurorehabilitation

Our results have several clinical implications. First, they extend knowledge of the effects of robot-mediated therapy. As pointed out by Krakauer [24], two critical questions should always be asked when assessing a rehabilitation technique: 1) whether gains persist for a significant period after training, and 2) whether gains generalize to untrained tasks. Previously we answered the first question and showed that clinical benefits induced by robot-mediated therapy are sustained even three years after end of treatment [17], [59], [75]. These results were confirmed in the recent Veterans Administration (VA) multicenter, randomized, controlled clinical trial reported in the New England Journal of Medicine which demonstrated that, on average, stroke patients retained (or further improved) gains six months after completion of training [19]. Here we answered the second question and demonstrated that the kinematic changes induced by robot-mediated therapy generalize to untrained tasks in the same workspace. One must take these results with the appropriate caveats: our results are valid for movements involving shoulder and elbow in the horizontal plane, and whether they extend beyond that needs to be verified. Our results challenge the traditional view held by many neurorehabilitation practitioners, i.e., that motor recovery in persons after stroke is always specific to the trained task. In both coarse and fine measures, subjects improved at circle drawing although they received no training for it.

Our results complement other results from our previous studies. First, we investigated the potential to increase the effectiveness of robot-mediated neurorehabilitation by developing new whole-arm, functionally-based robot therapy approaches [76]. Two approaches were investigated: 1) to train functional tasks with the robot ("top-down" approach), or alternatively 2) to train by aiming at impairment reduction at the capacity level with different robotic modules, breaking these functional tasks into subcomponents, and relying on the therapist to facilitate the carryover of observed impairment gains from robotic training into functional activities ("bottom-up" approach). The former approach was in line with current therapy views, while the latter was based on our previous research. Our hypothesis was that a robotic treatment protocol, properly targeted to emphasize a sequence and timing of sensory and motor stimuli similar to those naturally occurring in daily life tasks, could facilitate carryover of the observed gains in functional motor abilities (first approach). Our study suggested that at least for severe to moderate stroke patients the bottom-up approach is more effective, consistent with the results of others [32]. In fact, Pomeroy in the UK has been a proponent that robot-mediated therapy for severe to moderate stroke patients should focus on impairment rather than function (personal communication, Campus Biomedico, Rome, 2004). She recommends that as patients' impairments are reduced, therapists would then assist in translating these impairment gains into function for this population.

Second, we investigated the potential to increase the effectiveness of robot-mediated neurorehabilitation by training spatial movements for severe to moderate stroke patients [77]. Two approaches were investigated: 1) to train reaching in a gravity-compensated movement and against gravity on distinct days, or alternatively 2) to train both movements during the same session (spatial movement). The second approach was in line with current therapy views while the first was based on observations that suggest different motor controllers for reaching movements in a gravity-compensated environment and against gravity [78]. Our data showed that the latter approach was less effective than the former, probably due to another motor learning trait, namely “interference.”

Our results are consistent with those of these two studies, which suggest respectively that training simpler, nonfunctional movements may be more effective than training more complex, functional movements (at least for the very severe to moderate patients enrolled into our studies), and that motor recovery from stroke is similar to motor learning. In hindsight, one might speculate that if a model of motor learning and not motor adaptation characterizes motor recovery, then robot-mediated therapy should aim at training not necessarily functional tasks but rather a sequence of multiple, simpler tasks and rely on generalization of training within the workspace to further enhance beneficial therapeutic effects.

Acknowledgment

Dr. H. I. Krebs and Dr. 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.

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Biographies

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B. T. Volpe photograph and biography not available at the time of publication.

