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Chronic stroke survivors improve reaching accuracy by reducing movement variability at the trained movement speed.

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Title:

Chronic stroke survivors improve reaching accuracy by reducing movement variability at the trained movement speed.

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Abstract

Background: Recovery from stroke is often said to have "plateaued" after 6-12 months. Yet training can still improve performance even in the chronic phase. Here we investigate the biomechanics of accuracy improvements during a reaching task and test whether they are affected by the speed at which movements are practised.

Method: We trained 36 chronic stroke survivors (57.5 years, SD ±11.5; 10 females) over four consecutive days to improve endpoint accuracy in an arm-reaching task (420 repetitions/day). Half of the group trained using fast and the other half slow movements. The trunk was constrained allowing only shoulder and elbow movement for task performance.

Results: Before training, movements were variable, tended to undershoot the target and terminate in contralateral workspace (flexion bias). Both groups improved movement accuracy by reducing trial-to-trial variability; however, change in endpoint bias (systematic error) was not significant. Improvements were greatest at the trained movement speed and generalised to other speeds in the fast training group. Small but significant improvements were observed in clinical measures in the fast training group.

Conclusions: The reduction in trial-to-trial variability without an alteration to endpoint bias suggests that improvements are achieved by better control over motor commands within the existing repertoire. Thus, 4 days' training allows stroke survivors to improve movements that they can already make. Whether new movement patterns can be acquired in the chronic phase will need to be tested in longer-term studies. We recommend that training needs to be performed at slow and fast movement speeds to enhance generalisation.

Introduction

The majority of patients after stroke are left with deficits in upper limb function[1, 2]. Improvements in functional reaching can occur either by regaining the ability to make movements which were lost completely after the stroke [3], or by increasing the accuracy and/or speed of preserved movements[4, 5].

In the chronic phase after stroke multiple studies have shown that training can produce task-specific improvements even many years after stroke, although the speed of recovery slows[3, 6]. However, there are few detailed investigations of biomechanical changes induced by training in chronic stroke patients[3-5]. Some authors have argued that in the chronic phase all improvement is compensatory [4, 7], in that the goal is achieved by replacing lost abilities using other joints. This results in solutions that are not optimal for the task [8]. Thus, patients' movements may become more accurate with training but this may be achieved by increased trunk flexion during reaching[8-10]. However, improvement may occur through two other mechanisms. Even if patients do not recover lost function, they may recover better control of their movements, resulting in movements that are less variable from trial-to-trial, and hence on average more accurate[3, 11, 12]. Another possibility is that patients relearn to produce combinations of muscle activity lost due to stroke. Improvements in performance in this case would be detected as reduced endpoint bias and/or straighter trajectories.[3, 13] Additionally an important issue in motor learning is the speed-dependency of improvements. In a previous study[13], we found that if healthy adults practiced reaching at one speed they improved performance at that, but not at untrained speeds. After a neurological insult individuals tend to move slowly[14], possibly due to greater difficulties of generating activity[15], increases in stretch-reflexes [16], avoidance of increased interaction torques with higher velocities [17] or to compensate for decreases in accuracy[18-20]. However many movements such as catching a falling object, driving a car or stabilising yourself while on a bus rely on the ability to generate accurate, fast bursts of muscle activity[15]. Current clinical guidelines do not emphasize the need to train patients at a variety of movement speeds[21] and there are limited studies investigating how movement speed during training effects learning after stroke. Continual exposure to slow movements in daily behaviour and rehabilitation training may prevent regaining the ability to move accurately at fast speeds, or they may even reinforce the slowness of movement through use-dependent learning[13, 22].

We therefore investigated whether improvements in reaching are possible when practicing an arm-reaching task for four days when compensatory movements are minimised. We measured changes in endpoint accuracy in terms of endpoint bias and variability when patients trained either at fast or slow movement speed and analysed the effect of the training on the speed-accuracy trade-off function (SAT)[18, 23, 24]. We hypothesized that, as for healthy individuals, some of the movement improvements would be specific to the trained speed. More specifically, we predicted that improvements during fast reaching would be achieved only after training at the fast movement speed [5]. We further investigated how improvements in fast movements matter to clinical motor impairment measures, hypothesizing that improved ability to generate fast movements may have clinical relevance. Finally, we studied how different factors of impairment (sensory loss, spasticity, weakness) influence the ability to profit from training.

Materials and Methods

Subjects

This parallel-randomised (1:1 allocation) study was approved by the Joint Ethics Committee of University College London and the National Hospital for Neurology and Neurosurgery (NHNN). Patients were recruited from NNHN and charity stroke clubs and websites. (For clinical details, Supplementary data, Table I). Prior to participation, informed consent was obtained from each participant according to the Declaration of Helsinki. All patients met the following inclusion criteria: 1) Chronic stroke survivors (≥1 year history) with 2) persistent upper limb weakness (≤4 Medical Research Council (MRC) of either triceps or anterior deltoid muscles 3) Participants had to be able to perform the training task of ≥15 cm reach with the weight of the arm supported in a robotic manipulandum (Fig.1A). We excluded individuals with 1) history of previous stroke or other concomitant neurological or musculoskeletal disease, 2) cerebellar stroke, 3) proximal upper limb hypertonus ≥3 on Modified Ashworth scale (MAS), 4) severe sensory impairment ((light-touch <50% accuracy on 1g Bailey© monofilament sensory testing on dorsum and palm of hand). 5) Shoulder pain ≥3/10 on self-rated continuous visual analogue scale, 6) uncorrected visual impairment, 7) hemi-spatial neglect established by the Star Cancellation Task[25] and 8) cognitive and language impairment impeding co-operation in study protocol.

Clinical assessments were performed before and on the last day of the testing week by a neurologist (DH) blinded to training group allocation. Testing consisted of the Fugl-Meyer upper limb subset (/66), muscle strength (MRC grading) [26], sensory impairment(1g monofilament) and elbow flexor hypertonus (MAS) [27]. MAS scores were converted to a 6 point scale (0-5) prior to non-parametric analysis and are depicted as such throughout[28].

Reaching paradigm

Hand position was measured using a custom built 2D manipulandum (Fig.1A)[29], with an incremental quadrature encoder at each of the two joints (65.5k steps/revolution). This resulted in accuracy at the handle of ~0.03mm. Movement speed was calculated by differentiation of the position signal. All kinematic data were sampled at 200Hz. Participants were seated with forehead support, a shoulder strap and backrest support preventing compensatory movement in the sagittal and frontal plane while limiting shoulder girdle movement. Subjects held a handle (inset Fig.1A) or if required the hand was strapped onto the handle by a custom-made glove[13].

A forearm support eliminated gravity and vision of the hand was occluded by a mirror displaying visual feedback (Fig.1B). Feedback comprised of a 2 cm diameter starting box, a green cursor (0.5 cm diameter) representing manipulandum position and a circular 10 cm diameter target with a small black cross at its centre, which was located 20cm from the start box at an angle of zero degrees. A change of the target from an outline to a solid white colour indicated the start of a trial. Individuals were instructed to reach and terminate movement as close as possible to the centre of the target (centre cross) in their own time. When movement was initiated, the green cursor disappeared and only reappeared, displaying feedback of the end position (Fig.1C) for 1 second when movement stopped. Feedback was removed to prevent corrections during the movement because with corrections the relationship between speed and accuracy is complicated, as slower movements allow for more complete corrections. Visual feedback at the endpoint (knowledge of results[30]) is essential to prevent complete dis-calibration without knowledge of hand position, of the reaching movements and to motivate participants to move accurately. The robot was used primarily to measure movement however; assistance was provided to move the handle back to the starting position after the completion of each trial.

Initial assessment (pre) was performed on a Thursday and the final assessment on the following Friday (post-training). In these sessions reaching accuracy was established at four different speeds[13] depending on each individual's fastest movement ability. After task familiarization (15 repetitions with, and 15 without visual feedback of hand position), participants were encouraged to reach as quickly as possible in the 3rd block (Fig.1D). The 80th percentile or 4th shortest movement time was used to set the limit for the individual's fast movement time (Fig.1E dotted line, i.e. 460ms). Movements during fast reaching conditions had to be terminated faster than this limit (dark shaded area) which we found to be challenging but achievable in pilot testing. For the other three movement speeds the lower movement time limit was incrementally increased by 200ms resulting in this example, in limits of 460ms–660ms for medium fast (yellow) reaches, 660ms-860ms for medium slow (green) and slow (blue) between 860ms-1600ms while allowing some redundancy at the slow movement speed to increase ease of task peformance. This incremental increase allowed us to test individuals reaching accuracy at similar intervals along their SAT. The order of testing movement accuracy at the four movement speeds was randomized across patients. At every speed, reaching movements were repeated until twenty successful trials or a maximum of sixty trials were performed.

Training paradigm

Blocked, stratified randomisation to the fast or slow training group was performed after completion of the initial assessment. Sequentially numbered sealed envelopes contained group allocation stratified for functional impairment (Fugl-Meyer ≤50 or ≥51). Training sessions were always performed on the consecutive Monday to Thursday between the assessment sessions. All movements during the four training days were performed at the individually determined fast or slow movement time limit as described in the reaching paradigm. The trainer (UH) was not blinded to group allocation as the speed of movement was visually apparent and patients required prompting to perform movements at the correct speed. Patients were instructed to perform reaching movements in the robotic manipulandum, to a bulls-eye target for 420 reaches per day (7 blocks of 60 repeats) (Fig.1F). This protocol was established in pilot testing to achieve ≥400 movement repetitions in training[31, 32]. Movements had to be performed at the movement speed of the allocated group and were rewarded for endpoint accuracy to a maximum of 300 points (60x5 points) per block (Fig.1F). Five points were awarded for terminating in the bulls-eye (<1cm error) with incremental reduction to one point in the outer ring (4-5cm error). Accumulative points were displayed on the screen for each block and a beep indicated that the trial was successful within the speed limit and in the target area receiving at least 1 point. Movements that ended outside the target area and/or did not fall within the required movement limit were awarded zero points. Visual feedback of endpoint location was provided after each trial for 1 second. Participants were encouraged to increase their points per block and were reminded of their performance on the previous block and the previous day(s). Each training session lasted between 1-1½ hours.

Outcome measures

The primary outcome measure was spatial accuracy at movement end. We studied how accuracy changed due to training and how these reductions generalized to untrained speeds. As an overall measure of accuracy, we used average distance from the centre of the target (cm). This error could be further subdivided into the average deviation from the target (constant error) and the standard deviation around the mean endpoint(variable error) [33]. For some analyses, the error was further subdivided into parallel (i.e. movement direction) and perpendicular movement error (i.e. orthogonal to movement). To allow comparisons across individuals, movements of individuals with left hemiparesis were mirrored along the sagittal plane and data are presented as right arm movements for all participants.

For each trial, the maximum tangential movement speed of the hand was determined and averaged per individual for each tested target speed (maximum speed)[13]. The standard deviation around the mean was taken as a measure of variability of movement speed (movement speed variability).

Data Analysis

IBM SPSS software and custom written Matlab® (Mathworks) routines were used for data analysis ($p<=0.05$, distribution normality confirmed by Kolmogorov-Smirnov test).

Repeated measures ANOVAs (Greenhouse-Geisser corrected) were used to analyse performance during training BLOCK(7)*DAY(4)*GROUP(2) and change (day 1 compared to day 6) after training TIME(2)*MOVEMENT SPEED(4)*GROUP(2) and assessed by post-hoc Student's t-test, Holm-Bonferroni corrected for multiple comparisons if required. Fugl-Meyer and MAS scores were assessed by Wilcoxon Signed rank tests for change and Mann-Whitney U-Tests established group differences.

