Supplementary Material

Motor Tasks

All participants performed three different motor tasks, namely index finger-tapping, a reach-to-point task, and a reach-to-grasp-task. Each task was performed for 112 trials, including 28 trials per rTMS condition (contra- and ipsilesional aIPS, contralesional M1, sham stimulation). Movement onsets were indicated by a visual start signal and a brief acoustic tone to allow participants to focus on the visual target of the respective task.

In the *index finger-tapping task,* participants were instructed to perform repetitive vertical finger movements at maximal speed for 1.6 seconds. Participants were asked to aim at a tapping amplitude of 2.5 cm, indicated by a wooden block in front of their fingertip (Figure 1C, left panel).[1] Since finger-tapping tasks are relatively easy to implement under experimental conditions, they have been most commonly used in fMRI experiments after stroke [2], whereas more demanding tasks may be required to gain insights on motor recovery under real world circumstances. [3]

In a *reach-to-point task*, participants repetitively moved their index finger between two targets at maximum speed for 2.0 seconds. The distance between the targets was 15 cm in the sagittal plane and 5 cm in the vertical plane (Figure 1C, middle panel). This spatial arrangement required the participants to perform a forward and lifting movement using their arm, hand and index finger to reach the target. Compared with the finger-tapping task, the reach-to-point task probed higher visuomotor functions, i.e., visuomotor coordination and visuospatial attention.[4,5]

The *reach-to-grasp task* was implemented to further increase these demands by adding hand-object interaction.[6,7] Participants were instructed to reach for a 5 cm isometric wooden block, grasp it using their index finger and thumb, and lift it to a height of 10 cm. The distance between the starting position of the index finger and the center of the block was 15 cm, comparable to the pointing task. The target height for lifting the block was indicated by a plastic flag in front of the wooden block (Figure 1C, right panel). After lifting the block, participants were instructed to release the block and return the index finger to the starting position. Hence, the reach-to-grasp task represented a complex visuomotor condition probing hand motor performance resembling activities of daily living.

During all tasks, hand movements were recorded using a 3-D ultrasound-based motion analyzer system (CMS 20, Zebris Medical GmbH, Isny, Germany). Each movement was analyzed about four kinematic domains,[8] i.e., (i) efficiency, (ii) accuracy, (iii) smoothness and (iv) speed.

Kinematic assessment

Hand movements were recorded using a 3-D ultrasound-based motion analyzer system (CMS 20, Zebris Medical GmbH, Isny, Germany) with a sampling rate of 100 Hz. Markers were placed on the *dorsum* of the index finger and the thumb. The x-, y-, and z-directions of the position marker coordinates referred to the left-right, antero-posterior, and vertical (z) axis, respectively. All data were preprocessed using the SciPy package (https://www.scipy.org) for Python (version 3.5). Data were smoothed using a second-order low-pass 12 Hz Butterworth filter in forward and reverse directions, resulting in a fourth.order filtering. Next, data were segmented into single finger-tapping, pointing, or grasping movement cycles, respectively. Finger-tapping movements were divided by minima of index finger positions in the vertical plane, yielding single movements of ascending and descending finger positions. The beginning of a pointing or grasping movement was defined by the velocity of the fingertip marker, exceeding 5% of peak velocity. Likewise, the end of pointing or grasping was defined by a decrease in velocity below 5% of peak velocity near the starting position.[9] Each movement was analyzed with regards to four kinematic domains.[8] (i) efficiency, (ii) accuracy, (iii) smoothness and (iv) speed.

Importantly, establishing these dimensions allowed us to compare movement kinematics across very different motor tasks. *Efficiency* was assessed by inverted measures of movement time. That is, (i) the time of one finger-tapping movement, or (ii) the pointing time until the target was reached, or (iii) the grasping time until the cube was reached, respectively. *Accuracy* was measured by the inverted spatial distance [mm] of (i) the index finger from the target height (finger-tapping), (ii) the pointing target (pointing), and (iii) the lifted versus target height when lifting the wooden cube (grasping). *Smoothness* was measured by the inverted number of peaks in the velocity profile during (i) finger-tapping, (ii) reach-to-point or (iii) reach-to-grasp. *Speed* was assessed by the peak velocity during (i) finger-tapping, (ii) reach-to-point or (iii) reach-to-grasp. Thereby, the motor performance of each participant was examined by twelve kinematic features (three tasks x four dimensions) in total.