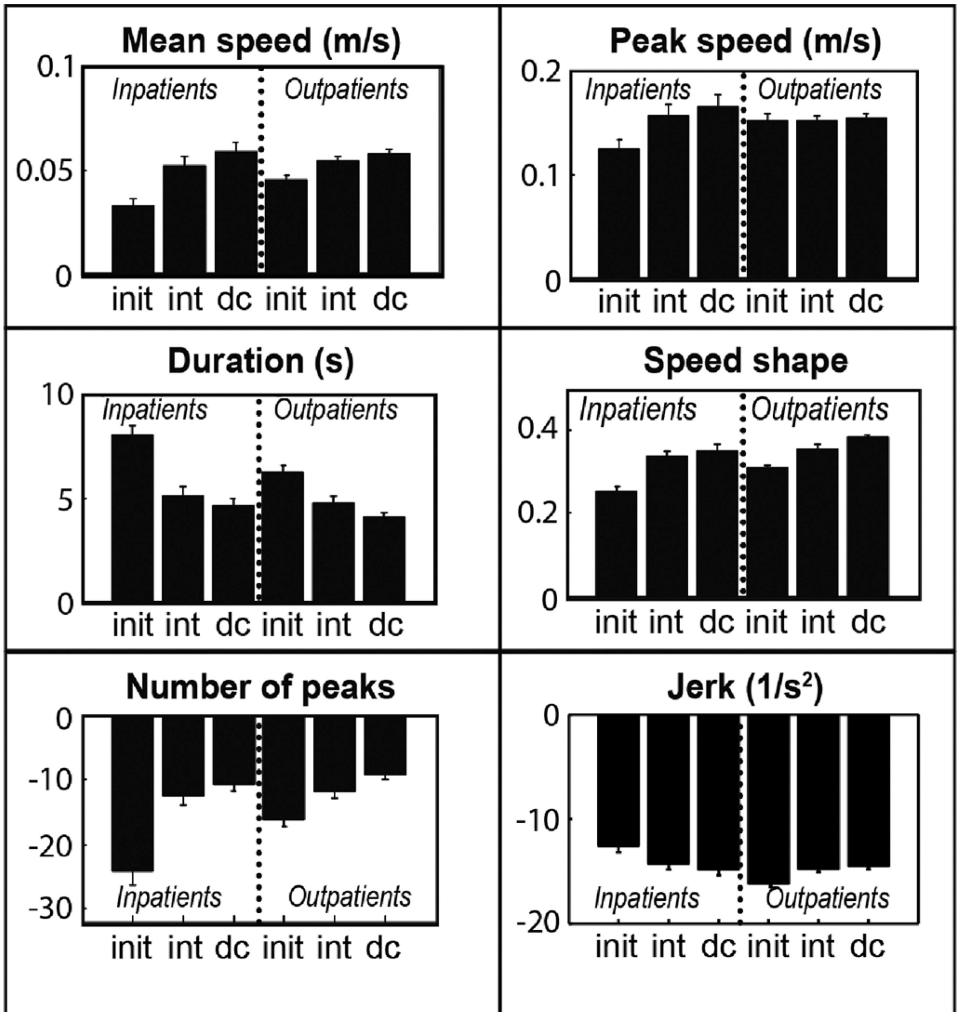
J. Stein photograph and biography not available at the time of publication.

C. Bever photograph and biography not available at the time of publication.

S. T. Mernoff photograph and biography not available at the time of publication.

S. E. Fasoli photograph and biography not available at the time of publication.

N. Hogan photograph and biography not available at the time of publication.



Change	Inpatients (n=42)	Outpatients (n=116)	P
Mean speed (m/s)	0.02* (8.17e-7)	0.01* (7.57e-9)	* (0.002)
Peak speed (m/s)	0.04* (8.32e-4)	0.003 (0.62)	* (0.001)
Duration (s)	-3.40* (3.0e-8)	-2.17* (2.18e-12)	* (0.02)
Speed shape	0.10* (2.23e-10)	0.07* (3.01e-24)	* (0.01)
Number of peaks	13.54* (2.44e-8)	7.07* (1.0e-10)	* (0.001)
Jerk ($1/s^2$)	-2.29* (0.001)	1.69* (9.53e-5)	* (1.70e-6)

Fig. 1.

