Reach Adaptation and Final Position Control Amid Environmental Uncertainty Following Stroke

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Abstract

We characterized how hemiparetic stroke survivors and neurologically intact individuals adapt reaching movements to compensate for unpredictable environmental perturbations. We tested the hypotheses that like unimpaired subjects, hemiparetic stroke survivors adapt using sensory information obtained during only the most recent movements and that the reliability of target acquisition decreases as the degree of sensorimotor impairment increases. Subjects held the handle of a 2-joint robotic arm which applied forces to the hand while reaching between targets in a horizontal plane. The robot simulated a dynamic environment which varied randomly in strength from one trial to the next. The trial sequence of perturbations had a non-zero mean value corresponding to information about the environment which subjects might learn. Stroke subjects were less effective at adapting reaches to the perturbations than control subjects. From a family of potential adaptation models, we found that the compensatory strategy patients used was the same as that used by neurologically-intact subjects. However, analysis of model coefficients found that the relative weighting of prior perturbations and prior movement errors on subsequent reach attempts was significantly depressed post-stroke. Regulation of final hand position was also impaired in the paretic limbs. Measures of trajectory adaptation and final position regulation deficits were significantly dependent on the integrity of limb proprioception and the amount of time post-stroke. But whereas model coefficients varied systematically with impairment level post-stroke, variability of final positioning in the contralesional limb did not. This difference suggests that these two aspects of limb control may be differentially impaired post-stroke.
Introduction

Upper limb hemiparesis is a frequent consequence of stroke which limits a survivor’s independence and quality of life (Vestling et al. 2003). Many reasons for reaching deficits in people with chronic hemiparesis have been proposed, including weakness (Chae et al. 2002), impaired limb sensation or joint proprioception (Mercier et al. 2004; Zackowski et al. 2004), disruption of spatial coordinate frameworks for reach planning (Rymer and Beer 2000), and deficits in the ability to isolate (individuate) and coordinate movement at the shoulder, elbow and wrist joints (McCrea et al. 2005; Zackowski et al. 2004). Of these, it has been suggested that the most important for reaching post-stroke are the ability to isolate movement at the shoulder, elbow and wrist joints (individuation) and the retention of intact sensation (Zackowski et al. 2004). Individuation is clearly necessary for moving the hand smoothly and directly between arbitrary locations within peripersonal space. But the role of intact limb sensation in reaching is less obvious since visual feedback suffices to inform spatial planning of movement, even in individuals entirely lacking limb proprioception (Gordon et al. 1995). Rather, proprioceptive estimates of limb state are needed to coordinate muscle torques across adjacent joints (Ghez et al. 1990; Sainburg et al. 1995; Sober and Sabes 2003), and they contribute importantly in compensating for performance errors via motor plan updating (i.e. motor adaptation; Scheidt et al. 2005).

Building on findings that some stroke survivors demonstrate improved movement patterns with training post-stroke (Winstein et al. 1999), recent experimental evidence suggests that residual motor adaptive capacity can be exploited to facilitate recovery of ‘normal’ movement kinematics by retraining the paretic arm in novel mechanical environments (Patton et al. 2006). However, the mechanisms underlying such improvements are not yet understood, and an impaired ability to anticipate changing environmental loads may be a key impediment to motor recovery in some individuals (Takahashi and Reinkensmeyer 2003). While recent studies have found that neurologically intact individuals compensate for novel mechanical environments using sensory information obtained during only the most recent movements (Scheidt et al. 2001; Thoroughman and Shadmehr 2000), it is not known
whether hemiparetic stroke patients use a similar strategy, and if so, whether the ability to adjust movements based on feedback of prior performance decreases as the degree of sensorimotor impairment increases.

Here we describe experiments using a planar robot to characterize how hemiparetic stroke survivors and neurologically-intact individuals adapt reaching movements to novel mechanical environments. Systems identification techniques previously developed to model motor adaptation in unimpaired subjects (Scheidt et al. 2001) characterized how sensory estimates of errors and loads experienced on recent trials contribute to motor command updating post-stroke. These techniques have the ability to distinguish performance deficits arising from changes in sensory information processing from those caused by biomechanical changes such as increased effective arm stiffness. We also examined the ability of subjects to coordinate shoulder and elbow motion at the end of reach in order to bring the hand to rest quickly and accurately at the target. We tested the hypothesis that like unimpaired subjects, hemiparetic stroke survivors compensate for novel mechanical environments during the reach using sensory information obtained during only the most recent movements. We also evaluated the secondary hypothesis that both the ability to adjust movements based on prior performance and the ability to terminate motion reliably at the desired target location decreases as the degree of sensorimotor impairment increases. Finally, we sought to evaluate how predictive trajectory control and final limb positioning might depend on experimental cofactors including integrity of limb proprioception, spasticity, patient age and the number of years since stroke. The results suggest that system identification techniques such as those described here may be helpful in identifying which patients would most likely benefit from adaptation-based rehabilitation therapies. Portions of this work have been presented in abstract form (Scheidt and Stoeckmann 2005).

Methods

12 unilateral, hemiparetic stroke survivors (SS) and 6 neurologically-intact (NI) control subjects gave informed consent to participate in this study in compliance with policies established by
Marquette University’s Office of Research Compliance and Northwestern University’s Office for Protection of Research Subjects. All SS were in the chronic stage of recovery, (at least 6 months post-stroke). These individuals, recruited from the pool of hemiparetic stroke outpatients of the Rehabilitation Institute of Chicago, all provided written consent allowing medical record review to identify the lesion site. Stroke survivors (SS) ranged in age from 38 to 75 years. Inclusion criteria for these subjects included that they were greater than 6 months post-stroke and that they possessed the ability to perform the desired reaching task. Exclusion criteria included: inability to give informed consent or follow 2-step directions, elbow strength less than 2- out of 5 ("poor minus") on the manual muscle testing scale, passive shoulder range of motion for flexion and abduction less than 90°, and/or shoulder pain in the test position of 75° to 90° abduction. The presence of contracture or shoulder subluxation did not exclude subjects from participating, unless it limited their ability to perform the task comfortably. NI control subjects, ranging in age from 35 to 58 years, were age-range matched to the stroke group. All subjects participated in a single experimental session lasting 2.5 to 3.0 hours (including assessment and setup time).