K-means clustering and multiple factor analysis

K-means is a nonhierarchical clustering approach based on an iterative algorithm, allowing to form subgroups based on multiple input variables.[10] To assign participants into clusters, variance is minimized between participants within clusters and maximized between clusters by computing the centroid of each cluster and subsequently reassigning participants to the clusters, resulting in minimal difference from the nearest centroid.

In the present study, the twelve kinematic features extracted from each of the 36 participants were z transformed and entered into a K-means clustering analysis as implemented in the R *stats* and *factoextra* packages. K = 2 was chosen due to the sample size and the hypothesis of subgrouping the patient cohort into patients with good motor outcome and patients with residual impairment based on their hand motor behavior.

To reduce dimensionality of the multi-dimensional dataset, we used all twelve kinematic variables to compute a multiple factor analysis (MFA) using the FactoMineR package (version 1.39) implemented in R.[11] The resulting first weighted principal component hence was defined to represent the *motor composite score* summarizing motor performance across tasks.[12,13]. A detailed overview on the MFA results is presented in Figure S1.

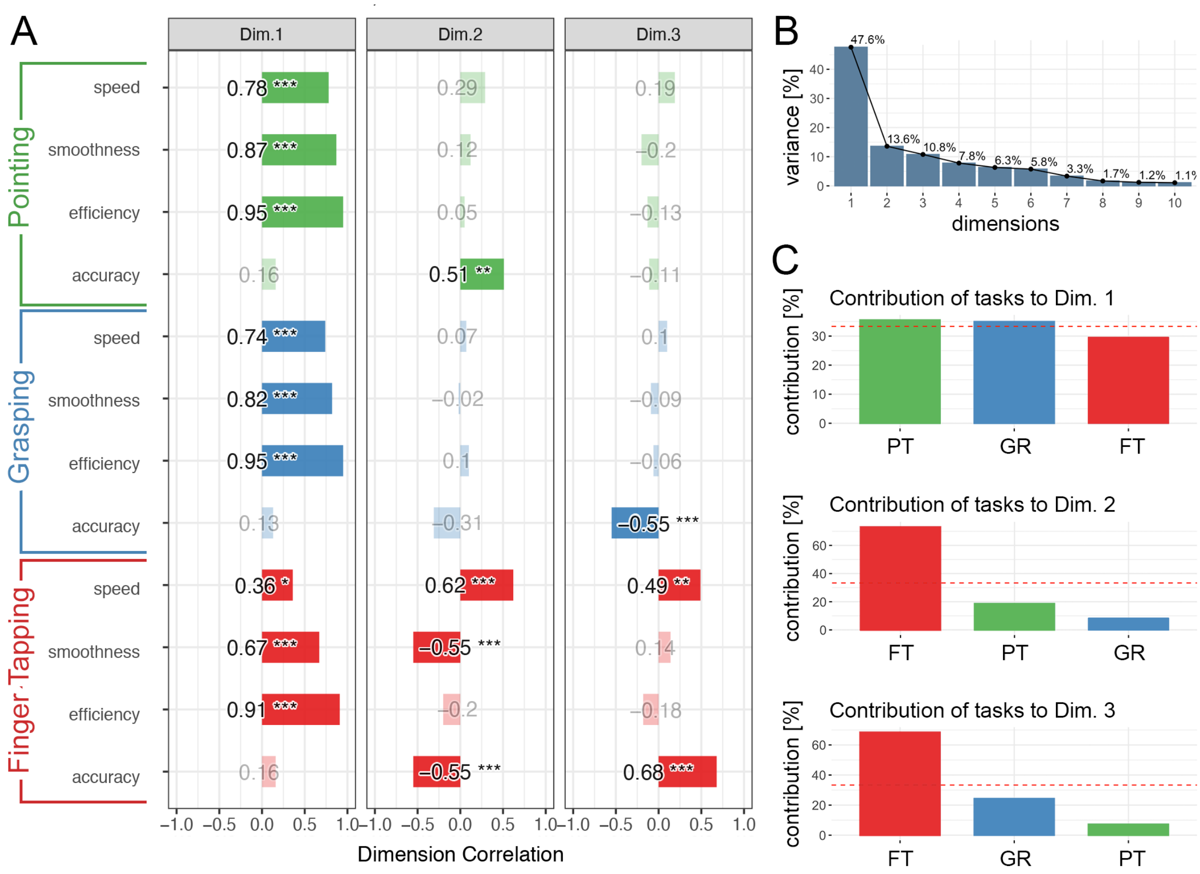

Figure S1. Three dimensions resulting from the MFA explained 71.73% of the variance of the kinematic data. **A)** Correlating each kinematic feature with these dimensions revealed that the first dimension is positively related to efficiency, smoothness, and speed of each task, reflecting overall motor performance across tasks. **B)** Notably, this dimension alone explained 47.1%, exceeding any other dimension as indicated by the scree plot. **C)** Contributions of tasks to each dimension. FT: finger-tapping, PT: pointing, GR: grasping.