Mean and standard error of kinematic outcome metrics for trained point-to-point movements for initial (init), mid-way or interim (int), and discharge (dc) evaluations. Table shows changes from admission to discharge for inpatients and outpatients (second and third column) and difference between changes in inpatients and outpatients (fourth column). P-values are reported in brackets. * indicates significance ($p < 0.05$).

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Change	Inpatients (n=42)	Outpatients (n=116)	P
Number	-3.96* (2.69e-4)	-5.05* (6.59e-13)	(0.36)
Peak (m/s)	0.025* (9.75e-6)	0.009* (1.01e-4)	* (6.53e-4)
Duration (s)	0.03 (0.054)	0.07* (4.44e-16)	* (0.003)
Overlap (s)	0.20* (1.02e-6)	0.08* (3.33e-16)	* (9.10e-6)
Interpeak distance (s)	-0.18* (5.46e-5)	-0.012 (0.24)	* (1.04e-7)
Mu (skewness)	-0.008 (0.28)	0.001 (0.71)	(0.23)
Sigma (kurtosis)	0.02* (0.04)	0.04* (0)	* (0.005)

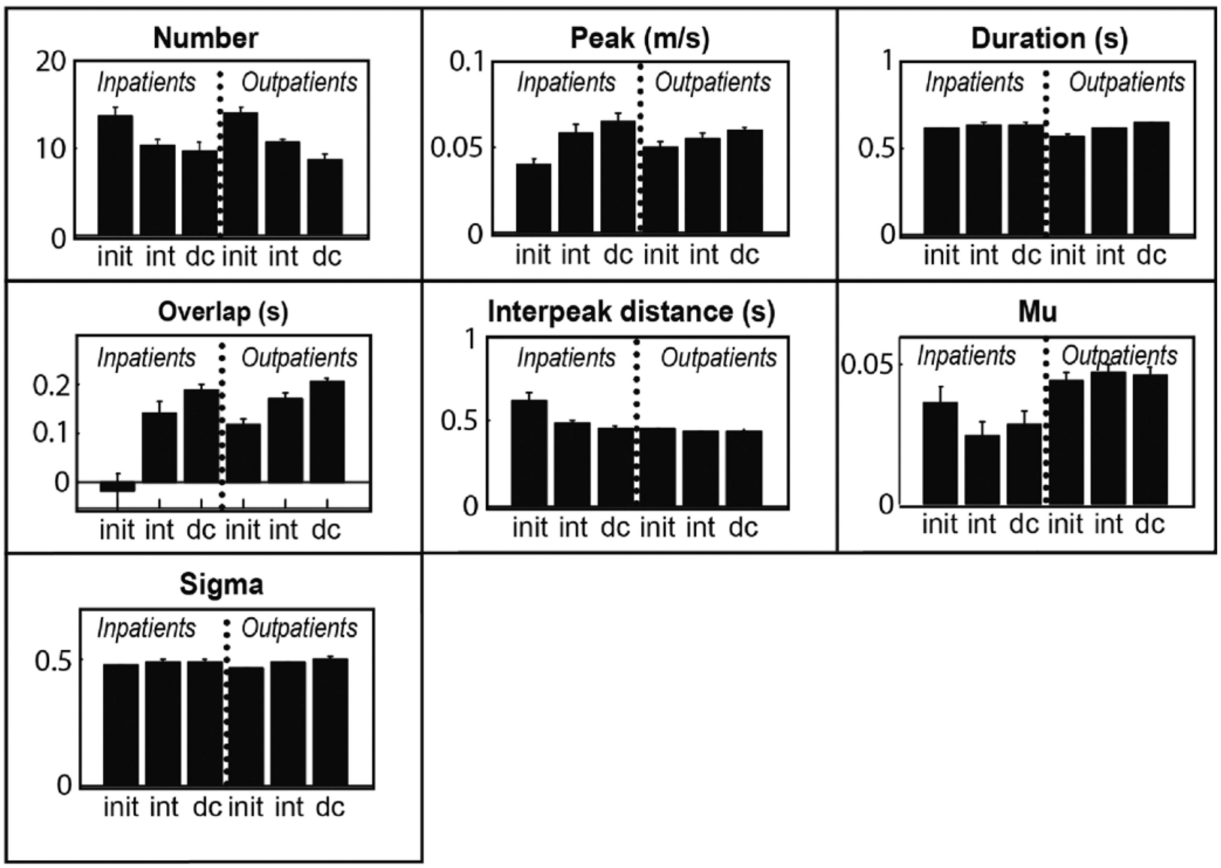

Fig. 2.
Similar to Fig. 1. Results of submovement analysis for trained point-to-point movements.