Immediately prior to experimental testing, the motor function for each stroke subject was assessed by the same licensed physical therapist while the subject was seated in an armless chair. Assessments included: 1) the upper extremity portion of the Fugl-Meyer (FM) Assessment of Physical Performance to assess motor control (Fugl-Meyer 1975), 2) the Modified Ashworth Scale (MAS) to assess spasticity at the shoulder, elbow and wrist, 3) goniometric assessment of active and passive range of motion at the shoulder, elbow and wrist joints, and 4) clinical evaluation of proprioception at the thumb, wrist, elbow and shoulder. In this last assessment, the subject was instructed to keep his/her eyes closed while the therapist randomly moved the tested joint “up” or “down”. When the joint stopped moving, the subject was to indicate joint position. Six repetitions were performed at each joint. If the response was brisk and accurate for every trial, proprioception was rated as “intact”. If the subject was unable to respond with any confidence, or if he/she made errors, proprioception was rated as “impaired”. To obtain an overall estimate of spasticity of the upper extremity, the modified
Ashworth scores were averaged across the joints tested (see also Zackowski et al. 2004). Subjects were assigned into four broad categories based on FM score: severely impaired (FM < 30; n=4), moderately-impaired (30 ≤ FM ≤ 50; n=4), mildly impaired (FM > 50; n=4) and unimpaired (NI) control subjects (n=6). One of the most severely impaired subjects was not able to complete the full protocol due to a claim of fatigue, and was therefore excluded from further analysis (see also Takahashi et al. 2006). Table 1 provides a description of subject characteristics for those individuals able to complete the experimental session. Upper extremity Fugl-Meyer scores for the included stroke survivors ranged from 13 to 58, reflecting a broad spectrum of motor impairment. Fugl-Meyer scores correlated weakly with spasticity score ($r^2 = 0.21$), although this relationship did not quite reach statistical significance ($p=0.074$). All subjects reported to have been right-hand dominant (pre-stroke for SS).

Insert Table 1 Here

Experimental Protocol

Subjects were seated in a high-backed chair and a chest harness was fastened around them to minimize trunk movement. For some stroke subjects, additional manual cues were provided to encourage limb (rather than trunk) motion during reaching. The arm was supported against gravity (between 75° and 90° abduction angle) using a light-weight, chair-mounted arm support. Direct view of the arm was occluded by an opaque screen mounted directly above the plane of hand motion. “Beginning” and “end” targets and a small cursor that tracked hand position at all times were projected onto the screen. Horizontal planar targets were separated by 15 cm and were aligned along a line in the parasagittal plane passing through the shoulder center of rotation. Thus, subjects reached the hand away from the body in the horizontal plane of the arm. Subjects were instructed to hold the handle of a two-joint robotic manipulator (Scheidt et al. 2001) and reach from the starting position to the target with a peak hand speed of 0.5 m/sec. After each reach, and during a delay period of 2.5 seconds, graphical feedback of hand speed indicated whether movement was too fast (> 0.6 m/sec),
too slow (< 0.4 m/sec) or just right. After this delay, the subject was instructed to relax as the robot moved the hand back to its initial location.

During the experimental session, subjects performed 300 reaches grouped into three blocks of trials for each arm, starting with the non-preferred limb (i.e. the contralesional arm for the stroke subjects and the non-dominant arm for the control subjects). This particular testing order was selected in order to minimize potential generalization of learning from the dominant to the non-dominant limb (Criscimagna-Hemminger et al., 2003). First, 50 movements were made with the robot handle moving freely (no perturbation) to allow subjects to learn the distance and timing of the task (baseline; BL). Subjects then made 200 movements in the presence of a velocity-dependent perturbation (a counter-clockwise, viscous curl force field; Figure 1A) whose magnitude varied pseudo-randomly from trial-to-trial (Figure 1B). These were the adaptation training trials (TRN). Finally, subjects performed an additional 50 trials without perturbation (washout; WO) in order to assess the persistence of the compensatory response acquired during training. Subjects could rest between trials as needed. These procedures were then repeated with the preferred limb.

Insert Figure 1 Here

During the adaptation block, the robot applied hand forces during the $i^{th}$ movement:

$$
\begin{bmatrix}
F_x \\
F_y
\end{bmatrix} = B_i \begin{bmatrix}
0 & -1 \\
1 & 0
\end{bmatrix} \begin{bmatrix}
\dot{x} \\
\dot{y}
\end{bmatrix}
$$

(1)

where $\dot{x}$ and $\dot{y}$ are the components of hand velocity along the medial/lateral ($x$) and proximal/distal ($y$) directions, $F_x$ and $F_y$ are the components of the force applied by the robot along the same directions. $B_i$ was a random real number between 0 and 30 (Ns/m) such that the amplitude of the perturbing force field varied randomly from trial to trial. Since subjects always moved along the positive y-direction, perturbing forces were always directed to the left. The magnitude of the environmental impedance $B_i$ remained constant for the duration of each movement and changed only between trials. Unbeknownst to the subjects, the distribution of perturbations had a non-zero mean
(15.2 Ns/m) corresponding to information about the perturbation sequence that they might learn (Figure 1C). By design, the sequence was constructed to insure insignificant correlation between perturbation magnitudes on consecutive trials. The significance of each correlation term was evaluated by comparing the correlation magnitude at each integer lag value to an estimate of the 95% confidence interval bounding zero correlation \(2\sigma \pm 2/\sqrt{N}\); Box et al. 1994). Each subject experienced the same perturbation sequence during adaptation training with both limbs.

\textit{Data analysis}

Instantaneous hand position was recorded at 150 samples per second using rotational encoders on the robot’s motors. Hand paths (Figure 1D) were low-pass filtered using a second order, zero-lag Butterworth filter with 20 Hz cutoff frequency prior to computing hand velocities (Figure 1E). We identified several kinematic features using an automated algorithm within the MATLAB programming environment (The Mathworks, Inc., Natick, MA). Each was verified visually and was manually adjusted if the algorithm erred. The hand’s starting point was defined as its x-y location 100 msec prior to movement onset (Figs. 1D and 1E; red). Movement onset was identified as the moment when the hand velocity first exceeded 0.1 m/sec at the beginning of a trial. The peak speed point included the hand’s x-y location and speed at the moment it reached its maximum speed (Figs. 1D and 1E; green). The hand’s penultimate position point was sampled at the moment its speed dropped (and remained) below 20% of its maximum value (Figs. 1D and 1E; blue). The hand’s final position point was defined as its x-y location 1.0 second after the penultimate position point was sampled (Figs. 1D and 1E; yellow).