Assessment of resting motor thresholds

Repetitive TMS was applied at an intensity of 90% of each individual's resting motor threshold (rMT). To adjust rTMS individually, each participant's motor threshold (rMT) was assessed by measuring amplitudes of motor evoked potentials (MEP) during single-pulse TMS over the M1 target coordinate, defined by the local fMRI activation maximum at the motor hand knob formation of the precentral gyrus.[14] Electromyographic (EMG) activity was recorded from the first dorsal interosseus (FDI) muscle of the hand contralateral to the stimulated hemisphere via Ag/AgCl surface electrodes (Tyco Healthcare, Neustadt, Germany) in a belly-tendon montage. The EMG signal was amplified, filtered (0.5 Hz high-pass and 30-300 Hz bandpass) and digitalized with a Powerlab 26T device, and analyzed using the LabChart software package (version 8, ADInstruments Ltd, Dunedin, New Zealand). The rMT was defined by an algorithm provided by the TMS motor threshold assessment tool (MTAT 2.0, http://www.clinicalresearcher.org/software.htm).[15,16] The MTAT has been shown to accurately estimate motor thresholds using less stimuli than the standard 5-out-of-10 rule which is especially useful in stroke patients to minimize the absolute number of TMS pulses.[17]

Definition of rTMS sites

As rTMS was applied at subject-specific coordinates, EPI images were only co-registered with the T1 volume but not spatially normalized. A relatively small Gaussian filter of 4 mm full-width-at-half-maximum (FWHM) was applied on EPI data to increase the signal-to-noise ratio to facilitate the identification of the task-related stimulation targets in aIPS. General linear models (GLM) at the single-subject level were corrected for movement-related nuisance employing six head motion parameters as covariates. The following single-subject activation maps were then used to define the regions of interest, serving as targets for rTMS. Consistent with our previous work,[1] the coordinates in the aIPS were identified by the nearest activation maximum in the medial anterior intraparietal sulcus close to the postcentral sulcus, i.e. a cortical region related to visuomotor coordinate transformation and reaching tasks.[18] During the rTMS session, the TMS coil was positioned tangentially to the scalp, applying a latero-medial current targeted hand movement-related neurons in the medial bank of the aIPS.[18,19] The stimulation site in the contralesional M1 was defined by the contralesional motor hotspot,[20,21] positioning the coil tangentially to the skull in a posterior-anterior current direction to elicit highest motor evoked potentials (MEP), targeting the posterior wall of the precentral gyrus at the hand knob formation.[22] As a control (sham) condition, stimulation was conducted over the parietooccipital vertex (Pz) in posterior-anterior direction with the coil tilted so that no cerebral tissue was targeted during stimulation.[23]

ANOVA of rTMS effects

Relative rTMS effects on motor behavior when interfering with a region (i.e. contralesional aIPS, ipsilesional aIPS, contralesional M1), compared to the sham condition, were tested for differences between groups, stimulation regions, tasks and kinematic features computing a repeated measures ANOVA using R (rstatix package version 0.7.0). The model of the ANOVA was designed with the between-subject factor GROUP (levels: "healthy controls", "patients with good motor outcome", "patients with residual impairment") and the within-subject factors DISTURBED REGION ("contralesional aIPS", "ipsilesional aIPS", "contralesional M1"), TASK ("finger-tapping", "pointing", "grasping"), and KINEMATIC FEATURE ("efficiency", "accuracy", "smoothness", "speed"). On all factor levels, rTMS effects were normally distributed, as assessed by Shapiro-Wilk's test of normality (p > 0.05).