The regression slope of performance change due to training was depicted in both training groups (intercept fixed to residual RMS Error of 0.93cm; +/-0.06 observed in healthy individuals, supplementary information Figure I). Regression coefficients were compared by t-statistics. A median split of sensory impairment (</≥80% sensory accuracy, mild(n=18), moderate(n=18)), muscle weakness (deltoid MRC =/≤4, mild(n=22), moderate(n=14)), and hypertonus (elbow flexors: MAS </≥2, mild(n=15), moderate(n=21)) assessed how impairments affected learning.

Results

36 Stroke survivors (57.5 years, SD ±11.5; 10 females) successfully trained at their target speeds (n=17 slow at average movement speed 32.2±0.3 cm/s and n=19 fast at 77.9±0.45cm/s) with no adverse events. The study participants comprised of 27 individuals with an infarct and nine haemorrhagic stroke survivors. The lesion site was cortical in 13 individuals, subcortical in six and nine patients presented with a combination (please see supplementary information Table 1). Lesion location was not known in the remaining 10 individuals. Intergroup comparison for lesion type, side or site did not demonstrate any group effect in this small sample. Over 4 days (day 2-5), reaching accuracy improved (Fig.2A; effect of DAY $F(3,102)=9.05$; $p<=0.001$ and BLOCK $F(6,204)=3.15$; $p=0.006$) and points awarded for hitting the target increased (Fig.2B; DAY $F(3,102)=20.83$; $p<0.001$ and BLOCK $F(6,204)=6.90$; $p<0.001$) for both training groups. (Movement speed fluctuated during the training days but no systemic change in speed was observed between days. Supplementary information Fig.II).

Accuracy improvements at trained and non-trained movement speeds

Before training, stroke survivors had poor endpoint accuracy at all four tested movement speeds without a difference in baseline performance for participants randomized to slow and fast training (Fig.2C&D). In a retention test, a day after the last training session (day 6), both groups improved their endpoint accuracy in comparison to performance on day 1 but the pattern of improvement differed for the two training groups (GROUP(2)xMOVEMENT SPEED(2) interaction, $F_{(3,102)}=2.884$, $p=0.039$). In the fast training group there was no difference between improvements at the trained fast speed and the untrained, slow speed ($t_{(18)}=0.23$, $p=0.821$) indicating broad generalisation. This was less efficient in the group that trained at the slow speed, who demonstrated greater improvements at the slow, trained movement speed than at the fast speed ($t_{(16)}=2.23$, $p=0.040$).

We next established to which extent this improvement was achieved by a reduction in endpoint bias and/or a reduction in endpoint variability by investigating the combined data of the two training groups.

Before training individuals demonstrated a bias to undershoot and terminate in the opposite workspace as indicated by the groups mean endpoint location and standard error of the mean (Fig.3A-D), generally indicative of an elbow and shoulder flexion bias (supplementary information Fig.IIIA). There was no interaction or significant change in the bias (rmANOVA: no effect of TIME) for both parallel ($F_{(1,35)}$=3.46, p=0.071) and perpendicular bias ($F_{(1,35)}$=2.64, p=0.113) at the 4 movement speeds. In comparison there was a reduction in endpoint variability of the movements after training (TIME $F_{(1,35)}$=37.714, p<=0.001) and this effect (Fig.3A-D) was confirmed by post-hoc Holm-Bonferroni corrected t-tests at all speeds(slow $t_{(35)}$=4.48, p<=0.001, med slow $t_{(35)}$=5.201, p<=0.001, med fast $t_{(35)}$=5.541, p<=0.001, fast $t_{(35)}$=2.156, p=0.038). The endpoint variability reduced in the parallel (under/overshoot) (TIME $F_{(1,35)}$=19.96, p<=0.001) and perpendicular directions (left/right bias) (TIME $F_{(1,35)}$=27.82, p<=0.001).

Movement speed variability

Although patients were required to move at specific speeds (supplementary information Fig.IV), their actual speed varied slightly from trial-to-trial (Fig.4). The variability of the peak speed was the same in both groups before training (no interaction $F_{(3,102)}$=1.11; p=0.348 or effect of GROUP $F_{(1,34)}$=0.61; p=0.440). Training altered this measure (Fig.4A-C) evident when the change at the 4 movement speeds are compared between the groups (Fig 4C) (GROUPxMovementSPEEDxTIME interaction, $F_{(2.5;83.5)}$=4.43; p=0.010). Post-hoc Holm-Bonferroni corrected t-tests indicated that the change was significant at the trained movement speed for the fast ($t_{(18)}$=3.03, p=0.029) and slow ($t_{(16)}$=2.985, p=0.026) group and only generalised to medium fast movements ($t_{(16)}$=3.404, p=0.015) in the slow training group.

The influence of baseline impairment and clinical measures on behavioural change

The RMS error of individuals with good baseline performance improved less than those with poor performance (Fig.5A), probably because of a floor effect, as movement error is never completely eliminated [34] (supplementary information Fig.I). This meant that the improvement in endpoint error was roughly proportional to the initial deficit[35]. The regression slopes of error reduction indicated a 20-30% improvement in performance (fast: m=0.76, SEM=0.66-0.87 and slow: m=0.72, SEM=0.60-0.84).

We asked whether the benefit of training varied between different subgroups of patients characterized by specific deficits. Severity of sensory impairment was the only factor that influenced learning (Fig.5B) as detected by the difference of the slope (Independent t-test, $t_{(34)}$=3.39, p=0.002) of the regression between the mildly (b=0.613, CI=0.52-0.71) and moderately (b=0.93, CI=0.76-1.09) impaired individuals. Neither the severity of hypertonus (mild: b=0.71, CI=0.51-0.91, moderate: b=0.69, CI=0.58-0.79, $t_{(34)}$=-0.21, p=0.86) nor muscle weakness (mild: b=0.87, CI=0.56–1.17, moderate: b=0.67, CI=0.58- 0.77, $t_{(34)}$=-1.20, p=0.237) influenced learning. This finding is maintained when excluding outliers with greater error, which could drive the reported effect (please see supplementary information Fig.V). We conclude that individuals with moderate sensory impairment improve least in this reaching task.

The influence of training on clinical measures of impairment

Elbow flexor hypertonus (MAS: Fig.6A), reduced in the group training at fast movement speed (related samples, Wilcoxon signed rank test, p=0.046, uncorrected for multiple comparison) but not for individuals training at slow speeds (p=0.581). Similarly the changes in Fugl-Meyer scores (Fig.6B) were significant for the fast (p=0.004, uncorrected for multiple comparison) but not the slow training group (p=0.230). Neither of these changes are however clinically meaningful (reduction in hypertonus MAS=0.21 SD=0.85 and increase in Fugl-Meyer score =1.84 SD=2.27).

Discussion

Our experiment showed that with 4 days' training chronic stroke survivors could improve reaching accuracy but correction for endpoint flexor bias was more difficult. Improvements in accuracy were achieved by reducing endpoint variability and were greatest at the trained speed but generalised to reaches made at untrained speeds. We recommend that training should be executed at a variety of speeds to maximize the breadth of generalization of improvements after training.

Reducing movement variability

Limiting compensatory trunk movement, while performing reaching movement, has been shown to be effective in improving movement quality in stroke survivors[36, 37]. Our set-up prevented trunk flexion and rotation and minimised shoulder girdle movement, permitting only elbow and shoulder movement for the performance of the reaching movement. The change in the speed-accuracy relationship[19, 20, 23], meant that at a retention test one day after training, patients could perform movements of a given speed more accurately than on the testing session before training. These improvements were not due to patients employing a different (i.e. "compensatory") strategy to achieve the same outcome. Instead, improved performance was the result of an established core characteristic of skill learning, namely reduced trial-to-trial variation of movement extent and peak velocity[12, 20]. A similar conclusion was reached recently by Kitago and colleagues[3]. The neural mechanisms underlying these changes are still unknown, but it seems likely that they are similar to those underlying reduction in variability in healthy adults who learn comparable tasks[20]. These improvements are possibly mediated by the recruitment of more neurons for the execution of the task[38], which effectively increases the neural signal-to-noise ratio[20] and improves performance.

Acquiring new movement patterns

Improvement in the speed-accuracy relationship is only one type of learning required after stroke[39]. Another component is re-acquiring movements that were lost and are not within the present movement repertoire. In our protocol, the reaching movement required a range of active elbow extension, which was not initially possible for all patients. It produced an endpoint bias, which often involved undershooting the target with a bias towards flexion. However, training produced very little change in endpoint bias so that we have no evidence for this type of learning in the present data. The implication is that within the confines of their damaged motor system, chronic patients can still learn to control variability but find it more difficult to regain new movement patterns. Whether the latter would be possible in sub-acute stroke or with more extensive training is an important question.

Influence of movement speed during training on performance changes

A recent paper demonstrated that chronic stroke survivors demonstrated long standing improvements in movement velocity and movement smoothness after performing only two training sessions consisting of 600 fast reaching movements [5]. However, limited evidence is available about the importance of performing training at different movement speed in stroke rehabilitation[2, 14] nor are recommendations to incorporate different movement speeds during training included in clinical guidelines[21]. While it is difficult to compare accuracy improvements across different movement speeds directly, as the task difficulty is different between speeds[18], our data clearly shows that improvements for faster movement speeds cannot be effectively achieved by training at slow speeds. Fast training also resulted in a small improvement in clinical scores, which could indicate that performing fast movements is important for recovery after stroke. While our data suggest that fast movements speed improve slightly different aspects of motor control than training at slower speeds, we can only speculate about the underlying mechanisms. One possibility is that generation of larger agonist bursts necessary for fast movements led to more neuronal recruitment and therefore better improvements in functions[38, 40]. Alternatively, it could be that the increased necessity to account for interaction torques (for example by stabilizing the shoulder) led to better learning outcome[17].

We suggest that training regimes for the upper limb should include a proportion of training with an emphasis on increasing movement speed, thereby also counteracting the general slowing of movements after stroke[14]. Our data show that training at fast speed did not increase hypertonus. However, at the current training intensity we found that training benefits were too small to be clinically relevant and did not lead to a change in the flexor bias. This can possibly be attributed to the fact that the short training period was insufficient to alter longer standing movement patterns.

The impact of impairment on learning and vice-versa

It is well established that muscle weakness, sensory loss and increased muscle tone influence motor control after stroke[41, 42]. Less is known of the effect of these impairments on learning. In the present study, we found that sensory impairment reduced learning, consistent with previous studies[42-44]. In contrast, we found no effect of increased tone or weakness. It is possible that removal of visual feedback during movement increased reliance on somatosensory feedback. If so, other types of training, using continuous visual feedback, might be less affected by sensory impairment.

Limitations

As this was a pilot study, there was no calculation of the number of subjects performed a priori to ensure study power and therefore a definitive trial would be required to validate these findings.

We investigated training at different movement speeds and therefore adjusted task difficulty according to each individual's maximum movement speed. The target location and size remained constant for all individuals irrespective of their arm length or reaching distance. Therefore, task difficulty was slightly different depending on each individual's initial ability but as we only included individuals who could end their movement within the 5cm target, we believe that similar strategies were still required throughout our sample. Although arm dominance has been found to influence the performance of reaching in stroke survivors movements [45], this study was not designed or powered to explore these aspects of motor learning.

The training period in this trial was too brief to allow for clinically meaningful changes in outcome measures and the long-term retention of the altered behaviour in our study was not explored however, the small improvement in impairment are encouraging and might indicate the potential utility of more intensive training.

Conclusion

A greater understanding of recovery mechanisms is required in order to tailor individualised rehabilitation protocols[2]. [3, 4, 13]This repetitive training protocol improved performance in line with previous findings [1, 2], despite training not being varied [46]. Our results show that performance improvement can be achieved without the use of compensatory strategies[4, 7]. Chronic stroke survivors improve reaching accuracy most notably at the trained movement speed by a reduction in movement variability. However, movement bias was not significantly changed. We can therefore conclude that in chronic stroke, improvements to the quality of existing movements is possible, however the ability to learn new movements or muscle synergies may take longer periods of training or need to be achieved by alternative training strategies. Over the short training period, we did not observe clinically relevant group differences in clinical outcomes. However, these may emerge over longer training periods, and if so a variety of movement speeds should be included during training as accuracy improvements achieved after slow movement training do not generalise to fast movements.