We then derived a number of secondary measures to assess ability to initiate movement toward the target, to adapt reaches to the presence of biased (yet random) environmental perturbations, and to acquire the target quickly and accurately. The initial movement direction was calculated as the interior angle between two lines – one connecting the hand’s starting point and its peak speed point (which generally occurred within the first 300 msec of the reach) and the second connecting the
hand’s starting location and the final target (the desired movement vector). We defined Movement Error (ε) as the hand’s perpendicular deviation from the desired movement vector at the peak speed point (Cirstea et al. 2003; Winstein et al. 1999). This measure of motor performance assumes that subjects intended to make straight-line movements with each hand. Kinematic hand path errors have previously been found to motivate motor adaptation during reaching (Scheidt et al. 2001; see also Scheidt et al. 2000).

To visualize the influence of perturbations of various field strengths on reach kinematics, we aligned hand trajectories in time with respect to movement onset and computed three average trajectories for each limb: movements made in the 30 weakest fields (Fig. 1C, blue), the 30 strongest fields (Fig. 1C, red) and the middle 30 field strengths (Fig. 1C, purple). We evaluated whether subjects demonstrated adaptive responses by computing the difference dθ between the average initial direction errors made in the 30 weakest adaptation block trials and the average computed during the last 30 baseline trials for each limb. Training trial deviations to the right of baseline (positive dθ values) are consistent with the formation of a predictive compensatory response.

We used multiple regression analysis to characterize whether subjects use information about prior kinematic performance and an estimate of prior perturbation strength to update motor commands for subsequent reaches (Scheidt et al. 2001). Specifically, we analyzed how well trial-by-trial performance could be described by limited-memory, autoregressive models with external inputs (i.e. ARX models; Ljung 1999) having the form:

\[
\varepsilon_i = \sum_{j=1}^{i-L} a_j \varepsilon_{i-j} + \sum_{k=0}^{i-M} b_k B_{i-k}
\]

(2)

where the \(a_j\) and \(b_k\) coefficients reflect the relative influence of previous movement errors (\(\varepsilon_{i-j}\)) and perturbation magnitudes (\(B_{i-k}\)) on subsequent movement errors, respectively. Since the perturbations were uncorrelated from one trial to the next, trial-by-trial correlations observed in a subject’s motor performance could not originate from the perturbation sequence itself but rather from information processing within the neuromotor controller. The constants L and M correspond to the minimum
number of memory elements (for movement errors and perturbation magnitudes, respectively) needed to describe the evolution of trial-by-trial errors. The family of model structures described by equation 2 can represent autoregressive processes having very limited memory requirements (eg. when both L and M are small), as well as processes having more complex dynamics. Importantly, stroke-related changes in model structure and/or coefficient values would reflect an altered ability to use sensory information from prior movement attempts to update motor commands for subsequent reach attempts.

To select the most parsimonious model structure to use for subsequent identification, we first averaged movement error on a trial-by-trial basis across subjects for each of three limb types: neurologically intact, contralesional and ipsilesional. (A distinction between dominant and non-dominant limbs in neurologically-intact subjects is beyond the scope of the present study). Given that the trial-series of movement errors observed during each adaptation block may be considered a stochastic realization of a motor response to the perturbation sequence \( B \), averaging across subjects reduces the effect of inter-subject execution variability on the structure estimation procedure. For each of the average datasets, we then used the systems identification toolbox \( \text{ident} \) within the Matlab computing environment (The Mathworks, Inc., Natick, MA) to fit all model structures of moderate complexity (L and M less than or equal to 10) to the first half of the \{perturbation, error\} time series data, and evaluated their ability to predict the sequence of errors in the second half. We used the minimum descriptor length (MDL) criterion (Ljung 1999) to identify the structure most consistent with the information filtering manifest in the trial series of errors observed during adaptation. Of all models considered, the MDL model is the one that minimizes a modified mean-square-error (MSE) function \( MSE_{MDL} = MSE(1 + n \log(k)/k) \) where \( n \) is the total number of parameters in the model being considered (L+M) and \( k \) is the number of data points in the estimation data set. Thus, the MDL criterion offers an efficient compromise between model complexity and the quality of fit to the data.

After analyzing the data in this way, the best fitting structure in each case was found to be identical to the structure previously found to efficiently model motor adaptation during reaching in neurologically intact human subjects (Scheidt et al. 2001, see also Results, below):
\[ e_i = a_i e_{i-1} + b_0 B_i + b_1 B_{i-1}. \] (3)

While other structure selection techniques were also evaluated (e.g. Akaike’s Information Criterion, Ljung 1999), the best improvement in data variance accounted for over the MDL choice was 1.6%, at a cost of considerable model complexity (i.e. four additional memory terms: 2 each for perturbations and errors). Thus, only the most recent errors and perturbations influence the updating of motor commands on subsequent movement attempts.

Using this model structure, we sought to determine whether deficits in reaching following stroke might reflect an impaired ability to effectively utilize memories of prior errors and/or perturbation strengths to update motor commands. Parameter estimates (i.e. coefficients \( a_i \), \( b_0 \) and \( b_1 \)) for each limb of each subject were obtained by re-fitting the model to the individual subject adaptation block data. Importantly, model coefficient \( a_i \) estimates the relative influence of movement error in any given trial on the subsequent trial’s movement error. Coefficient \( b_0 \) estimates the limb’s effective mechanical compliance which varies from subject to subject due to factors such as differences in limb inertia and effectiveness of online feedback correction, etc. Consequently, we factored out these limb-dependent variations in effective limb compliance when computing the relative influence of the most recent perturbation on upcoming reach performance (i.e. the ratio \(-b_i/b_0\)).

We next evaluated the ability of subjects to bring the hand to rest quickly and accurately within the neighborhood of the target. Endpoint accuracy was assessed by computing the 95% confidence interval (CI) ellipse for the mean location of final hand positions (Oliveira et al. 1996; Johnson and Wichern 1998). Movements were considered accurate, on average, if the ellipse encompassed the target location. Endpoint precision was assessed by computing the area \( A \) of the 95% CI ellipse for the entire distribution of final positions for each limb (see Fig 7A). The inter-limb difference in precision (i.e the difference in ellipse areas \( \Delta = A_{\text{non-preferred}} - A_{\text{preferred}} \)) was then computed to compare final posture regulation across arms within subjects. Finally, we sorted the contralesional arm adaptation block trials based on perturbation strength and then computed separate precision ellipse areas for the
half with the strongest perturbations and the half with the weakest perturbations. This was done to assess whether muscular weakness might have influenced endpoint variability post-stroke.