Effect	DFn	DFd	F-value	p-value	ges
main effects					
group	2.0	33.0	1.75	0.190	0.004
task	1.7	54.4	0.99	0.364	0.004
region	**2.0**	**66.0**	**2.92**	**0.061**	**0.004**
kin_feature	1.6	52.1	2.97	0.072	0.011
Interaction effects					
group:task	3.3	54.4	1.73	0.167	0.012
group:region	**4.0**	**66.0**	**0.69**	**0.601**	**0.002**
group:kin_feature	3.2	52.1	3.35	0.024 *	0.024
task:region	**3.0**	**99.6**	**2.54**	**0.061**	**0.005**
task:kin_feature	2.2	71.5	1.07	0.354	0.009
region:kin_feature	**2.6**	**86.9**	**2.29**	**0.092**	**0.007**
group:task:region	**6.0**	**99.6**	**0.43**	**0.857**	**0.002**
group:task:kin_feature	4.3	71.5	1.81	0.131	0.030
group:region:kin_feature	**5.3**	**86.9**	**0.51**	**0.777**	**0.003**
task:region:kin_feature	**3.3**	**107.9**	**1.53**	**0.207**	**0.010**
group:task:region:kin_feature	**6.5**	**107.9**	**0.76**	**0.617**	**0.010**

Table S1. Summary of repeated measures ANOVA, which solely showed a significant interaction for the factors stimulation GROUP x KINEMATIC FEATURE, F(3.2, 52.1) = 3.35, $p < 0.024$. However, this effect was not region-specific. Interactions of interest (prominent rows) involving the stimulated region, were not significant. Degrees of Freedom are depicted in the numerator (DFn) and in the nominator (DFd). ges: Generalized Eta-Squared as a measure of effect size.

Upper limb recovery

To compare patients' motor deficit during our study with the initial deficit, NIHSS upper limb score of all patients were obtained during the chronic phase as well as acute phase after stroke. Comparing these scores between the acute and chronic phase revealed a significant difference when computing Mann-Whitney Tests across all patients ($P < 0.001$), but also separately for each subgroup (high kinematic performance: $P = 0.009$, low kinematic performance: *P* = 0.020). To assess the degree of recovery, the delta between timepoints was calculated (Score during the chronic minus the acute phase). We further tested if this degree of recovery was higher in patients who performed better in the kinematic measures using a non-paired, one-sided Mann-Whitney Test, indicating that kinematic high performers had undergone a higher degree of recovery than kinematic low performers (*P* = 0.033).

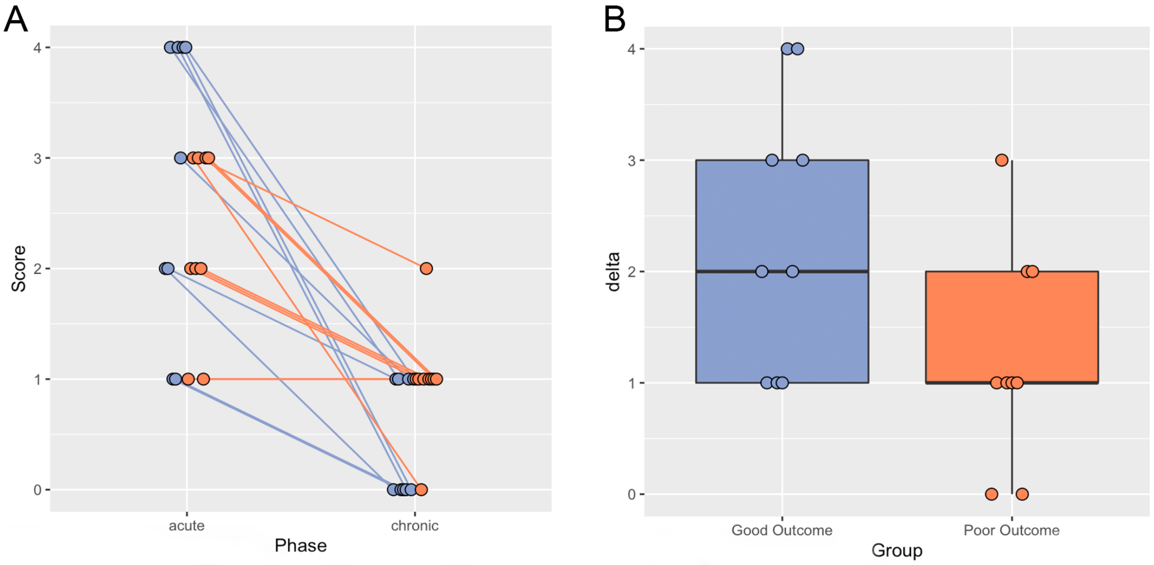

Figure S2. NIHSS upper limb scores in the acute and chronic phase after stroke in patients with near to normal kinematic outcome (blue) and residual deficits (orange) **A)** Parallel plots indicate changes of NIHSS upper limb scores from the acute to chronic phase post-stroke. Note that data points are jittered horizontally to allow the discrimination of single patients **B)** The difference (delta) of the motor score between the chronic and acute phase reflect the degree of recovery, indicating a more substantial recovery of upper limb deficits in the patient subgroup with good kinematic outcome (*P* = 0.033).