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Figure legends

Figure 1. Reaching protocol. A) Experimental set-up. B-C) Experimental display during accuracy testing. Target (5cm radius) with centre cross, positioned at 20 cm distance. Hand position is displayed to participant as a green dot at the start (B) and at the end (C) but not during the reaching movement. D-E) Method of determining individual movement speed limits. D) Example data of movement times for 15 trials when attempting fast reaching. indicating) The 80th percentile is indicated by a dotted line (Fig.1E). Therefore the fast movement limit is less than 460ms (red) with incremental increase of 200ms for medium fast (460-660ms orange), medium slow (660-880 green) and slow (880-1600ms blue). F) Bullseye display of target during training days with points as feedback of endpoint accuracy.

Figure 2. Change in amount of endpoint error. A) The mean endpoint error (RMS ±SEM) for fast (red) and slow (blue) group reduced during the training days. B) The mean points (±SEM) per training block reduced for both training groups over the training days. C) RMS (±SEM) error at the four individually set target speeds before (unfilled) and after (filled) training for the fast and D) slow training group.

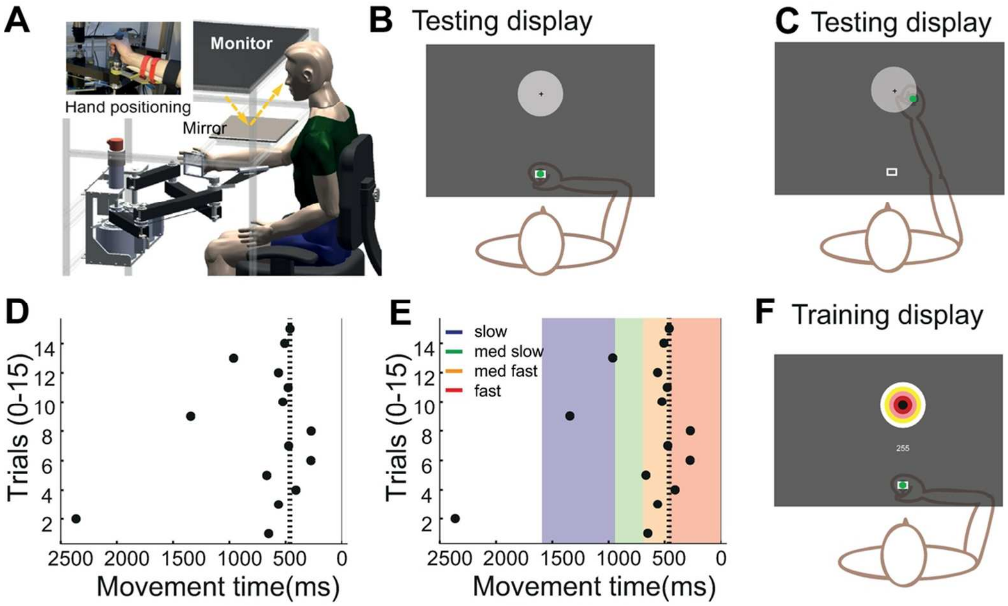
Figure 3. Endpoint variability and bias. **M**ean endpoint bias and variability (SD) in relationship to the target centre (0,0) at the four movement times (A slow, B medium slow, C medium fast, D fast) before (dashed) and after training (solid). The change in endpoint bias was not significant, however the reduction in endpoint variability was significant at all movement speed. Participants tended to undershoot and end movement in the contralateral workspace (flexor bias). Data of individuals with left hemiplegia are mirrored along the sagittal plane and data are presented as right arm movements for all participants.

Figure 4. Change in movement speed variability. Mean peak speed variability (±SEM) for the slow, medium slow, medium fast and fast movement speed before (unfilled) and after (filled) training for the A) fast (red) and B) slow (blue) training group. C) Mean change in movement speed variability at the 4 tested movement speed for the fast (red) and slow (blue) training group. A significant change in maximum speed variability was detected at the training speed for both groups as well as at the medium fast speed for the slow training group.

Figure 5. Effect of baseline ability and impairment on learning. A) Correlation of baseline RMS error with the post training performance on an individual basis for the fast (red) and

slow (bluet) training group. The performance floor of 0.928cm is depicted by a dotted line. B) Correlation of pre and post training measures of all individuals divided into groups of mild (grey) and moderate (black) sensory impairment, hypertonus and muscle weakness.

Figure 6. Functional outcome measures. A) Mean elbow flexor hypertonus (MAS) and B) Fugl-Meyer score for the fast (red) and slow (blue) training groups before (unfilled) and after (filled) training.



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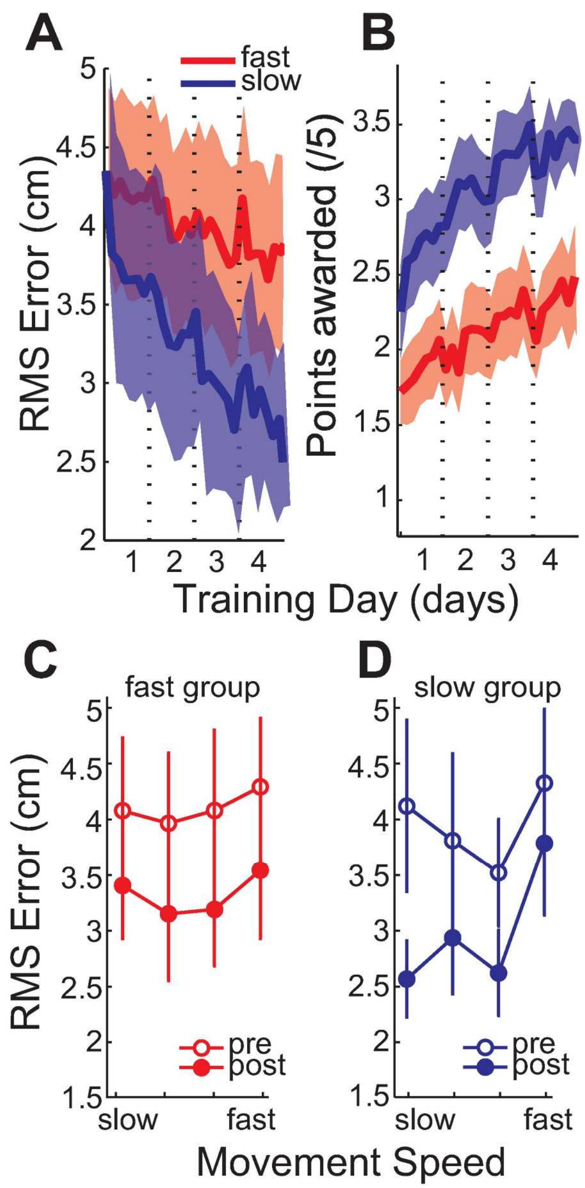

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Fig.2

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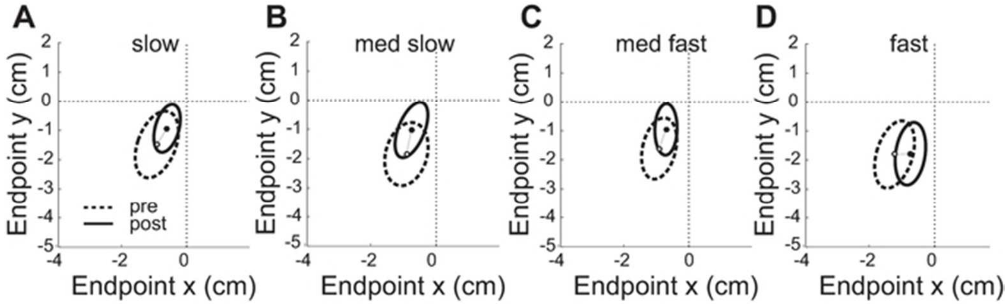

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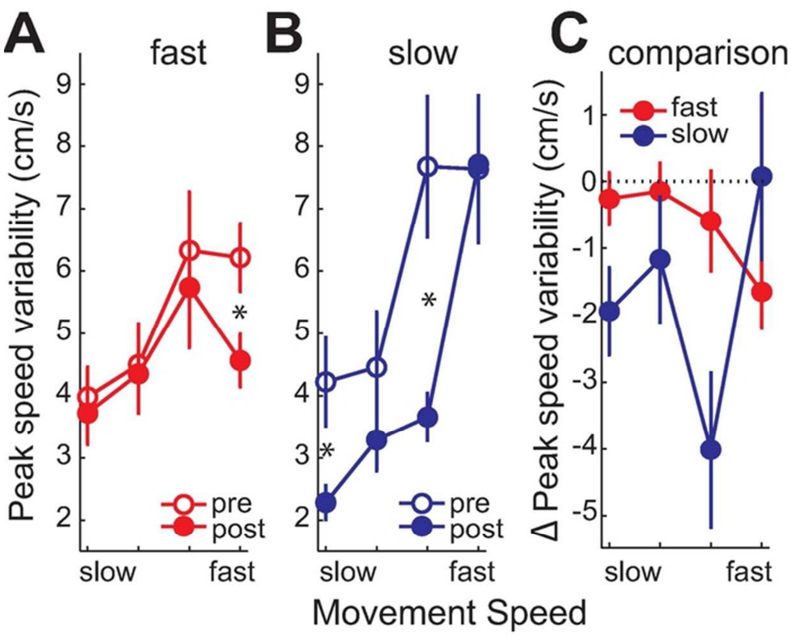

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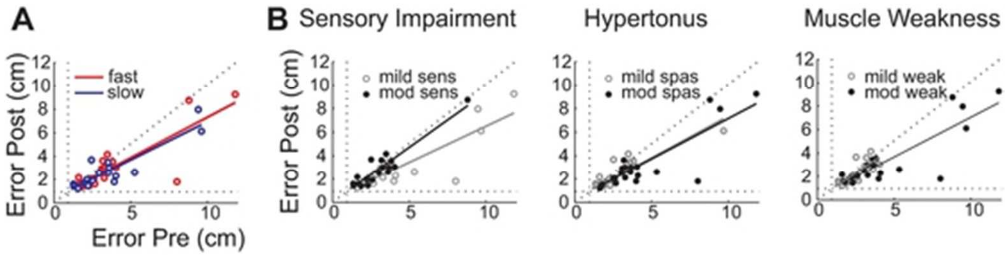

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47x11mm (300 x 300 DPI)

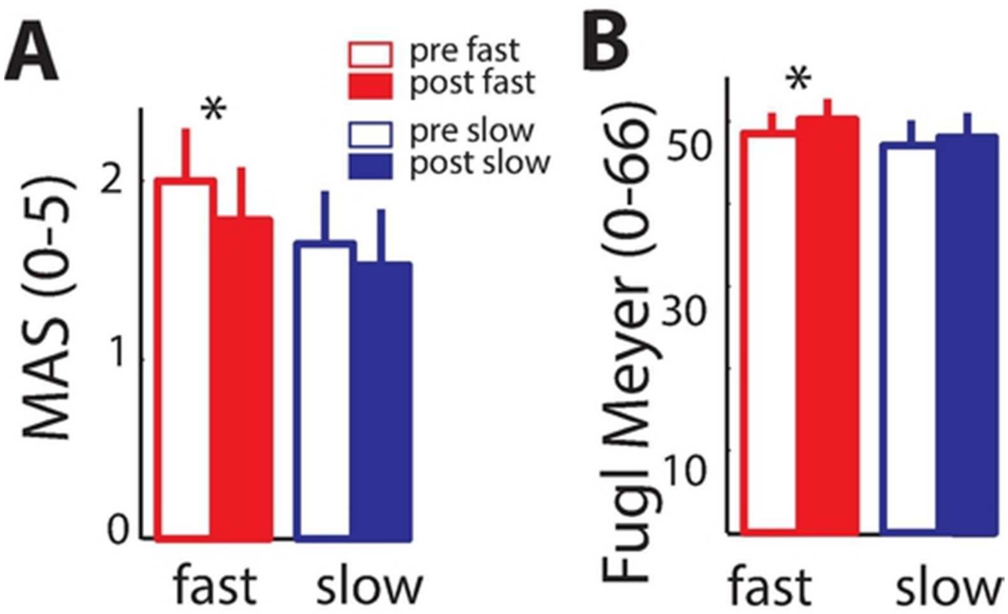

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Fig.6
42x26mm (300 x 300 DPI)

Online Supplement

Title:

Chronic stroke survivors improve reaching accuracy by reducing movement variability at the trained movement speed.