**Statistical analysis**

Two main hypotheses were tested. First, we hypothesized that like unimpaired subjects, hemiparetic stroke survivors adapt to uncertain environments using sensory feedback obtained during the most recent reach attempts to update commands for subsequent reaches. Second, we hypothesized that the ability to adjust movements based on prior performance and the ability to terminate motion reliably at the desired target location decreases as the degree of sensorimotor impairment increases.

To check whether subjects had made similar movements with both limbs independent of impairment group membership, we analyzed average peak hand speed using a 2-way, repeated measures analysis of variance (ANOVA) with limb (preferred, non-preferred) as the within subject factor, and group (ni, mildly-, moderately-, or severely-impaired) as the between subjects factor. To assess whether each subject group had compensated for the environmental perturbations while reaching, we performed planned, one-sided, one-sample t-tests to determine whether $d\theta$ was significantly greater than zero for each limb within each subject group. To determine whether stroke subjects used memories of prior performances to update subsequent reaches (thereby compensating for perturbation), we performed one-sided, one-sample, Tukey t-tests to assess whether model coefficients $a_1$ and $b_1$ were significantly greater than zero for each subject group. We used separate Tukey paired t-tests to determine whether model coefficient $a_1$, $b_0$, and the ratio $-b_1/b_0$ were altered in the contralesional limb relative to the ipsilesional limb of stroke subjects and Tukey two-sample t-tests to compare between the contralesional limbs of stroke survivors and control limbs. Two-way, repeated measures ANOVAs were then used to evaluate whether model coefficients varied with limb (preferred, non-preferred) and/or impairment level. We used separate 1-way ANOVAs to assess whether integrity of limb proprioception influenced model coefficient $a_1$, and the ratio $-b_1/b_0$. Finally,
we used regression analyses to assess whether model coefficients varied systematically with experimental cofactors including spasticity, age and amount of time post-stroke.

To assess accuracy of hand positioning at the end of movement, we used 2-way, mixed model repeated measures ANOVA to evaluate whether the average distance between the hand’s final position and the target varied systematically across subject groups (ni, mildly-, moderately-, or severely-impaired) and between limbs (non-preferred and preferred). To determine whether weakness was a prime cause of increased endpoint variability in the contralesional limb, we used a paired t-test to compare variability ellipse areas between adaptation block trials with the strongest perturbations and trials with the weakest perturbations. To assess inter-limb differences in the precision with which subjects could bring the hand to rest within the neighborhood of the target, we analyzed the trial-by-trial variability in final positioning as quantified by $\Delta$. Because the distribution of $\Delta$ values was decidedly non-normal, we used a non-parametric Mann-Whitney two-sample rank test to assess whether this factor varied systematically between the stroke and neurologically intact subjects. A nonparametric Kruskal-Wallis test was used to assess whether $\Delta$ varied systematically across impairment level post-stroke (mild, moderate, or severe). A final Mann-Whitney test was performed to determine whether $\Delta$ varied systematically with the integrity of contralesional limb proprioception. Regression analyses were used to examine whether $\Delta$ varied systematically with experimental cofactors including spasticity, age or amount of time post-stroke. Regression analyses were also used to determine whether $\Delta$ varied systematically with either model coefficient $a_1$, or the ratio -$b_1/b_0$.

All statistical testing was carried out within the Minitab computing environment (Minitab, Inc., State College, PA). Effects were considered statistically significant at the $\alpha=0.05$ level.

Results

*Kinematic performance during baseline and perturbation training*
Given our restrictive inclusion criteria, it is not surprising that all subjects were able to acquire the target with both limbs by the end of the 2.5 second pause following each reaching movement (as shown in Figure 2 for a representative subject selected from each impairment level group). The initial phase of baseline movements was well-directed toward the target, with the deviation from the ideal straight line hand path averaging less that ±5° across limbs and subject groups (Fig 2; BL). While multiple peaks in hand speed profiles were observed most frequently in the impaired limbs of stroke subjects (eg. Fig. 1E), the first peak was consistently the largest. After acclimating to the task during baseline practice, mean peak hand speed for all groups and both limbs did not fall significantly outside the desired range (0.4 to 0.6 m/sec; p>0.237 in all eight cases). ANOVA found that mean peak hand speed did not vary by subject group (F(3,33)=1.80, p=0.197), but did vary by limb within the desired range of hand speeds (F(1,33)=7.74; p=0.017) with peak speed in the preferred limb (0.51 ±0.11 m/s) greater than that in the non-preferred limb (0.44 ±0.13 m/s). No interaction between group and limb was observed.

Not all subjects were able to adapt their reaching movements to the environmental perturbations. When training in the presence of viscous curl perturbations, movements made in the strongest fields were always deflected in the direction of the field (Fig 2, red traces). Performance in the weakest fields varied by subject group (Fig 2, blue traces; see also Fig 3). NI subjects consistently demonstrated clear evidence of compensation for the force fields since reaches against the weakest fields generated large errors in the direction opposite to the imposed forces (Fig 2, blue traces). These rightward deflections resulted in dθ values significantly greater than zero for both the preferred and non-preferred arms of NI subjects (p=0.013 and p=0.002, respectively; Fig. 3). Mildly- and moderately-impaired subjects overcompensated with their preferred, ipsilesional arms (mildly-impaired: p=0.034; moderately-impaired: p=0.001) whereas only the mildly-impaired subjects as a group did so with their non-preferred contralesional arm (p=0.026). The most severely-impaired subjects did not demonstrate rightward deflections of hand trajectory in the weakest fields with either...
arm (p>0.35 in both cases). Rather, two of the three severely-impaired subjects had negative $d_0$ values, providing no evidence for feedforward compensation in these subjects.

**Insert Figure 3 Here**

Although over-compensation provides evidence that some impaired subjects had adjusted their feed-forward motor commands to counter the effects of perturbation, it is possible that this compensation was simply due to aim adjustment at the beginning of training, rather than by trial-by-trial updating of reaching movements as demonstrated by neurologically intact subjects (Scheidt et al. 2001; Takahashi et al. 2001; Thoroughman and Shadmehr 2000). Consequently, we re-evaluated the ability of limited memory models of motor adaptation (Eqn 2) to predict trial-by-trial changes in hand path error observed during motor adaptation following stroke.