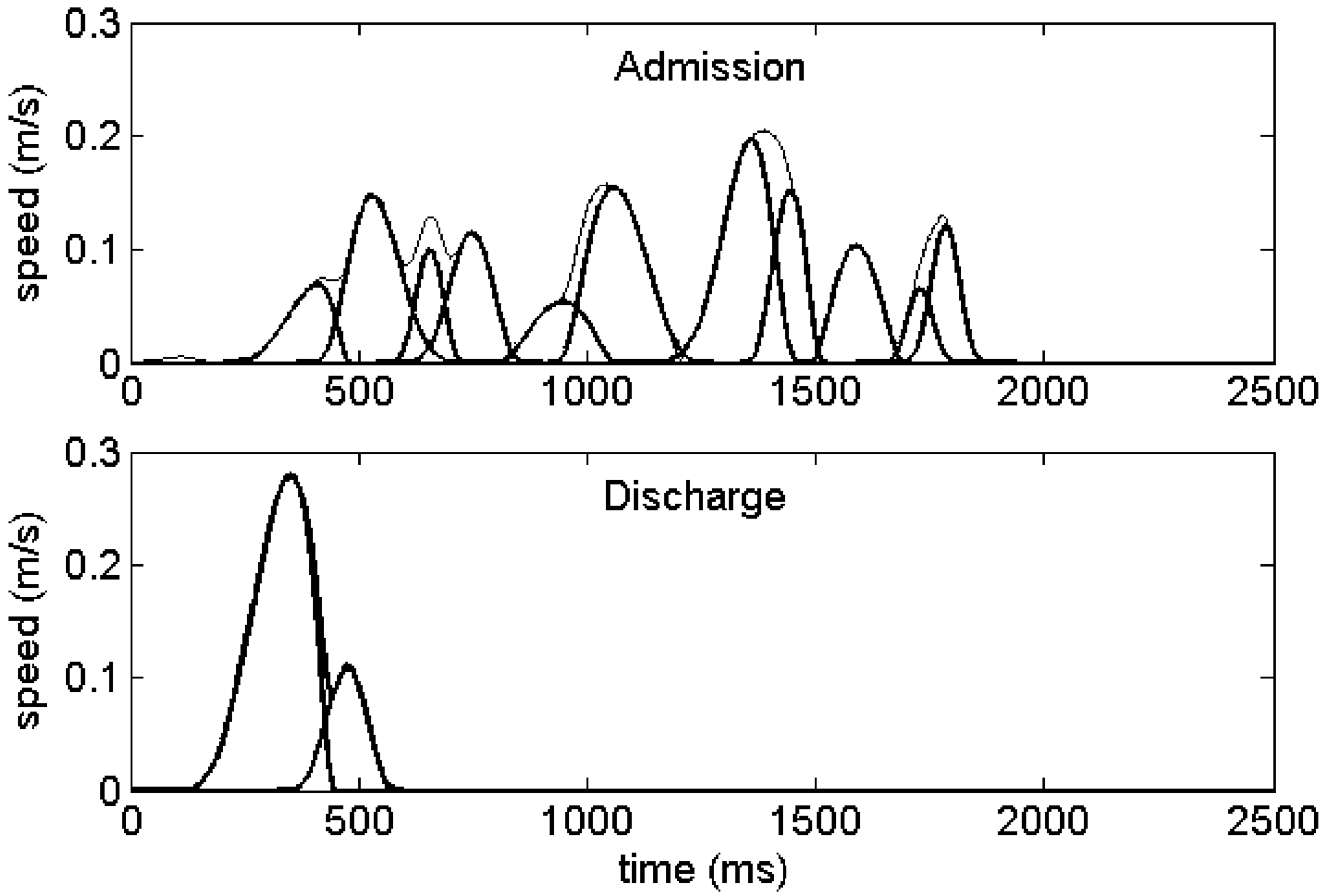

Fig. 3.

Representative submovement changes from admission to discharge. Lighter and darker lines represent speed profiles and decomposing submovements. Submovement number decreased from 11 to 2, duration increased from 0.20 to 0.23 ms, overlap increased from 0.16 to 0.21 s, amplitude increased from 0.11 to 0.41 m/s, and interpeak distance decreased from 0.48 to 0.41 s. Symmetry changed from 0.11 and 2×10^{-4} and kurtosis changed from 0.57 to 0.69.

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Change	Inpatients (n=42)	Outpatients (n=116)	P
Mean speed (m/s)	0.05* (1.03e-5)	0.007 (0.11)	* (1.76e-6)
Peak speed (m/s)	0.07* (5.28e-4)	-0.01 (0.10)	* (5.33e-6)
Duration (s)	-1.14* (0.02)	-0.35 (0.31)	(0.22)
Speed shape	0.10* (1.76e-6)	0.05* (1.39e-12)	* (4.54e-4)
Number of peaks	5.45* (0.002)	2.35* (0.02)	(0.10)
Jerk ($1/s^2$)	-0.41 (0.34)	1.31* (0.001)	* (0.01)
Axes ratio	0.22* (3.36e-9)	0.11* (5.1e-15)	* (1.05e-4)