Authors:

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Running title: Reaching training at different speeds

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Flow Diagram:

Supplemental Table I. Clinical presentation of research participants

Patient ID	Age	Weak UL	Months since onset	Fugl-Meyer pre	Fugl-Meyer post	MAS-pre	MAS-post	Sensation	Weakness	Stroke type	Lesion location
Fast											
2	30	R	132	40	41	3	3	mild	3	haem	unknown
4	52	L	32	38	37	3	3	mild	3	infarct	cortical
7	66	R	60	59	61	1	0	mod	3	infarct	unknown
9	55	L	120	58	60	3	3	mild	3	haem	mixed
10	49	L	15	32	32	3	2	mod	1	infarct	cortical
11	54	L	12	51	49	3	3	mod	3	infarct	cortical
14	88	R	84	61	60	1	1	mod	3	infarct	cortical
15	60	L	36	48	54	3	3	mild	3	infarct	sub-cort
17	69	L	84	61	60	0	0	mod	4	haem	cortical
19	47	L	72	55	57	3	3	mild	4	infarct	sub-cort
21	53	L	30	46	50	3	3	mod	4	infarct	mixed
22	62	L	13	49	51	3	3	mod	4	haem	cortical
24	68	L	22	24	26	1	1	mild	3	infarct	cortical
25	58	R	42	49	52	1	1	mild	3	infarct	unknown
27	49	R	28	49	49	3	3	mild	4	infarct	mixed
30	74	L	15	63	64	0	0	mod	3	infarct	cortical
33	49	L	52	39	43	3	2	mild	1	infarct	sub-cort
34	47	R	72	62	62	0	0	mod	4	infarct	mixed
36	50	L	19	38	42	2	2	mild	2	haem	mixed
Mean	**56.8**	**R=6**	**49.5**	**48.0**	**49.8**	**2**	**1.8**	**mild=10**	**3.1**	**haem=5**	**c=8, s=3**
Slow											
1	42	R	60	41	44	3	3	mod	4	haem	unknown
3	69	L	24	58	62	0	0	mod	4	infarct	cortical
5	47	L	28	57	58	3	3	mild	2	infarct	mixed
6	56	R	48	41	37	3	3	mild	2	infarct	sub-cort
8	37	L	30	62	62	2	2	mod	3	haem	sub-cort
12	54	L	20	64	64	0	0	mod	4	infarct	unknown
13	52	R	184	34	38	0	0	mod	3	infarct	unknown
16	69	L	18	55	56	1	1	mod	4	infarct	mixed
18	57	R	60	38	34	3	1	mild	3	infarct	cortical
20	52	R	100	28	32	3	3	mild	3	infarct	cortical
23	41	R	121	30	32	3	3	mod	3	infarct	cortical
26	62	L	25	49	54	2	1	mild	4	haem	mixed
28	45	L	30	55	57	1	3	mod	4	haem	sub-cort
29	63	R	18	58	56	2	0	mod	4	infarct	unknown
31	65	L	82	32	33	1	2	mild	2	infarct	unknown
32	71	R	17	62	57	0	0	mild	4	infarct	cortical
35	61	R	96	37	42	1	1	mild	2	infarct	mixed
Mean	**55.5**	**R=9**	**56.5**	**47.1**	**48.1**	**1.6**	**1.5**	**mild= 8**	**3.2**	**haem=4**	**c=5, s=3**

Abbreviations: ID=identifier, Aff UL=affected upper limb, MAS=modified Ashworth Scale, haem=haemorrhagic, Mm= muscle, mod=moderate, sub-cort=sub-cortical

Supplemental Table II. Performance characteristics for all subjects when performing slow reaching movements

ID	Movement Time		Max Speed		RMS Error		Constant Error				Variable Error			
							Parallel		Perpendicular		Parallel		Perpendicular	
Fast	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
2	1166.8	1252.7	29.04	27.07	2.52	2.75	-1.04	-1.91	0.49	-0.47	0.94	1.45	2.05	1.32
4	1504.0	1148.4	21.44	30.70	9.01	2.03	-5.43	-0.03	-6.69	-0.44	2.01	1.21	2.47	1.60
7	1171.3	1072.5	42.05	39.18	4.32	3.68	2.12	0.25	0.34	0.56	2.53	3.50	2.96	2.16
9	1254.5	1433.3	17.77	14.19	10.70	9.26	-10.40	-9.07	-1.90	-0.87	2.16	1.67	1.23	0.86
10	1017.5	992.1	30.04	40.32	11.06	8.91	-8.13	-7.06	-6.94	-4.32	0.80	1.99	3.24	3.22
11	1000.2	992.2	31.73	34.19	2.65	2.55	-1.42	-1.19	0.50	-1.19	1.96	1.75	1.55	0.79
14	1262.4	1151.7	27.34	23.41	1.82	3.00	0.17	-2.63	-0.07	-0.60	1.96	1.21	0.91	0.69
15	1191.8	1114.6	23.94	26.51	2.22	2.14	-1.06	-1.17	-0.41	-0.42	1.70	1.57	0.95	0.84
17	971.4	942.5	33.59	35.95	4.21	4.24	3.30	3.88	-1.57	-0.34	1.82	1.14	1.38	1.25
19	1070.0	1096.7	26.94	30.61	3.30	2.20	-2.63	-1.13	-1.14	0.58	1.33	1.41	0.99	1.12
21	1110.9	1101.4	26.90	24.52	3.39	4.22	-2.20	-2.19	0.28	-2.10	2.11	2.76	1.49	1.07
22	1380.6	1049.8	31.20	34.77	5.05	3.68	1.58	-0.49	3.17	2.93	2.04	1.59	3.00	1.58
24	1114.7	1080.8	25.35	26.90	2.22	2.65	-0.67	0.55	-0.50	-0.44	1.49	2.37	1.43	1.20
25	1171.3	1104.1	26.14	24.86	2.68	2.22	-1.11	-1.27	-2.11	-1.22	0.89	0.98	0.87	1.14
27	1151.5	1097.4	24.59	26.11	3.18	3.10	-2.89	-2.74	-0.31	-0.21	1.10	1.28	0.76	0.79
30	972.4	1045.0	32.40	30.87	1.71	1.49	0.04	0.75	-0.89	-0.65	1.08	0.94	1.05	0.73
33	1724.7	1382.3	30.49	37.71	2.85	2.50	-1.10	0.39	-1.93	-2.08	1.88	1.15	0.98	0.82
34	1061.8	1111.1	29.00	27.28	2.49	1.77	-0.49	-0.35	-0.37	0.03	2.27	1.59	0.97	0.94
36	1257.0	1214.5	33.47	27.19	2.04	2.29	1.41	-0.89	-0.14	0.66	1.09	1.60	1.11	1.26
Mean	**1187.1**	**1125.4**	**28.60**	**29.60**	**4.1**	**3.4**	**-1.6**	**-1.4**	**-1.1**	**-0.6**	**1.6**	**1.6**	**1.5**	**1.2**
Slow														
1	983.1	950.9	31.11	29.71	5.34	2.99	-0.68	-1.25	-2.87	-1.72	1.55	1.04	4.22	1.95
3	1186.3	948.9	35.10	37.55	1.69	1.42	0.32	0.84	0.55	0.02	1.26	0.70	0.95	0.93
5	1208.2	1183.5	27.70	29.41	2.80	1.25	-1.33	0.24	-1.67	0.17	0.95	0.74	1.60	0.98
6	1205.0	1092.4	11.34	19.98	13.44	6.53	-13.20	-6.23	-0.85	-1.47	1.62	0.60	2.25	1.18
8	1191.1	1145.3	33.60	27.96	3.63	3.56	1.61	0.89	-0.29	-2.61	5.17	1.24	2.19	1.94
12	1072.2	1083.2	30.45	28.98	1.57	1.20	0.25	-0.47	0.09	-0.26	1.37	1.14	0.76	0.64
13	1069.2	1020.5	27.90	34.78	3.12	1.55	-1.35	-0.82	0.85	0.16	2.39	1.24	1.33	0.69
16	1071.0	1023.5	29.22	31.58	1.75	4.29	-0.21	3.77	0.33	1.30	1.57	1.34	1.41	0.85
18	1306.1	1068.6	37.43	29.34	7.88	2.56	2.94	-0.12	-4.63	-1.35	6.36	1.47	2.77	1.54
20	1226.8	1143.3	26.03	26.13	5.56	2.63	-2.83	-0.77	-3.54	-1.95	2.01	0.92	3.09	1.39
23	1210.6	1349.2	25.76	22.82	3.49	3.00	0.73	0.57	0.73	-1.24	2.18	1.71	2.69	2.07
26	1014.4	1028.1	29.61	29.85	1.48	1.51	-0.03	0.83	-0.51	0.77	1.24	0.88	0.99	0.59
28	1179.7	1173.9	25.63	25.53	3.06	2.39	-1.62	-0.50	0.19	-1.64	2.65	1.41	1.81	1.17
29	816.7	859.0	45.21	39.25	2.08	1.73	-0.39	-0.37	-0.44	-0.46	1.20	1.07	1.91	1.35
31	1227.0	899.1	38.76	40.93	2.87	1.83	-0.50	-0.66	1.38	-0.84	2.11	0.87	1.69	1.20
32	1306.0	1191.7	23.94	27.45	2.10	1.30	0.13	0.40	0.12	0.29	2.31	1.07	1.10	0.62
35	1450.4	1625.9	21.50	21.33	8.18	3.85	-7.25	-3.69	-2.20	-0.34	2.17	1.03	2.67	0.91
Mean	**1160.2**	**1105.1**	**29.43**	**29.56**	**4.1**	**2.6**	**-1.4**	**-0.4**	**-0.8**	**-0.7**	**2.2**	**1.1**	**2.0**	**1.2**

Measurement units: Movement Time at slow speed (ms), Maximum movement speed at slow speed (cm/s), All Error at trained speed (cm)

Supplemental Table III. Performance characteristics for all subjects when performing fast reaching movements