**Post-stroke preservation of adaptation model structure (but not coefficient values)**

For each of the three average responses considered (neurologically intact, ipsilesional arm, and contralesional arm), movement errors elicited by interaction with the robot were reasonably well-described as a linear function of perturbation magnitude (Fig 4A) and an exponential function of trial number (Fig 4B). We therefore used linear systems analysis techniques to characterize how subjects use information from prior performances to guide motor adaptation. Of all candidate models of moderate complexity having the form of Equation 2, the model of equation 3 was identified as the minimum descriptor length (MDL) structure of choice for each of the three average responses, with 92.5% data variance accounted for (VAF) in the neurologically intact response, 89.7% VAF in the ipsilesional arm response, and 78.8%, VAF in the contralesional arm response. Thus, equation 3 captures the average trial-by-trial changes in movement error at peak velocity regardless of whether subjects had had a stroke or not, and if they had, regardless of which arm was considered.

**Insert Figure 4 Here**
Parameter $a_1$ in equation 3 evaluates the extent to which memory of the most recent movement error influences performance on the subsequent reach attempt. 1-sample Tukey t-tests found that coefficient $a_1$ was significantly greater than zero for each group ($p<0.05$ in all cases), and thus all subject groups used memory of the most recent kinematic performance to guide updating of motor plans for subsequent movement attempts. However, coefficient $a_1$ varied systematically with arm type (neurologically intact, ipsilesional and contralesional; Fig. 4C). Tukey t-tests found that both the contralesional and ipsilesional coefficient values were significantly lower than intact limb values ($p=0.001$ and $p=0.018$, respectively), but not different from one another ($p=0.584$).

The ratio $-b_1/b_0$ evaluates the relative extent to which memory of the most recent perturbation influences performance on the subsequent reach (Fig. 4D). Here again, Tukey t-tests found that contralesional values were significantly less than both intact values ($p<0.001$) and ipsilesional values ($p=0.042$), which were themselves less than intact values ($p=0.016$).

Model parameter $b_0$ provides an estimate of the limb's effective mechanical compliance (i.e. the slope of the regression lines in Fig 4A). Tukey t-tests found that coefficient $b_0$ varied systematically with arm type (Fig. 4E) in that contralesional values were significantly lower than intact limb values ($p=0.040$). While this is perhaps to be expected since clinical assessments frequently find hemiparetic limbs to be stiffer than normal (i.e. less compliant), intentional stiffening of the limb via co-activation of agonist/antagonist muscles incurs excess energetic costs, especially in trials with small perturbations. Thus, compensation via limb stiffening is considered less efficient than a memory-based approach.

For the intact limbs, 78% of the average data variance could be explained using just the current perturbation, with 14.5% of the remaining data variance captured by the memory-dependent model terms. For ipsilesional limbs, 81% of the variance could be explained by the current perturbation whereas 8.7% of the remaining variance was captured by the memory-dependent terms. For the contralesional limbs, 75% of the variance could be explained by the current perturbation whereas only 3.8% of the remaining variance was captured by adding the two memory terms, consistent with the finding of reduced model coefficient values highlighted in Figures 4C and 4D above.
We then asked whether adaptation model coefficients vary with impairment level post-stroke. For model coefficient $a_1$, two-way ANOVA found main effects of subject group (ni, mildly-, moderately-, or severely-impaired; $F_{(3,33)}=7.72, p=0.003$) and limb (preferred, non-preferred; $F_{(1,33)}=7.12, p=0.019$). No interaction between group and limb was found. Post-hoc Tukey t-tests found that $a_1$ for the non-preferred limbs of severely- and moderately-impaired groups was significantly lower than for the mildly-impaired and intact subject groups ($p<0.025$ in each case), which did not differ one from the other (Fig 5A). No significant differences in $a_1$ were observed between groups using the preferred arm. The ratio $-b_1/b_0$ also varied both by group ($F_{(3,33)}=10.07, p=0.001$) and by limb ($F_{(1,33)}=7.63, p=0.016$; Fig. 5B). The interaction between these factors was also significant ($F_{(3,33)}=4.10, p=0.030$). Post-hoc Tukey t-tests found that $-b_1/b_0$ for the non-preferred limbs of severely-impaired subjects was significantly less than those for the other three groups ($p < 0.038$ in each case). The ratios for both the moderately- and mildly-impaired subject groups were significantly lower than those for the intact subjects ($p < 0.001$ and $p=0.001$, respectively), but did not differ from each other. No significant differences were observed between groups using the preferred arm ($p>0.209$ in all cases). Paired t-tests found that the difference in the ratios between preferred and non-preferred limbs reached statistical significance only for the most severely-impaired subjects ($p=0.050$). In contrast, ANOVA found no main effect of either group or limb on coefficient $b_0$ ($p=0.080$ and $p=0.138$, respectively) and no significant interaction effects.

Considering only the stroke subject results (i.e. excluding the NI subject data), regression analyses found no significant variation in contralesional limb model coefficients with either spasticity or age, ($p>0.37$ in all cases). Regression analyses found that only $-b_1/b_0$ varied systematically on the contralesional side with time post-stroke ($p=0.027$). This suggests that during the chronic stage of
recovery, the influence of prior perturbations on subsequent motor commands may be reduced progressively with time post-stroke.

**Practical consequence of altered sensorimotor adaptation**

Since the sequence of perturbations used in the current experiments had a non-zero mean, we regarded it as a ‘noisy step’ change in perturbation strength which subjects could adapt to. We therefore simulated the responses to deterministic steps to show more clearly how steady-state error can change depending on particular coefficient values. As shown in Figure 5C, the model's coefficients predict adaptation as well as variable degrees of error reduction (or increases) in response to a step change in perturbation strength. Here, we predict time series of movement errors for the case where no adaptive compensation is applied (i.e. when $a_1=b_1=0$, in which case the simulated error would equal -1.0; gray trace) as well as using coefficient values from the non-preferred limb of one subject selected from each group (see Table 2). The selected subjects highlight typical performance for each group, except for the severely-impaired subject who was selected to illustrate how improperly-tuned adaptation can result in poorer performance than if previous perturbations and errors had been ignored entirely. The adaptive strategy used by the intact subject is clearly better able to reduce steady-state errors than that of the three stroke subjects, with steady-state errors for the most severely-impaired subject predicted to increase over the simulation without adaptation. Similar results were obtained from simulations driven by the actual perturbation sequence used in this study (two examples of which are shown in Figure 5D). Here, the average error in the last 100 trials was predicted to be greater in magnitude for the severely-impaired limb (dark solid line) than the neurologically intact limb (thin solid line). This was consistent with the actual observed performance (dashed lines), with steady-state errors of -0.2 cm and -0.7 cm for the neurologically-intact and severely-impaired subjects, respectively. Models derived from the other stroke-impaired limbs also demonstrated increases in steady-state error above and beyond those predicted for the neurologically intact limb.
Influence of proprioceptive integrity on post-stroke adaptation