Stroke Lesions

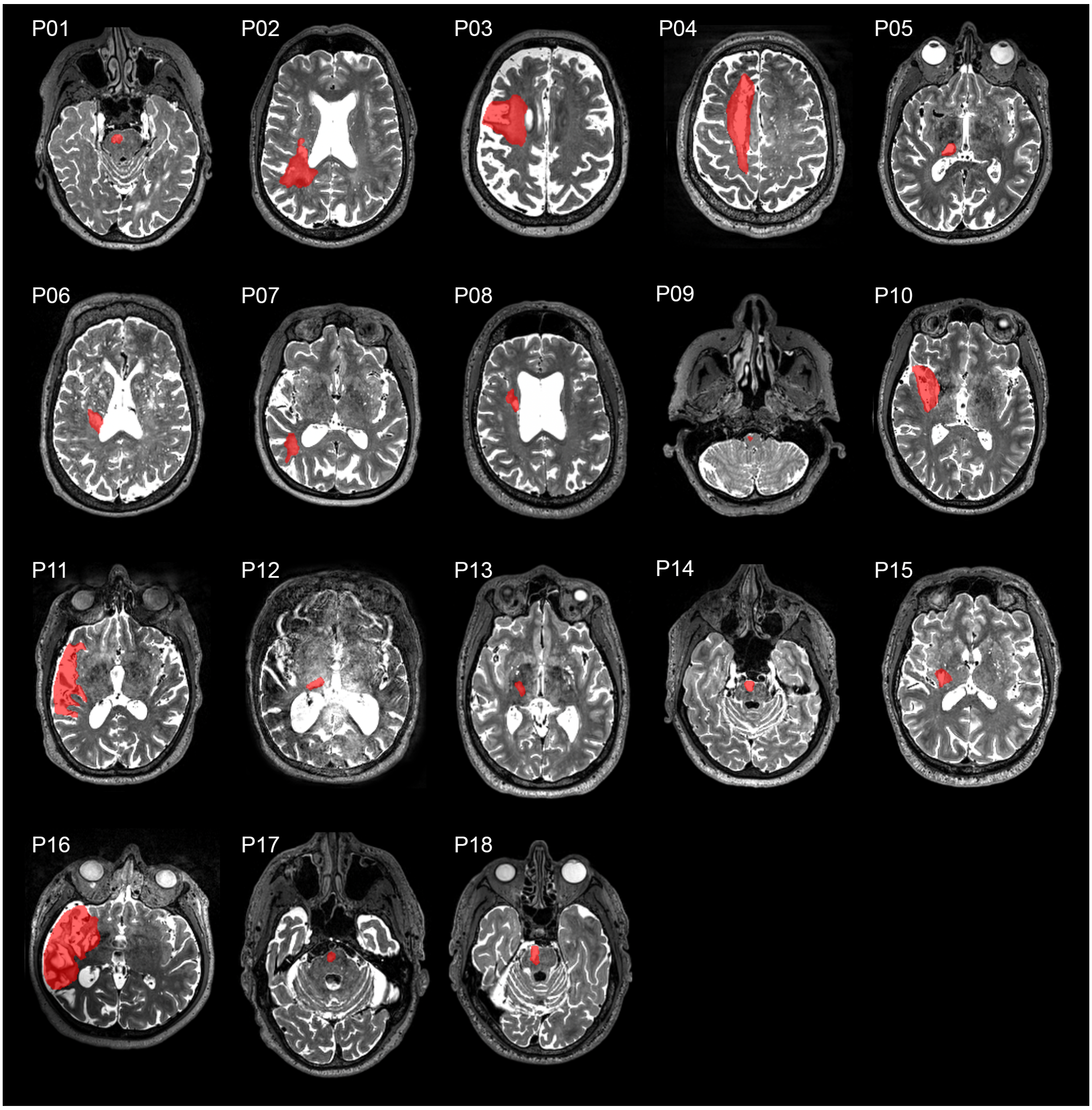

Figure S3. Individual patients' stroke lesion maps displayed in T2-weighted MRI images. All images were flipped along the midsagittal plane, so that lesions are commonly displayed on the left.

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