ID	Movement Time		Max Speed		RMS Error		Constant Error				Variable Error			
							Parallel		Perpendicular		Parallel		Perpendicular	
Fast	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
2	398.1	407.5	94.84	96.45	2.52	1.83	-0.15	-0.17	-0.79	0.23	1.18	1.12	2.21	1.43
4	396.4	405.8	59.89	79.42	7.04	2.07	-6.51	-0.88	-1.90	-1.17	1.14	0.88	1.81	1.17
7	431.7	472.5	82.07	71.31	4.22	7.04	0.21	-5.91	-2.43	2.41	3.16	2.90	3.76	2.20
9	724.2	482.9	21.44	33.48	13.05	11.11	-12.90	-11.00	-0.78	-1.39	1.13	0.95	1.07	1.16
10	426.1	359.1	83.10	65.65	8.36	8.78	-5.61	-8.09	-5.69	-1.82	2.18	1.31	1.19	3.18
11	385.0	332.1	65.23	85.50	5.56	4.29	-5.46	-3.92	-0.02	0.18	1.00	1.11	0.68	1.41
14	631.1	589.5	59.23	51.16	1.85	1.90	1.52	-1.49	0.28	-0.85	0.70	1.25	0.79	0.60
15	470.5	468.8	66.62	73.75	2.41	1.84	-1.28	0.37	-1.22	-1.28	1.57	1.23	1.01	0.53
17	387.5	380.9	90.26	100.26	2.25	3.87	0.77	3.03	0.86	-0.94	1.41	2.01	1.34	0.96
19	345.4	417.4	115.56	100.28	2.26	1.39	-1.33	-0.38	-0.63	0.42	1.69	0.87	1.37	0.95
21	452.2	425.9	61.54	71.03	3.98	3.86	-3.63	-3.39	-0.82	-0.02	0.95	1.24	1.16	1.42
22	469.6	423.8	91.86	99.03	3.98	3.58	-1.84	-2.62	2.08	0.72	1.56	1.27	3.00	2.00
24	412.9	412.5	85.53	86.51	3.29	2.55	1.96	1.96	-1.45	-0.70	1.70	1.33	1.56	1.16
25	538.8	478.5	64.12	72.41	2.87	1.66	0.43	0.41	-2.37	-0.81	1.01	1.02	1.23	0.94
27	466.9	502.6	78.68	62.82	4.05	3.45	-3.08	-2.87	-1.99	-1.38	1.17	0.97	1.30	0.94
30	408.8	381.2	95.34	99.02	2.76	1.64	1.53	-0.23	0.02	-1.07	1.91	0.83	1.36	0.91
33	735.0	803.9	47.77	56.80	4.52	2.58	-3.55	-1.38	-2.27	-1.90	1.58	0.74	0.55	0.80
34	404.4	402.1	115.37	98.90	2.19	1.38	0.04	0.20	-0.43	-0.16	1.88	1.06	1.21	0.85
36	486.3	531.5	69.48	74.25	4.41	2.51	-3.30	-1.13	-2.34	-1.64	1.78	0.99	0.80	1.22
Mean	**472.1**	**456.8**	**76.21**	**77.79**	**4.3**	**3.5**	**-2.2**	**-2.0**	**-1.2**	**-0.6**	**1.5**	**1.2**	**1.4**	**1.3**
Slow														
1	407.5	363.3	152.65	99.96	3.81	3.09	2.51	-1.42	1.88	-1.81	1.06	1.16	3.14	1.84
3	365.6	361.3	92.37	102.18	1.58	2.05	0.05	0.36	-0.27	1.55	1.21	1.57	1.04	0.89
5	433.8	476.5	93.63	77.87	5.76	2.92	-2.88	-0.73	-3.40	-0.99	1.24	1.35	2.08	1.57
6	439.3	347.9	47.37	52.58	9.04	10.29	-9.52	-10.04	-8.63	-10.10	2.49	1.70	1.28	1.04
8	420.0	400.3	108.32	107.51	4.85	3.59	1.37	1.73	2.60	2.24	2.12	2.19	4.64	2.25
12	430.7	417.1	89.15	81.23	2.09	3.03	-0.65	-1.07	-0.92	-2.30	1.51	1.63	0.94	0.90
13	521.8	466.2	71.44	70.80	3.49	1.35	1.97	0.37	2.95	0.13	1.73	1.05	1.23	0.87
16	459.6	455.0	65.52	71.98	2.89	4.68	-2.03	2.24	-2.47	0.21	1.24	4.92	0.71	0.64
18	467.5	504.2	78.78	70.72	3.91	2.89	-0.74	1.34	-1.30	0.96	1.54	1.35	1.70	1.39
20	546.3	528.9	69.39	67.98	3.90	2.52	-0.71	-1.59	1.66	-1.11	2.75	1.54	3.95	1.45
23	506.5	498.2	61.96	59.19	2.94	2.52	-0.79	-2.56	-0.67	-1.65	1.66	1.67	2.16	1.64
26	440.7	448.8	80.73	73.44	2.23	1.55	1.51	-0.66	1.34	0.81	1.54	1.73	0.87	0.74
28	408.7	431.8	75.43	67.10	2.58	3.18	-1.65	-1.09	-1.95	-2.29	1.30	2.27	1.15	1.21
29	412.2	432.5	84.27	77.23	3.21	2.70	-2.88	-1.90	-1.13	-1.66	2.46	1.25	2.41	1.70
31	529.4	627.6	75.27	56.50	6.07	5.13	-5.06	-3.00	-5.00	-3.23	2.74	1.16	2.15	1.70
32	536.9	535.0	74.93	68.25	2.83	2.35	1.64	0.81	2.07	0.78	1.63	1.42	1.10	1.26
35	737.1	923.3	43.85	47.21	12.26	10.56	-9.46	-8.27	-8.57	-8.21	1.52	1.37	3.24	3.47
Mean	**474.3**	**483.4**	**80.30**	**73.63**	**4.3**	**3.8**	**-1.6**	**-1.5**	**-1.3**	**-1.6**	**1.7**	**1.7**	**2.0**	**1.4**

Measurement units: Movement Time at fast speed (ms), Maximum movement speed at fast speed (cm/s), All Error at trained speed (cm)

Figure I. Reduction in RMS error in healthy individuals

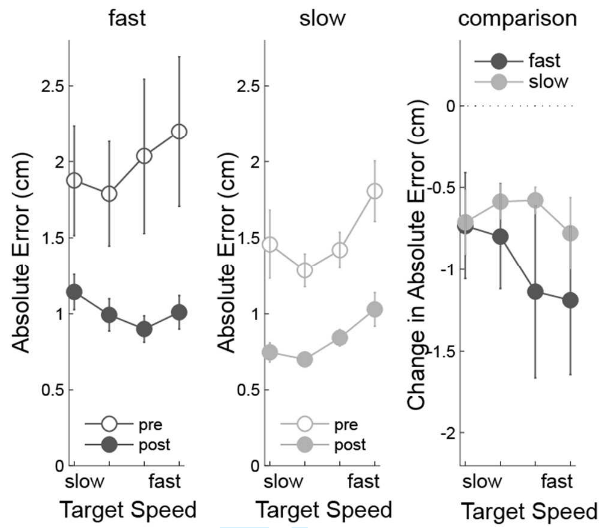


Figure I. Change of RMS error in healthy individuals for fast (dark grey) and slow (light grey) training group at all set target speeds. The error before training (unfilled) and after training (filled) is measured for the fast and slow training group at slow, medium slow, medium fast and fast movement speed. The amount of change in RMS error is compared between the two groups at all target speeds.

In this set of healthy individuals (n=14, female=8, age=25.3 years) learning and a reduction in RMS error is observed in both training groups (effect of TIME $F_{(1,12)}$=15.363, p=0.002) after the same amount of training as performed in the stroke group. There is however no interaction or effect of Group indicating that the improvement between these two training groups was not different. Error is never quite eliminated after training and the mean endpoint error for all participants at all target speeds was 0.928cm(+/- 0.271) which we propose to be the performance floor in this protocol.

Figure II. Performance change in stroke patients during training

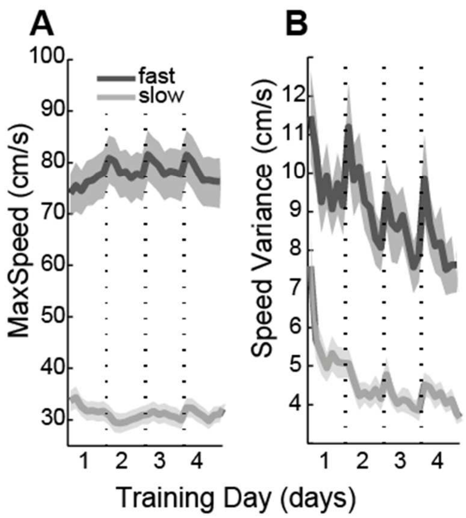


Figure II. Reaching performance during training days (Day 1-4). A). Mean movement speed for fast (dark grey) and slow (light grey) group per training block (7/day) for the 4 training days. B) Mean maximum speed variability (SD) for the two groups for each training block on the 4 training days.

Patients in the two training groups performed training at different movement speeds and both groups demonstrated learning; they reduced their endpoint error and gained greater reward points for improved accuracy. In addition we noted that they reduced the trial-to-trial variability of their movement speed over the four training days (Fig IIA-B). Changes in performance between and during each day were investigated by a 3-way ANOVA - DAY(4)*BLOCK(7)*GROUP(2).

A main effect of GROUP ($F_{(1,34)}$=91.85, p<0.001) confirms the difference in movement speed (Fig IIA) between groups as instructed by the protocols. An additional interaction ($F_{(18,612)}$=31.35, p=0.003) shows that changes over the blocks from day to day differed between the two groups. In the fast training group individuals increased their movement speed from the first to the last block on the first training day whereas on subsequent days they slowed down over the course of each daily session. Bonferroni-corrected post-hoc t-tests, only reached significance on day 3 ($t_{(18)}$=3.37, p=0.018). In comparison, the slow training group reduced their movement speed on the first training day ($t_{(16)}$=2.35, p=0.032) and then remained stable over the remaining days. This may indicate that patients training at the fast movement speed tired over the course of the training session.

Finally, maximum movement speed variability reduced throughout training (Fig IIB). Both groups demonstrated a continuous reduction in maximum speed variability in an effect of DAY ($F_{(3,102)}$=9.72; p<0.001) as well as an effect of BLOCK within each day ($F_{(6,204)}$=4.29; p<0.001). As expected variability of movement increased with greater movement speed, GROUPS ($F_{(1,34)}$=27.91; p<0.001), being higher in the fast training group. However, no interaction was observed, indicating that the reduction in variability was similar in both groups over the practice days.

Despite overall reductions in movement speed variability during training, figure IIB suggests that these improvements were not fully retained from day-to-day, particularly for the fast training group. Forgetting (i.e. a return towards the previous days performance level) could indeed be confirmed in the fast group on the first two training days (paired t-test $t_{(18)}$=-2.36, p=0.030 and $t_{(18)}$=-2.40, p=0.027) and for the slow group from the third to the fourth day ($t_{(16)}$=-3.86, p=0.001).

Figure III. Distribution of error and individual differences

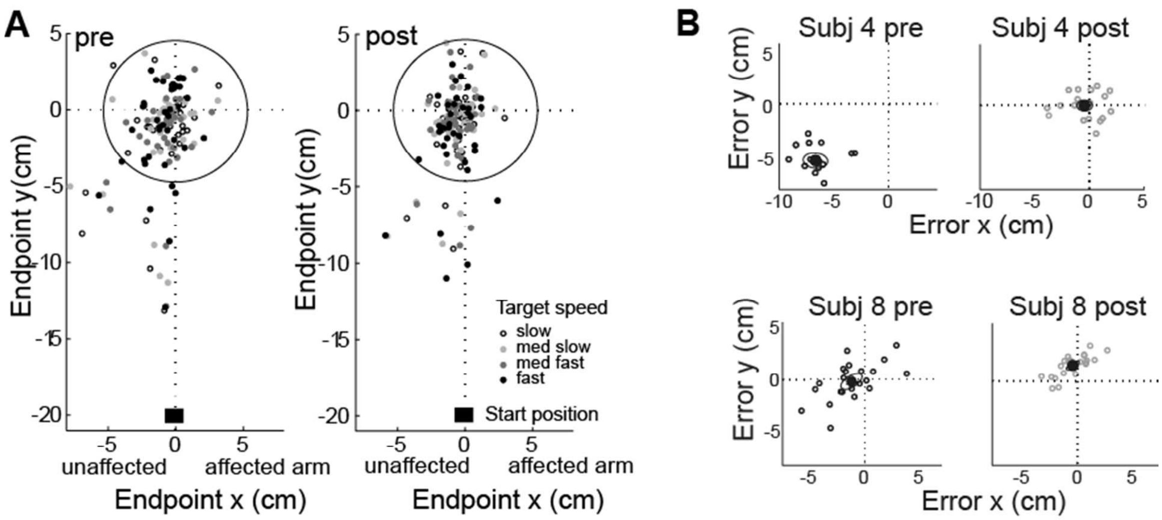


Figure III. A) Average movement endpoint in relation to the start point, target centre and circumference for each subjects at slow (unfilled), medium slow (light grey), medium fast (dark grey) and fast (black) movement speed before (pre) and after (post) training. B) For example, subject 4 had a clear bias of endpoint location which improved after training without changing the variability. In comparison subject 8 had large variance of reaching endpoints, which reduced after training while the small bias remained unchanged. No consistent cause for this distribution could be detected in this small data-set when investigating patient age, lesion site and side.