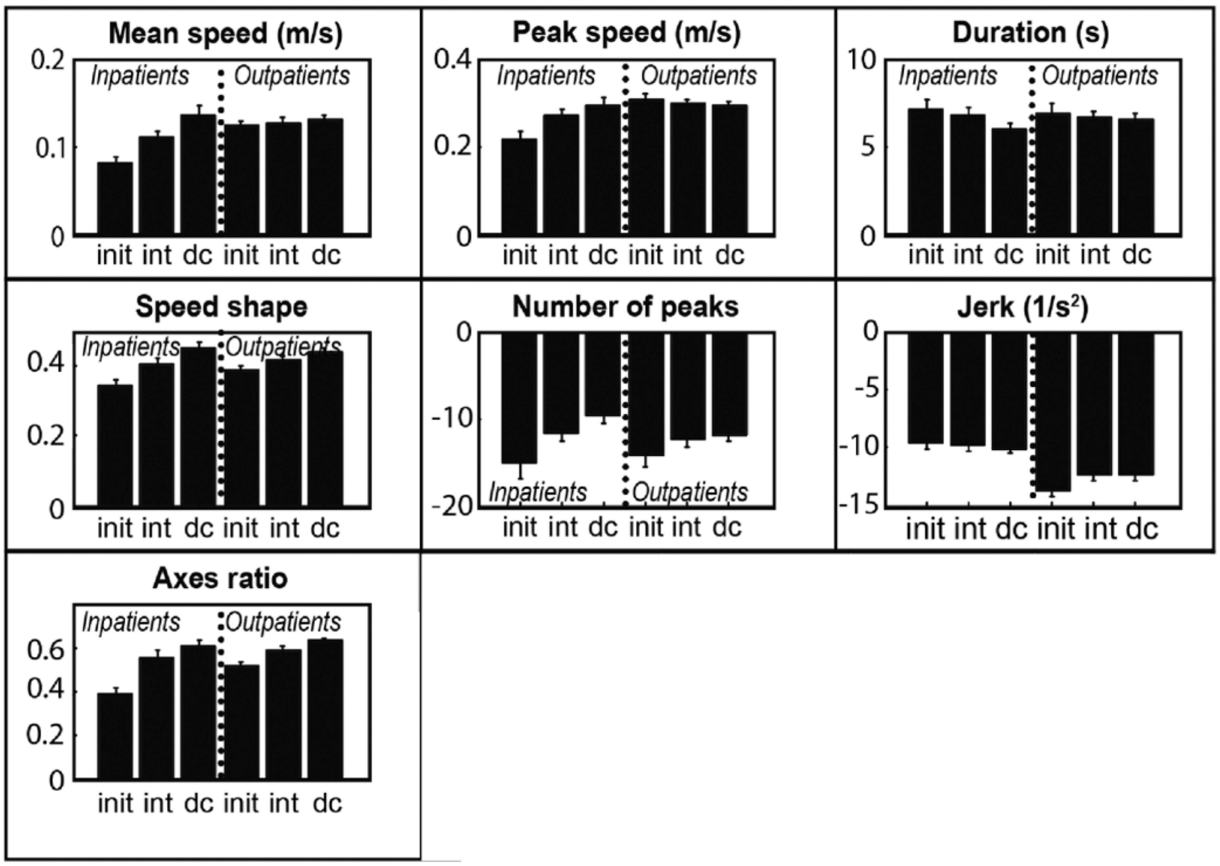

Fig. 4.

Similar to Fig. 1 for untrained circle drawing movements.

Change	Inpatients (n=42)	Outpatients (n=116)	P
Number	-1.55 (0.053)	-1.54* (0.01)	(0.99)
Peak (m/s)	0.059* (6.77e-6)	0.009 * (0.03)	* (2.79e-6)
Duration (s)	0.09* (5.73e-5)	0.09* (2.90e-13)	(0.91)
Overlap (s)	0.14* (0.004)	0.05* (6.65e-9)	* (0.003)
Interpeak distance (s)	-0.04 (0.39)	0.05* (8.29e-5)	* (0.009)
Mu (skewness)	0.01 (0.50)	-0.006 (0.25)	(0.20)
Sigma (kurtosis)	0.05* (4.87e-4)	0.05* (8.29e-12)	(0.92)