ANOVA found that coefficient $a_1$ in non-preferred limbs varied systematically with the integrity of limb proprioception ($F_{(1,15)}=6.94$, $p=0.019$; Fig. 6A), as did the ratio $-b_1/b_0$ ($F_{(1,15)}=9.60$, $p=0.007$; Fig. 6B). In both cases, the values were depressed when proprioception was impaired. In the preferred limb, ANOVA also found a main effect of proprioception on both coefficient $a_1$ ($F_{(1,15)}=8.06$, $p=0.012$) and the ratio $-b_1/b_0$ ($F_{(1,15)}=7.00$, $p=0.018$), suggesting that control deficits arising from impaired proprioception may not be limited to the contralesional limb post-stroke. Finally, we reanalyzed the model coefficients using two-way ANOVA after excluding subjects with known proprioceptive deficits and found coefficient dependencies on impairment level (but not limb) similar to those described in the paragraphs above. This suggests that proprioceptive integrity, as measured clinically, does not suffice to explain all of the variability in adaptation model coefficients across impairment levels.

Precision, but not accuracy of final limb position regulation is degraded post-stroke

We next evaluated each subject’s ability to terminate movement quickly and accurately within the neighborhood of the target. As shown for a representative subject from each impairment group, final hand positions were approximately centered about the target location, even for the most severely-impaired subjects (Figure 7A). Across many trials, all subject groups were equally accurate with both limbs. One-sample t-tests found that endpoint centroids did not fall significantly outside of the target region ($p>0.574$ in all cases). ANOVA found that the average distance between the hand’s final position and the target did not vary across subject groups ($F_{(3,33)}=2.16$, $p=0.142$) or between limbs ($F_{(1,33)}=2.51$, $p=0.133$). In contrast, the spatial variability of final hand position clearly depended both on subject group and limb (Fig. 7A). Whereas the 95% confidence interval areas provide no
compelling evidence for limb-specific differences in final position variability in intact subjects (paired t-test: \(p=0.103\)), the CI areas for contralesional arms were greater than those for ipsilesional arms in all but one stroke subject (SS7). Paired t-test found no significant difference between 95% CI areas calculated separately for the strongest and weakest trials in the contralesional arm \(p=0.104\), providing no support for the idea that muscle weakness was a prime cause of increased endpoint variability post-stroke.

**Insert Figure 7 Here**

When the ellipse areas for the ipsilesional arm were plotted against those for the contralesional arm, the vast majority of stroke subjects lay above the line of unit slope (Fig 7B), having positive \(\Delta\) values. A Mann-Whitney two-sample rank test found that \(\Delta\) was significantly greater for stroke subjects than for neurologically intact subjects \(p=0.002\). However, upon excluding the neurologically-intact subjects from the analysis, a Kruskal-Wallis test found no systematic variation between \(\Delta\) and the three impairment level groups \(p=0.181\), suggesting that final position variability is uniformly elevated in the contralesional limb as compared to the ipsilesional limb post-stroke. A final rank sum test found that stroke subjects with impaired proprioception had greater spatial variability on the involved side than did stroke subjects with intact proprioception \(p=0.010\). Thus, some of the variation in final position regulation across subjects likely resulted from variations in the integrity of limb proprioception. Regression analyses found no significant variation in \(\Delta\) with spasticity or age \(p>0.32\) in each case), although there was a significant negative correlation with time post-stroke \(p=0.042\). This suggests that within subjects, final position regulation may equalize progressively with time across limbs during the chronic stage of stroke recovery.

**Comparison of trajectory adaptation and final position regulation**

To evaluate whether there might exist a common factor contributing to the observed deficits in trajectory adaptation and final position regulation, we plotted the inter-limb difference in confidence
interval ellipse areas ($\Delta$) against adaptation model coefficients $a_i$ (Fig 8A) and $-b_i/b_0$ (Fig 8B).

Separate regressions of $\Delta$ on $a_i$ and $b_i/b_0$ found significant correlation between these performance measures ($r^2 = 0.37$, $p=0.009$ and $r^2 = 0.47$, $p=0.002$ respectively; solid lines). Subjects with impaired proprioception usually had small $a_i$ and $-b_i/b_0$ values as well as large $\Delta$ values, suggesting that this factor contributes importantly to deficits in both trajectory adaptation and final position regulation. But even after excluding those subjects with obvious proprioceptive deficits, there remains a small, but significant correlation between impaired final position regulation and impaired adaptation ($\Delta$ vs. $a_i$: $r^2 = 0.37$, $p=0.027$; $\Delta$ vs. $-b_i/b_0$: $r^2 = 0.55$, $p=0.004$; dashed lines).

Insert Figure 8 Here

**Discussion and Conclusions**

We compared how hemiparetic stroke survivors and neurologically-intact individuals adjust reaching movements to compensate for unpredictable environmental dynamics. We used systems identification techniques to analyze trial-by-trial changes in hand trajectory, finding that the adaptive strategy used by stroke survivors is similar in form to that used by neurologically intact individuals.

We characterized the extent to which memories of prior perturbations and prior movement errors influenced subsequent reach attempts by fitting a linear model of motor adaptation to the behavioral data. Model coefficients values varied strongly with impairment severity, most notably in the contralesional arm, consistent with our original hypothesis. In contrast, final position accuracy was not degraded in either limb post-stroke, although final position variability was uniformly elevated in the contralesional arms as compared to both ipsilesional arms and arms of neurologically intact subjects.

This increase in final position variability was independent of impairment level. Whereas measures of trajectory adaptation and final position variability were both dependent on the integrity of limb proprioception and the amount of time post-stroke (but not spasticity or age), differences in the
sensitivity of trajectory adaptation and final limb positioning to impairment level suggest that these two aspects of limb control may be differentially impaired post-stroke.