The reaching task was initially challenging for the stroke survivors as demonstrated by the poor endpoint accuracy at the various movement speed seen before training (Fig IIIA). Patients showed a consistent bias to undershoot at all target speeds and a tendency to end the movement in the opposite workspace. We investigated whether for the whole group, training at the two movement speeds reduced either the bias or the variability of the endpoint. The size of these two types of errors could be relatively unrelated (Fig IIIB).

Figure IV. Maximum movement speed

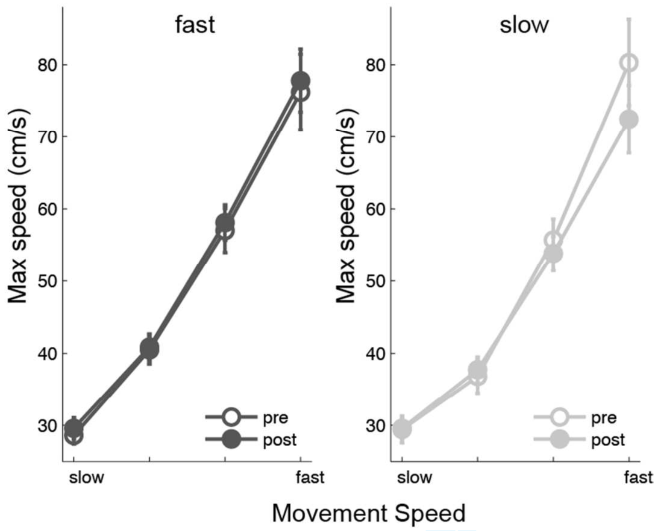


Figure IV. Maximum movement speed. Maximum movement speed before (unfilled) and after (filled) training for the A) fast (dark grey) and B) slow (light grey) movement speed for the 4 target speeds.

In addition to movement accuracy, success at this task also depended on the ability to perform the required movement in the pre-determined movement time. Performance changes could therefore also be observed as reduced variability of the maximum movement speed (Fig.4), specifically at the trained speed. The maximum velocity during the four movement times was very similar between the two training groups and did not change significantly after the training.

Figure V. Linear regression of performance change when excluding outliers

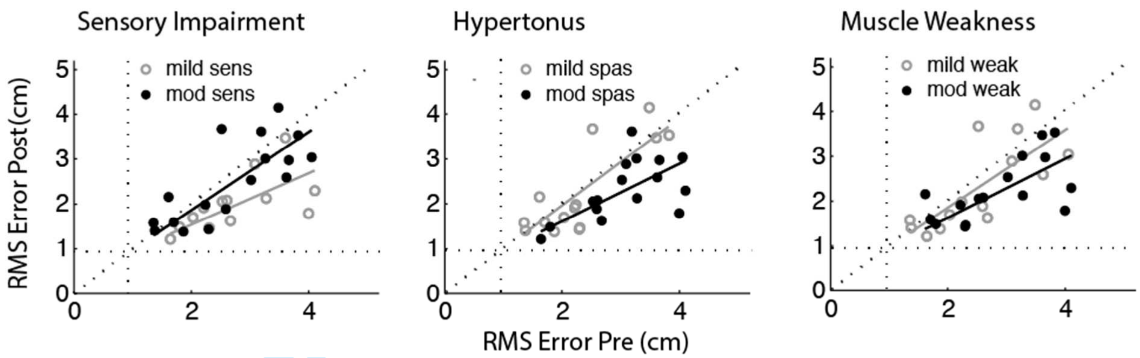
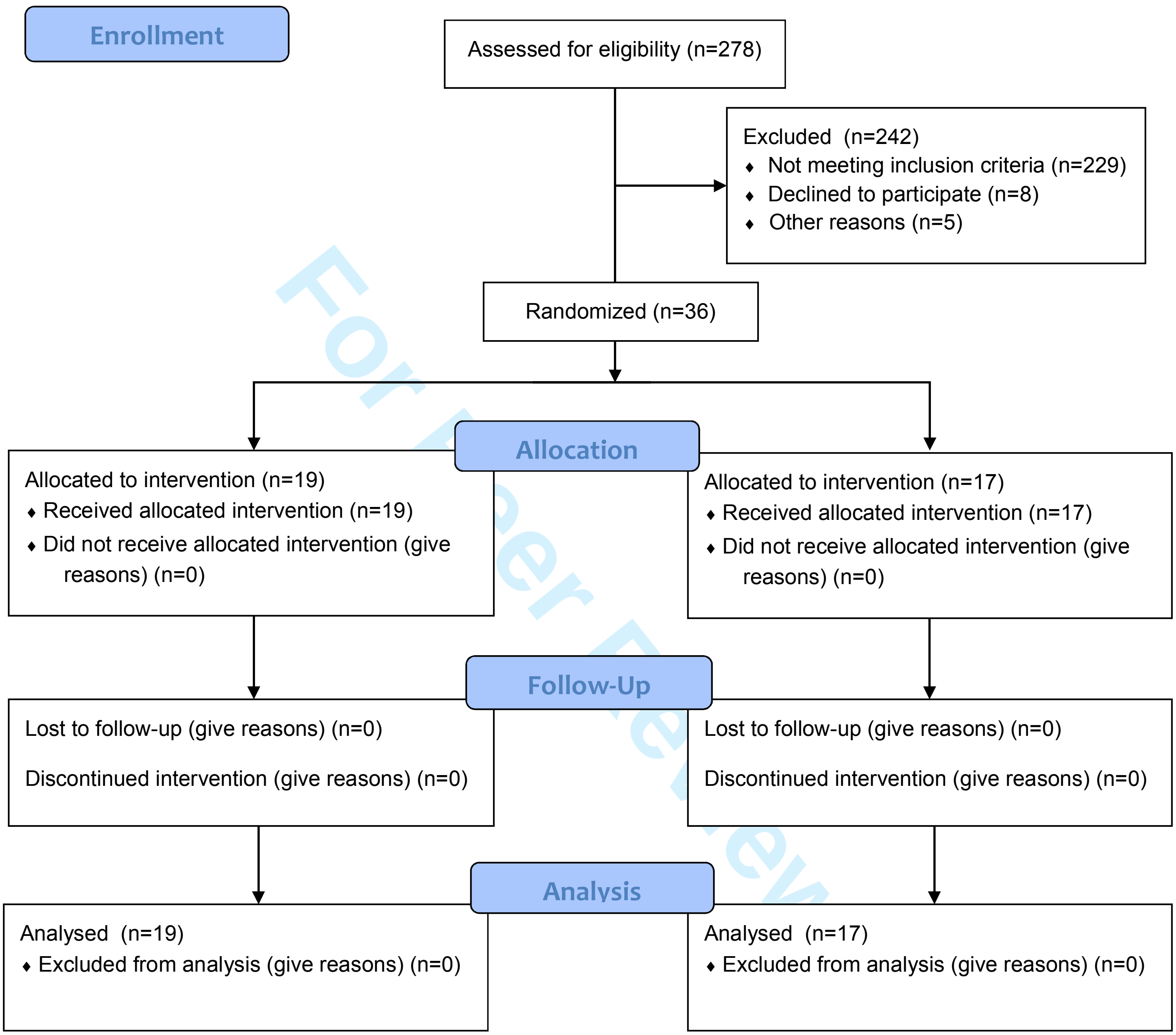


Figure V Correlation of pre and post endpoint error divided by severity of Sensory Impairment(Fig VA), Spasticity (Fig VB) and muscle weakness (Fig VC) for the subgroup of individuals with a baseline RMS error smaller than 5cm.

Analyses of subgroup of patient's with a mean RMS error<=5. We observed the same influence of sensory impairment on learning as observed when all data was included. The regression slope between individuals with mild (b=0.57, CI=0.41-0.73) and moderately (b=0.87, CI=0.73-1.01) impaired sensation differed ($t_{(28)}$=2.89, p=0.007). Furthermore in this subgroup contrary to expectations, individuals with moderate hypertonus (b=0.64, CI=0.52-0.77) demonstrated greater learning ($t_{(28)}$=-2.95, p=0.006) than individuals with mild hypertonus (b=0.97, CI =0.78-1.16) but muscle weakness still had no effect on learning in this subgroup of stroke survivors (mild: b=0.0.865, CI=0.686-1.044, moderate: b=0.66, CI=0.51-0.80, $t_{(28)}$=-1.86, p=0.074).

CONSORT 2010 Flow Diagram



Title:

Chronic stroke survivors improve reaching accuracy by reducing movement variability at the trained movement speed.

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Abstract

Background: Recovery from stroke is often said to have "plateaued" after 6-12 months. Yet training can still improve performance even in the chronic phase. Here we investigate the biomechanics of accuracy improvements during a reaching task and test whether they are affected by the speed at which movements are practised.

Method: We trained 36 chronic stroke survivors (57.5 years, SD ±11.5; 10 females) over four consecutive days to improve endpoint accuracy in an arm-reaching task (420 repetitions/day). Half of the group trained using fast and the other half slow movements. The trunk was constrained allowing only shoulder and elbow movement for task performance.

Results: Before training, movements were variable, tended to undershoot the target and terminate in contralateral workspace (flexion bias). Both groups improved movement accuracy by reducing trial-to-trial variability; however, change in endpoint bias (systematic error) was not significant. Improvements were greatest at the trained movement speed and generalised to other speeds in the fast training group. Small but significant improvements were observed in clinical measures in the fast training group.

Conclusions: The reduction in trial-to-trial variability without an alteration to endpoint bias suggests that improvements are achieved by better control over motor commands within the existing repertoire. Thus, 4 days' training allows stroke survivors to improve movements that they can already make. Whether new movement patterns can be acquired in the chronic phase will need to be tested in longer-term studies. We recommend that training needs to be performed at slow and fast movement speeds to enhance generalisation.

Introduction

The majority of patients after stroke are left with deficits in upper limb function[1, 2]. Improvements in functional reaching can occur either by regaining the ability to make movements which were lost completely after the stroke [3], or by increasing the accuracy and/or speed of preserved movements[4, 5].

In the chronic phase after stroke multiple studies have shown that training can produce task-specific improvements even many years after stroke, although the speed of recovery slows[3, 6]. However, there are few detailed investigations of biomechanical changes induced by training in chronic stroke patients[3-5]. Some authors have argued that in the chronic phase all improvement is compensatory [4, 7], in that the goal is achieved by replacing lost abilities using other joints. This results in solutions that are not optimal for the task [8]. Thus, patients' movements may become more accurate with training but this may be achieved by increased trunk flexion during reaching[8-10]. However, improvement may occur through two other mechanisms. Even if patients do not recover lost function, they may recover better control of their movements, resulting in movements that are less variable from trial-to-trial, and hence on average more accurate[3, 11, 12]. Another possibility is that patients relearn to produce combinations of muscle activity lost due to stroke. Improvements in performance in this case would be detected as reduced endpoint bias and/or straighter trajectories.[3, 13] Additionally an important issue in motor learning is the speed-dependency of improvements. In a previous study[13], we found that if healthy adults practiced reaching at one speed they improved performance at that, but not at untrained speeds. After a neurological insult individuals tend to move slowly[14], possibly due to greater difficulties of generating activity[15], increases in stretch-reflexes [16], avoidance of increased interaction torques with higher velocities [17] or to compensate for decreases in accuracy[18-20]. However many movements such as catching a falling object, driving a car or stabilising yourself while on a bus rely on the ability to generate accurate, fast bursts of muscle activity[15]. Current clinical guidelines do not emphasize the need to train patients at a variety of movement speeds[21] and there are limited studies investigating how movement speed during training effects learning after stroke. Continual exposure to slow movements in daily behaviour and rehabilitation training may prevent regaining the ability to move accurately at fast speeds, or they may even reinforce the slowness of movement through use-dependent learning[13, 22].