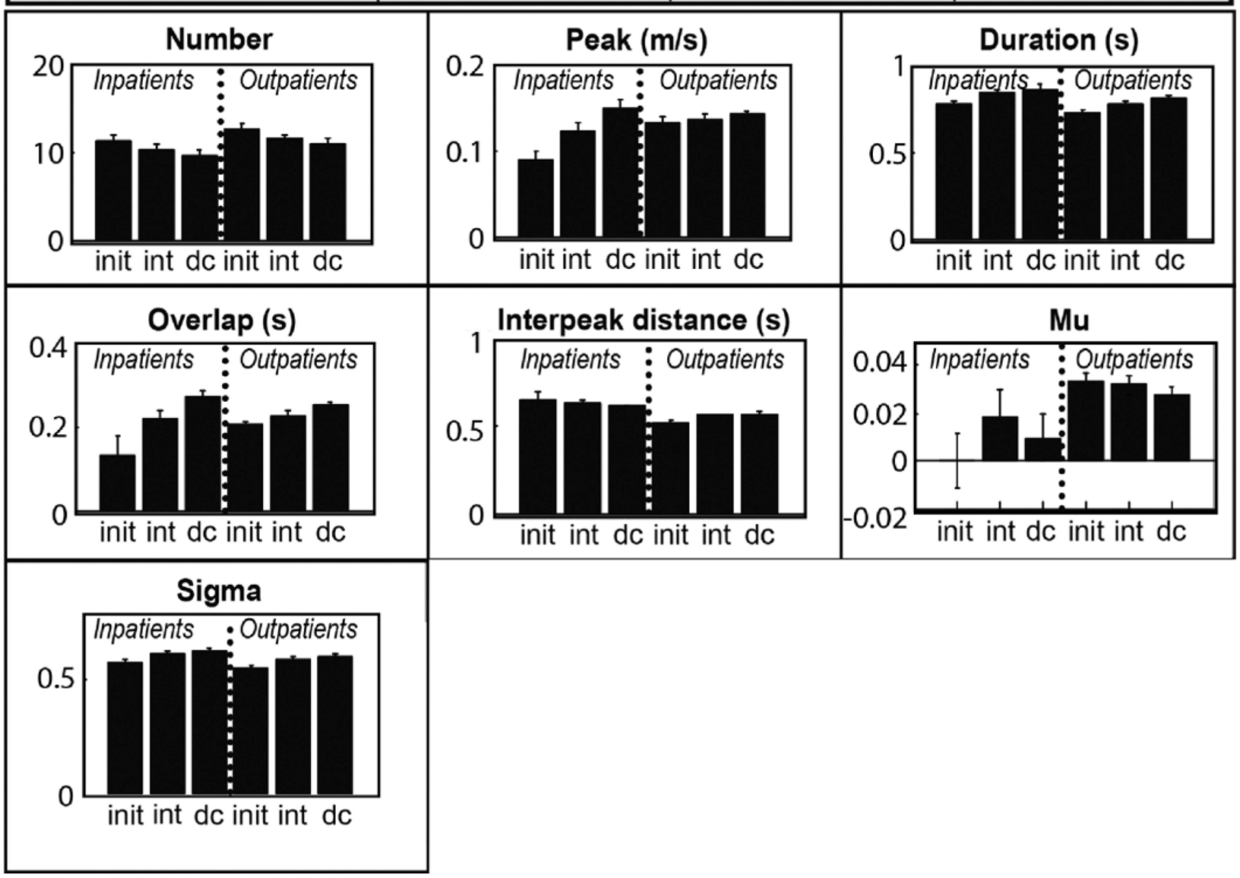

Fig. 5.

Similar to Fig. 1. Results of submovement analysis for untrained circle drawing movements.

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TABLE I

Summary Demographics of Each Group. Values Represent the Percentage (%) or the Mean (Standard Error)

Characteristic	Inpatients (n=42)	Outpatients (n=116)
Gender, male	57%	63%
Age (years)	61.3 (1.8)	58.8 (1.2)
Lesion side, right	77%	54.7%
Time since stroke (days)	19.1 (1.2)	1150 (90)
Fugl-Meyer Admission (66)	10.02 (1.14)	20.47 (1.15)
Fugl-Meyer Discharge (66)	22.70 (2.28)	24.35 (1.27)

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TABLE II

Pearson's Correlation Between Mean Values of the Variables Extracted From Trained Point-to-Point and Untrained Circle Drawing Movements. For Each Variable, Mean Values for Admission, Interim and Discharge for Trained Point-to-Point Movements for Inpatients and Outpatients Were Arranged in a Vector and Correlated With the Corresponding Mean Values for Untrained Circle Movements

Variable	Correlation
Mean speed (m/s)	0.90* (0.01)
Peak speed (m/s)	0.83* (0.04)
Duration (s)	0.72 (0.10)
Speed shape	0.93* (0.007)
Number of peaks	0.85* (0.03)
Jerk ($1/s^2$)	0.75 (0.08)
Submovement number	0.93* (0.005)
Submovement peak (m/s)	0.88* (0.02)
Submovement duration (s)	0.85* (0.03)
Submovement overlap (s)	0.83* (0.04)
Submovement interpeak distance (s)	0.56 (0.24)
Submovement Mu (Skewness)	−0.22 (0.67)
Submovement Sigma (Kurtosis)	0.92* (0.008)

*indicates statistically significant correlations. P values are reported in brackets