Proprioceptive contributions to movement planning, reach adaptation and final position regulation

The relative importance of proprioception in movement planning appears to depend on whether the limb position feedback is to be used to specify kinematic or dynamic aspects of the movement: Whereas limb state estimates for computing intended movement direction and extent rely almost exclusively on visual feedback (Sober and Sabes 2003), computations of the muscle forces and/or joint torques needed to execute the desired reach relies mostly on proprioceptive feedback (Sober and Sabes 2003). Feedback from muscle and joint proprioceptors also contributes importantly to the evaluation of limb position during movement for the conditional execution of movement sequences (Cordo 1994; Verscheuren 1999). Here we have shown that when arm proprioception is impaired post-stroke, prior trajectory errors have less impact on upcoming movements than in subjects with ostensibly intact proprioception (Fig 5, left). It seems unlikely that planning errors, caused by misestimating initial limb position, can explain this observation since all of the subjects were able to direct initial hand movements to the target with both arms during baseline practice and since erroneous initial limb position estimates would have given rise to systematic errors in reach direction (Scheidt et al. 2005). Rather, our findings suggest that in addition to its other roles, proprioception contributes importantly to the estimation of kinematic performance during movement for subsequent updating (adaptation) of motor commands.

The trial-by-trial variability of final hand position for the contralesional arm was much greater than that for the ipsilesional arm. Poor final position regulation could arise from at least four neuromuscular deficiencies. First, rapid goal-directed movements, such as those performed in the current study, normally elicit balanced cocontractions of opposing muscles at the shoulder and elbow joints in order to stabilize the hand at its desired final location (Gribble and Ostry 1998). Because muscles are viscoelastic actuators, errors in either scaling or balancing coactivation of opposing muscles would
degrade the ability to acquire a properly-specified final limb configuration (cf. Scheidt and Ghez 2006). Indeed, abnormal coupling between agonists and antagonists within the paretic limb are a common observation post-stroke (Beer et al. 1999; Dewald et al. 1995; Reinkensmeyer et al. 1999), and might have contributed here as well. Alternatively, central specification of the desired limb configuration could itself be impaired, thus leading to improperly targeted reaches. This deficit could arise from a distortion of the spatial representation of target location used for final position planning (cf. Rymer and Beer 2000). This alternative is unlikely here since the average movement accuracy at the end of the initial reach was not measurably impaired post-stroke. Third, weakness (Chae et al. 2002) or activation deficits (McCrea et al. 2005) in the muscles of the contralesional arm might have caused subjects to exert greater effort with that limb than with the ipsilesional arm. If there normally is a causal link between increased effort and increased motor output variability as suggested (Jones et al. 2002), then increased variability of final position might simply have been the consequence of contralesional arm neuromuscular deficits. This alternative too is unlikely, since a comparison of movement variability from trials performed with the strongest and weakest perturbations found no significant difference between them. Finally, increased noise either in sensory pathways or in the execution of desired motor commands could give rise to suboptimal weighting of the visual and proprioceptive feedback used to estimate limb state at the end of movement (Beers et al. 1996; 1999; Smeets et al. 2005; see also Speers RA 2002) thereby leading to positioning errors. Indeed, variability was greatest for subjects with impaired proprioception. While the current results can not resolve the question of why final position variability increased so dramatically in the contralesional limb, we anticipate that future experiments analyzing inter-limb differences in agonist/antagonist muscle coactivity at the end of reaching may be able to resolve this question.

While nearly all stroke subjects studied here demonstrated impaired final position regulation with the contralesional limb, evidence for impaired trajectory adaptation with that limb was harder to demonstrate for the less-impaired stroke survivors. Increased effective stiffness of the contralesional limbs of stroke survivors evidently reduced hand deflections caused by transient perturbations during movement (Fig 4A). In spite of this, these limbs demonstrated elevated hand position variability at the
end of movement (i.e. when feedback mechanisms presumably regulate limb position about the desired posture; see Fig 7). This raised the question of whether deficits in trajectory adaptation and deficits in final position regulation might be the result of distinct pathologies. The idea that limb movement and position control may be controlled by separate neural systems is supported by recent single unit recording data in primates (Kurtzer et al. 2005) as well as by recent psychophysical evidence in neurologically intact human subjects (Bagesteiro and Sainburg 2003; Dizio and Lackner 1995; Scheidt and Ghez 2006; 2004) Separation of posture and movement control function is also suggested by the different time frames over which trajectory adaptation and limb posture regulation eliminate performance errors; whereas adaptation is considered a feedforward process with motor command updating occurring from one trial to the next, final limb position regulation requires cancellation of errors on a moment-by-moment basis (Scheidt and Ghez, 2004; Suminski et al., 2006).

To explore this issue, we used regression analyses to determine the extent to which deficits in final position regulation co-vary with reduction in model coefficient values (Fig 8). Much of the negative correlation between final position and trajectory variables was due to the unusual values presented by subjects with demonstrably impaired proprioception: Subjects with impaired proprioception who demonstrated greater final hand position variability also tended to demonstrate a decreased ability to use sensory information from prior movements to update motor commands on subsequent reach attempts. Decreased contribution of prior performance errors to motor command updating post-stroke might simply reflect a natural adjustment in sensorimotor memory weighting, driven by increased uncertainty in limb trajectory estimates that result from deficits in proprioceptive sensory information processing. But even after removing these subjects from the analysis, there remained a small but significant negative correlation. This may have been the result of an inability of our clinical assessment of proprioceptive integrity to detect mild proprioceptive impairment in some subjects. Future studies wishing to differentiate impairments of trajectory formation from those of final limb positioning will require more rigorous and quantitative assessment of residual proprioceptive capacity in order to minimize potential confounds introduced by possibly undetected deficits in limb position sense.
Clinical implications