We therefore investigated whether improvements in reaching are possible when practicing an arm-reaching task for four days when compensatory movements are minimised. We measured changes in endpoint accuracy in terms of endpoint bias and variability when patients trained either at fast or slow movement speed and analysed the effect of the training on the speed-accuracy trade-off function (SAT)[18, 23, 24]. We hypothesized that, as for healthy individuals, some of the movement improvements would be specific to the trained speed. More specifically, we predicted that improvements during fast reaching would be achieved only after training at the fast movement speed [5]. We further investigated how improvements in fast movements matter to clinical motor impairment measures, hypothesizing that improved ability to generate fast movements may have clinical relevance. Finally, we studied how different factors of impairment (sensory loss, spasticity, weakness) influence the ability to profit from training.

Materials and Methods

Subjects

This parallel-randomised (1:1 allocation) study was approved by the Joint Ethics Committee of University College London and the National Hospital for Neurology and Neurosurgery (NHNN). Patients were recruited from NNHN and charity stroke clubs and websites. (For clinical details, Supplementary data, Table I). Prior to participation, informed consent was obtained from each participant according to the Declaration of Helsinki. All patients met the following inclusion criteria: 1) Chronic stroke survivors (≥1 year history) with 2) persistent upper limb weakness (≤4 Medical Research Council (MRC) of either triceps or anterior deltoid muscles 3) Participants had to be able to perform the training task of ≥15 cm reach with the weight of the arm supported in a robotic manipulandum (Fig.1A). We excluded individuals with 1) history of previous stroke or other concomitant neurological or musculoskeletal disease, 2) cerebellar stroke, 3) proximal upper limb hypertonus ≥3 on Modified Ashworth scale (MAS), 4) severe sensory impairment ((light-touch <50% accuracy on 1g Bailey© monofilament sensory testing on dorsum and palm of hand). 5) Shoulder pain ≥3/10 on self-rated continuous visual analogue scale, 6) uncorrected visual impairment, 7) hemi-spatial neglect established by the Star Cancellation Task[25] and 8) cognitive and language impairment impeding co-operation in study protocol.

Clinical assessments were performed before and on the last day of the testing week by a neurologist (DH) blinded to training group allocation. Testing consisted of the Fugl-Meyer upper limb subset (/66), muscle strength (MRC grading) [26], sensory impairment(1g monofilament) and elbow flexor hypertonus (MAS) [27]. MAS scores were converted to a 6 point scale (0-5) prior to non-parametric analysis and are depicted as such throughout[28].

Reaching paradigm

Hand position was measured using ~~All kinematic data were acquired in~~ a custom built 2D manipulandum (Fig.1A)[29], with an incremental quadrature encoder at each of the two joints (65.5k steps/revolution). This resulted in accuracy at the handle of ~0.03mm. Movement speed was calculated by differentiation of the position signal. All kinematic data were sampled at 200Hz.~~.~~ Participants were seated with forehead support, a shoulder strap and backrest support preventing compensatory movement in the sagittal and frontal plane while limiting shoulder girdle movement. Subjects held a handle (inset Fig.1A) or if required the hand was strapped onto the handle by a custom-made glove[13]. ~~while the hand position was recorded at a sampling frequency of 200Hz.~~

A forearm support eliminated gravity and vision of the hand was occluded by a mirror displaying visual feedback (Fig.1B). Feedback comprised of a 2 cm diameter starting box, a green cursor (0.5 cm diameter) representing manipulandum position and a circular 10 cm diameter target with a small black cross at its centre, which was located 20cm from the start box at an angle of zero degrees. A change of the target from an outline to a solid white colour indicated the start of a trial. Individuals were instructed to reach and terminate movement as close as possible to the centre of the target (centre cross) in their own time. When movement was initiated, the green cursor disappeared and only reappeared, displaying feedback of the end position (Fig.1C) for 1 second when movement stopped. Feedback was removed to prevent corrections during the movement because with corrections the relationship between speed and accuracy is complicated, as slower movements allow for more complete corrections. Visual feedback at the endpoint (knowledge of results[30]) is essential to prevent complete dis-calibration without knowledge of hand position, of the reaching movements and to motivate participants to move accurately. The robot was used primarily to measure movement however; assistance was provided to move the handle back to the starting position after the completion of each trial.

Initial assessment (pre) was performed on a Thursday and the final assessment on the following Friday (post-training). In these sessions reaching accuracy was established at four different speeds[13] depending on each individual's fastest movement ability. After task familiarization (15 repetitions with, and 15 without visual feedback of hand position), participants were encouraged to reach as quickly as possible in the 3rd block (Fig.1D). The 80th percentile or 4th shortest movement time was used to set the limit for the individual's fast movement time (Fig.1E dotted line, i.e. 460ms). Movements during fast reaching conditions had to be terminated faster than this limit (dark shaded area) which we found to be challenging but achievable in pilot testing. For the other three movement speeds the lower movement time limit was incrementally increased by 200ms resulting in this example, in limits of 460ms–660ms for medium fast (yellow) reaches, 660ms-860ms for medium slow (green) and slow (blue) between 860ms-1600ms while allowing some redundancy at the slow movement speed to increase ease of task peformance. This incremental increase allowed us to test individuals reaching accuracy at similar intervals along their SAT. The order of testing movement accuracy at the four movement speeds was randomized across patients. At every speed, reaching movements were repeated until twenty successful trials or a maximum of sixty trials were performed.

Training paradigm

Blocked, stratified randomisation to the fast or slow training group was performed after completion of the initial assessment. Sequentially numbered sealed envelopes contained group allocation stratified for functional impairment (Fugl-Meyer ≤50 or ≥51). Training sessions were always performed on the consecutive Monday to Thursday between the assessment sessions. All movements during the four training days were performed at the individually determined fast or slow movement time limit as described in the reaching paradigm. The trainer (UH) was not blinded to group allocation as the speed of movement was visually apparent and patients required prompting to perform movements at the correct speed. Patients were instructed to perform reaching movements in the robotic manipulandum, to a bulls-eye target for 420 reaches per day (7 blocks of 60 repeats) (Fig.1F). This protocol was established in pilot testing to achieve ≥400 movement repetitions in training[31, 32]. Movements had to be performed at the movement speed of the allocated group and were rewarded for endpoint accuracy to a maximum of 300 points (60x5 points) per block (Fig.1F). Five points were awarded for terminating in the bulls-eye (<1cm error) with incremental reduction to one point in the outer ring (4-5cm error). Accumulative points were displayed on the screen for each block and a beep indicated that the trial was successful within the speed limit and in the target area receiving at least 1 point. Movements that ended outside the target area and/or did not fall within the required movement limit were awarded zero points. Visual feedback of endpoint location was provided after each trial for 1 second. Participants were encouraged to increase their points per block and were reminded of their performance on the previous block and the previous day(s). Each training session lasted between 1-1½ hours.

Outcome measures

The primary outcome measure was spatial accuracy at movement end. We studied how accuracy changed due to training and how these reductions generalized to untrained speeds. As an overall measure of accuracy, we used average distance from the centre of the target (cm). This error could be further subdivided into the average deviation from the target (constant error) and the standard deviation around the mean endpoint(variable error) [33]. For some analyses, the error was further subdivided into parallel (i.e. movement direction) and perpendicular movement error (i.e. orthogonal to movement). To allow comparisons across individuals, movements of individuals with left hemiparesis were mirrored along the sagittal plane and data are presented as right arm movements for all participants.

For each trial, the maximum tangential movement speed of the hand was determined and averaged per individual for each tested target speed (maximum speed)[13]. The standard deviation around the mean was taken as a measure of variability of movement speed (movement speed variability).

Data Analysis

IBM SPSS software and custom written Matlab® (Mathworks) routines were used for data analysis ($p<=0.05$, distribution normality confirmed by Kolmogorov-Smirnov test).

Repeated measures ANOVAs (Greenhouse-Geisser corrected) were used to analyse performance during training BLOCK(7)*DAY(4)*GROUP(2) and change (day 1 compared to day 6) after training TIME(2)*MOVEMENT SPEED(4)*GROUP(2) and assessed by post-hoc Student's t-test, Holm-Bonferroni corrected for multiple comparisons if required. Fugl-Meyer and MAS scores were assessed by Wilcoxon Signed rank tests for change and Mann-Whitney U-Tests established group differences.

The regression slope of performance change due to training was depicted in both training groups (intercept fixed to residual RMS Error of 0.93cm; +/-0.06 observed in healthy individuals, supplementary information Figure I). Regression coefficients were compared by t-statistics. A median split of sensory impairment (</≥80% sensory accuracy, mild(n=18), moderate(n=18)), muscle weakness (deltoid MRC =/≤4, mild(n=22), moderate(n=14)), and hypertonus (elbow flexors: MAS </≥2, mild(n=15), moderate(n=21)) assessed how impairments affected learning.

Results

36 Stroke survivors (57.5 years, SD ±11.5; 10 females) successfully trained at their target speeds (n=17 slow at average movement speed 32.2±0.3 cm/s and n=19 fast at 77.9±0.45cm/s) with no adverse events. The study participants comprised of 27 individuals with an infarct and nine haemorrhagic stroke survivors. The lesion site was cortical in 13 individuals, subcortical in six and nine patients presented with a combination (please see supplementary information Table 1). Lesion location was not known in the remaining 10 individuals. Intergroup comparison for lesion type, side or site did not demonstrate any group effect in this small sample. Over 4 days (day 2-5), reaching accuracy improved (Fig.2A; effect of DAY $F(3,102)=9.05$; $p<=0.001$ and BLOCK $F(6,204)=3.15$; $p=0.006$) and points awarded for hitting the target increased (Fig.2B; DAY $F(3,102)=20.83$; $p<0.001$ and BLOCK $F(6,204)=6.90$; $p<0.001$) for both training groups. (Movement speed fluctuated during the training days but no systemic change in speed was observed between days. Supplementary information Fig.II).

Accuracy improvements at trained and non-trained movement speeds

Before training, stroke survivors had poor endpoint accuracy at all four tested movement speeds without a difference in baseline performance for participants randomized to slow and fast training (Fig.2C&D). In a retention test, a day after the last training session (day 6), both groups improved their endpoint accuracy in comparison to performance on day 1 but the pattern of improvement differed for the two training groups (GROUP(2)xMOVEMENT SPEED(2) interaction, $F_{(3,102)}=2.884$, $p=0.039$). In the fast training group there was no difference between improvements at the trained fast speed and the untrained, slow speed ($t_{(18)}=0.23$, $p=0.821$) indicating broad generalisation. This was less efficient in the group that trained at the slow speed, who demonstrated greater improvements at the slow, trained movement speed than at the fast speed ($t_{(16)}=2.23$, $p=0.040$).

We next established to which extent this improvement was achieved by a reduction in endpoint bias and/or a reduction in endpoint variability by investigating the combined data of the two training groups.

Before training individuals demonstrated a bias to undershoot and terminate in the opposite workspace as indicated by the groups mean endpoint location and standard error of the mean (Fig.3A-D), generally indicative of an elbow and shoulder flexion bias (supplementary information Fig.IIIA). There was no interaction or significant change in the bias (rmANOVA: no effect of TIME) for both parallel ($F_{(1,35)}$=3.46, p=0.071) and perpendicular bias ($F_{(1,35)}$=2.64, p=0.113) at the 4 movement speeds. In comparison there was a reduction in endpoint variability of the movements after training (TIME $F_{(1,35)}$=37.714, p<=0.001) and this effect (Fig.3A-D) was confirmed by post-hoc Holm-Bonferroni corrected t-tests at all speeds(slow $t_{(35)}$=4.48, p<=0.001, med slow $t_{(35)}$=5.201, p<=0.001, med fast $t_{(35)}$=5.541, p<=0.001, fast $t_{(35)}$=2.156, p=0.038). The endpoint variability reduced in the parallel (under/overshoot) (TIME $F_{(1,35)}$=19.96, p<=0.001) and perpendicular directions (left/right bias) (TIME $F_{(1,35)}$=27.82, p<=0.001).

Movement speed variability

Although patients were required to move at specific speeds (supplementary information Fig.IV), their actual speed varied slightly from trial-to-trial (Fig.4). The variability of the peak speed was the same in both groups before training (no interaction $F_{(3,102)}$=1.11; p=0.348 or effect of GROUP $F_{(1,34)}$=0.61; p=0.440). Training altered this measure (Fig.4A-C) evident when the change at the 4 movement speeds are compared between the groups (Fig 4C) (GROUPxMovementSPEEDxTIME interaction, $F_{(2.5;83.5)}$=4.43; p=0.010). Post-hoc Holm-Bonferroni corrected t-tests indicated that the change was significant at the trained movement speed for the fast ($t_{(18)}$=3.03, p=0.029) and slow ($t_{(16)}$=2.985, p=0.026) group and only generalised to medium fast movements ($t_{(16)}$=3.404, p=0.015) in the slow training group.

The influence of baseline impairment and clinical measures on behavioural change

The RMS error of individuals with good baseline performance improved less than those with poor performance (Fig.5A), probably because of a floor effect, as movement error is never completely eliminated [34] (supplementary information Fig.I). This meant that the improvement in endpoint error was roughly proportional to the initial deficit[35]. The regression slopes of error reduction indicated a 20-30% improvement in performance (fast: m=0.76, SEM=0.66-0.87 and slow: m=0.72, SEM=0.60-0.84).

We asked whether the benefit of training varied between different subgroups of patients characterized by specific deficits. Severity of sensory impairment was the only factor that influenced learning (Fig.5B) as detected by the difference of the slope (Independent t-test, $t_{(34)}$=3.39, p=0.002) of the regression between the mildly (b=0.613, CI=0.52-0.71) and moderately (b=0.93, CI=0.76-1.09) impaired individuals. Neither the severity of hypertonus (mild: b=0.71, CI=0.51-0.91, moderate: b=0.69, CI=0.58-0.79, $t_{(34)}$=-0.21, p=0.86) nor muscle weakness (mild: b=0.87, CI=0.56–1.17, moderate: b=0.67, CI=0.58- 0.77, $t_{(34)}$=-1.20, p=0.237) influenced learning. This finding is maintained when excluding outliers with greater error, which could drive the reported effect (please see supplementary information Fig.V). We conclude that individuals with moderate sensory impairment improve least in this reaching task.

The influence of training on clinical measures of impairment

Elbow flexor hypertonus (MAS: Fig.6A), reduced in the group training at fast movement speed (related samples, Wilcoxon signed rank test, p=0.046, uncorrected for multiple comparison) but not for individuals training at slow speeds (p=0.581). Similarly the changes in Fugl-Meyer scores (Fig.6B) were significant for the fast (p=0.004, uncorrected for multiple comparison) but not the slow training group (p=0.230). Neither of these changes are however clinically meaningful (reduction in hypertonus MAS=0.21 SD=0.85 and increase in Fugl-Meyer score =1.84 SD=2.27).

Discussion

Our experiment showed that with 4 days' training chronic stroke survivors could improve reaching accuracy but correction for endpoint flexor bias was more difficult. Improvements in accuracy were achieved by reducing endpoint variability and were greatest at the trained speed but generalised to reaches made at untrained speeds. We recommend that training should be executed at a variety of speeds to maximize the breadth of generalization of improvements after training.

Reducing movement variability

Limiting compensatory trunk movement, while performing reaching movement, has been shown to be effective in improving movement quality in stroke survivors[36, 37]. Our set-up prevented trunk flexion and rotation and minimised shoulder girdle movement, permitting only elbow and shoulder movement for the performance of the reaching movement. The change in the speed-accuracy relationship[19, 20, 23], meant that at a retention test one day after training, patients could perform movements of a given speed more accurately than on the testing session before training. These improvements were not due to patients employing a different (i.e. "compensatory") strategy to achieve the same outcome. Instead, improved performance was the result of an established core characteristic of skill learning, namely reduced trial-to-trial variation of movement extent and peak velocity[12, 20]. A similar conclusion was reached recently by Kitago and colleagues[3]. The neural mechanisms underlying these changes are still unknown, but it seems likely that they are similar to those underlying reduction in variability in healthy adults who learn comparable tasks[20]. These improvements are possibly mediated by the recruitment of more neurons for the execution of the task[38], which effectively increases the neural signal-to-noise ratio[20] and improves performance.

Acquiring new movement patterns

Improvement in the speed-accuracy relationship is only one type of learning required after stroke[39]. Another component is re-acquiring movements that were lost and are not within the present movement repertoire. In our protocol, the reaching movement required a range of active elbow extension, which was not initially possible for all patients. It produced an endpoint bias, which often involved undershooting the target with a bias towards flexion. However, training produced very little change in endpoint bias so that we have no evidence for this type of learning in the present data. The implication is that within the confines of their damaged motor system, chronic patients can still learn to control variability but find it more difficult to regain new movement patterns. Whether the latter would be possible in sub-acute stroke or with more extensive training is an important question.

Influence of movement speed during training on performance changes

A recent paper demonstrated that chronic stroke survivors demonstrated long standing improvements in movement velocity and movement smoothness after performing only two training sessions consisting of 600 fast reaching movements [5]. However, limited evidence is available about the importance of performing training at different movement speed in stroke rehabilitation[2, 14] nor are recommendations to incorporate different movement speeds during training included in clinical guidelines[21]. While it is difficult to compare accuracy improvements across different movement speeds directly, as the task difficulty is different between speeds[18], our data clearly shows that improvements for faster movement speeds cannot be effectively achieved by training at slow speeds. Fast training also resulted in a small improvement in clinical scores, which could indicate that performing fast movements is important for recovery after stroke. While our data suggest that fast movements speed improve slightly different aspects of motor control than training at slower speeds, we can only speculate about the underlying mechanisms. One possibility is that generation of larger agonist bursts necessary for fast movements led to more neuronal recruitment and therefore better improvements in functions[38, 40]. Alternatively, it could be that the increased necessity to account for interaction torques (for example by stabilizing the shoulder) led to better learning outcome[17].

We suggest that training regimes for the upper limb should include a proportion of training with an emphasis on increasing movement speed, thereby also counteracting the general slowing of movements after stroke[14]. Our data show that training at fast speed did not increase hypertonus. However, at the current training intensity we found that training benefits were too small to be clinically relevant and did not lead to a change in the flexor bias. This can possibly be attributed to the fact that the short training period was insufficient to alter longer standing movement patterns.

The impact of impairment on learning and vice-versa

It is well established that muscle weakness, sensory loss and increased muscle tone influence motor control after stroke[41, 42]. Less is known of the effect of these impairments on learning. In the present study, we found that sensory impairment reduced learning, consistent with previous studies[42-44]. In contrast, we found no effect of increased tone or weakness. It is possible that removal of visual feedback during movement increased reliance on somatosensory feedback. If so, other types of training, using continuous visual feedback, might be less affected by sensory impairment.

Limitations

As this was a pilot study, there was no calculation of the number of subjects performed a priori to ensure study power and therefore a definitive trial would be required to validate these findings.

We investigated training at different movement speeds and therefore adjusted task difficulty according to each individual's maximum movement speed. The target location and size remained constant for all individuals irrespective of their arm length or reaching distance. Therefore, task difficulty was slightly different depending on each individual's initial ability but as we only included individuals who could end their movement within the 5cm target, we believe that similar strategies were still required throughout our sample. Although arm dominance has been found to influence the performance of reaching in stroke survivors movements [45], this study was not designed or powered to explore these aspects of motor learning.

The training period in this trial was too brief to allow for clinically meaningful changes in outcome measures and the long-term retention of the altered behaviour in our study was not explored however, the small improvement in impairment are encouraging and might indicate the potential utility of more intensive training.

Conclusion

A greater understanding of recovery mechanisms is required in order to tailor individualised rehabilitation protocols[2]. [3, 4, 13]This repetitive training protocol improved performance in line with previous findings [1, 2], despite training not being varied [46]. Our results show that performance improvement can be achieved without the use of compensatory strategies[4, 7]. Chronic stroke survivors improve reaching accuracy most notably at the trained movement speed by a reduction in movement variability. However, movement bias was not significantly changed. We can therefore conclude that in chronic stroke, improvements to the quality of existing movements is possible, however the ability to learn new movements or muscle synergies may take longer periods of training or need to be achieved by alternative training strategies. Over the short training period, we did not observe clinically relevant group differences in clinical outcomes. However, these may emerge over longer training periods, and if so a variety of movement speeds should be included during training as accuracy improvements achieved after slow movement training do not generalise to fast movements.

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Figure legends

Figure 1. Reaching protocol. A) Experimental set-up. B-C) Experimental display during accuracy testing. Target (5cm radius) with centre cross, positioned at 20 cm distance. Hand position is displayed to participant as a green dot at the start (B) and at the end (C) but not during the reaching movement. D-E) Method of determining individual movement speed limits. D) Example data of movement times for 15 trials when attempting fast reaching. indicating) The 80th percentile is indicated by a dotted line (Fig.1E). Therefore the fast movement limit is less than 460ms (red) with incremental increase of 200ms for medium fast (460-660ms orange), medium slow (660-880 green) and slow (880-1600ms blue). F) Bullseye display of target during training days with points as feedback of endpoint accuracy.

Figure 2. Change in amount of endpoint error. A) The mean endpoint error (RMS ±SEM) for fast (red) and slow (blue) group reduced during the training days. B) The mean points (±SEM) per training block reduced for both training groups over the training days. C) RMS (±SEM) error at the four individually set target speeds before (unfilled) and after (filled) training for the fast and D) slow training group.

Figure 3. Endpoint variability and bias. **M**ean endpoint bias and variability (SD) in relationship to the target centre (0,0) at the four movement times (A slow, B medium slow, C medium fast, D fast) before (dashed) and after training (solid). The change in endpoint bias was not significant, however the reduction in endpoint variability was significant at all movement speed. Participants tended to undershoot and end movement in the contralateral workspace (flexor bias). Data of individuals with left hemiplegia are mirrored along the sagittal plane and data are presented as right arm movements for all participants.

Figure 4. Change in movement speed variability. Mean peak speed variability (±SEM) for the slow, medium slow, medium fast and fast movement speed before (unfilled) and after (filled) training for the A) fast (red) and B) slow (blue) training group. C) Mean change in movement speed variability at the 4 tested movement speed for the fast (red) and slow (blue) training group. A significant change in maximum speed variability was detected at the training speed for both groups as well as at the medium fast speed for the slow training group.

Figure 5. Effect of baseline ability and impairment on learning. A) Correlation of baseline RMS error with the post training performance on an individual basis for the fast (red) and

slow (bluet) training group. The performance floor of 0.928cm is depicted by a dotted line. B) Correlation of pre and post training measures of all individuals divided into groups of mild (grey) and moderate (black) sensory impairment, hypertonus and muscle weakness.

Figure 6. Functional outcome measures. A) Mean elbow flexor~~biceps~~ hypertonus (MAS) and B) Fugl-Meyer score for the fast (red) and slow (blue) training groups before (unfilled) and after (filled) training.