Consistent with previous reports that motor learning is preserved after stroke (Winstein et al. 1999), we found that a limited-memory strategy of motor adaptation is largely preserved in all but the most severely-impaired individuals. Our results confirm and extend a previous report finding that many stroke survivors demonstrate reduced ability to form and/or implement internal models for controlling the contralesional arm during reaching (Takahashi and Reinkensmeyer 2003). Indeed, the systems identification techniques described above appear capable of identifying stroke survivors who retain residual adaptive capacity in the paretic limb, and may also have potential to track improvements in adaptive capacity with recovery. The sensitivity and specificity of these techniques should be explored in a longitudinal study in order to ascertain whether they could be used to identify stroke survivors who might best benefit from additional sensorimotor therapies intended to retrain trajectory formation and final position control with the involved limb. For example, a recent review of treatment interventions for the paretic upper limb of stroke survivors concludes that sensorimotor training can enhance recovery, with positive effects being maintained up to 12 months after discharge from treatment (Barreca and et 2003). We know that practice and exposure alone are not enough (Carey 2005). Rather, positive training effects and transfer can be obtained only when the practiced tasks have a high degree of specificity to the desired outcome, there is variation in training stimuli, and feedback is provided intermittently. These key components could easily be integrated into a robotic treatment program. As suggested previously by others (Emken and Reinkensmeyer 2005; Wei et al. 2005), it may even be beneficial to manipulate sensory feedback during training such that motor adaptation to novel environmental dynamics is accelerated. In this way, it might be possible to promote improved motor function beyond the trained reaching movements, thereby improving the stroke survivor’s ability to contend with the unpredictable environmental dynamics that frequently occur during activities of daily living.
Acknowledgements

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<th>spasticity</th>
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\(^1\) i = ischemic; h = hemorrhagic

\(^2\) R=right; L=left; MCA = middle cerebral artery; ACA = anterior cerebral artery; BG = basal ganglia

\(^3\) prop = integrity of proprioceptive sense in the contralesional arm

\(^4\) FM= Fugl-Meyer score; upper extremity portion

\(^5\) This subject had a left visual field deficit which did not interfere with his ability to perform the required task. We were unable to obtain medical records for this subject and were thus unable to verify lesion location.
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Bolded entries indicate subjects for whom responses were simulated in Figure 4D.
**FIGURE LEGENDS**

**Figure 1:** Description of the environmental perturbations and identification of kinematic performance features. A) Viscous curl force field perturbation applied to the subject’s hand during reaching. The hand force was directed perpendicular to the instantaneous hand speed, with a magnitude proportional to that speed. B) Sequence of gains used to scale perturbation of panel A on a trial-by-trial basis. C) Distribution of perturbation gains in panel B. Shading indicates those trials used in subsequent analyses to compute average performance in the weakest (blue), strongest (red) and average (purple) force field perturbations. D) Sample hand path with the locations indicated for starting point (red), peak velocity point (green), penultimate position point (blue) and final position point (yellow). E) Sample hand speed profile with vertical markers indicating the time of kinematic fiducial points indicated for panel D. The horizontal dashed line indicates the threshold value (0.1 m/sec) used to identify movement onset.

**Figure 2:** Average hand trajectories for the non-preferred and preferred limbs (left and right panels, respectively) for representative subjects from the neurologically intact (NI), mildly-impaired, moderately-impaired, and severely-impaired subject groups. Within each panel, the left-most trace displays the average hand paths during baseline (BL) training without perturbation. The middle traces display average trajectories from those training block movements in the weakest (blue), strongest (red) and average fields (purple). Shading represents 95% confidence intervals about the mean trajectory. The right-most trace displays the average hand paths obtained during the last 30 null-field trials after training. Scale bars indicate 5 cm displacements in both the x (lateral) and y (forward) directions.

**Figure 3:** Average difference $d\theta$ between the initial direction errors observed in the weakest force field trials compared to those observed during baseline practice for the non-preferred and preferred limbs (left and right bar clusters, respectively). Deflections in the direction opposed to the imposed perturbations (consistent with overcompensation in the weakest force field trials) are indicated by
positive dθ values. Asterisks indicate those limbs and subject groups demonstrating significant overcompensation (p<0.05), consistent with adaptation to the approximate mean of the perturbation sequence. Error bars indicate ±1 standard deviation.

**Figure 4:** Analysis of memory-based motor adaptation model coefficients during reaching as a function of limb type (neurologically intact, ipsilesional, and contralesional). A) Regression analysis demonstrating that the imposed perturbations were reasonably effective in eliciting proportional errors in hand trajectories. Solid lines indicate separate regressions for the average responses from neurologically intact limbs (black, 78% VAF), ipsilesional limbs (blue, 81% VAF), and contralesional limbs (red, 75%). B) Time series plot and best-fit exponential model of average responses from neurologically intact limbs (black), ipsilesional limbs (blue), and contralesional limbs (red). An adaptive reduction in error was observed in each average response. C) Coefficient analysis for adaptation model term a1. D) Coefficient analysis for the ratio -b1/b0. E) Coefficient analysis for adaptation model term b0.

**Figure 5:** Analysis of adaptation model coefficients as a function of impairment level (neurologically intact, mildly-, moderately-, and severely-impaired) and limb (non-preferred and preferred). A) Coefficient analysis for adaptation model term a1. B) Coefficient analysis for the ratio -b1/b0. C) Simulations demonstrating the varying effectiveness of selected models to a hypothetical step change in perturbation strength. Prior to simulation, and to facilitate direct comparison of responses across subjects, we normalized b0 to -1.0 in each case, and then re-computed the b1 coefficients ensuring that the ratio -b1/b0 remained unchanged. For the simulated intact subject, the perturbation causes an initial increase in error which is reduced greatly within 3 to 5 trials. Simulated subjects from the mildly- and moderately-impaired groups show some reduction in error, but much less than the intact subject. The simulated subject from the severely-impaired group predicts adaptive performance that is worse than if the subject had not employed a memory-based adaptation strategy (the grey trace labeled NONE). D) Steady-state errors were also predicted in response to random perturbations. Here we show simulated responses of a neurologically-intact (light thin line) and severely-impaired (dark thick
limb to the random perturbation sequence used experimentally. Only the second half of the experiment was simulated so that the model responses could be compared directly to the steady-state errors actually observed in these limbs (horizontal dashed lines).

**Figure 6:** Analysis of adaptation model coefficients as a function of non-preferred limb proprioceptive status (intact or impaired). A) Coefficient analysis for adaptation model term $a_1$. B) Coefficient analysis for the ratio $-b_1/b_0$.

**Figure 7:** Final hand position analysis. A) Final hand position plots for the non-preferred (left panel) and preferred limbs (right panel) from representative subjects from each group relative to the target position (red square). Yellow ellipses indicate the 95% confidence boundaries of the distribution of final positions. Bars provide 2.5 cm scales in both the x and y directions. B) Comparison of the 95% confidence ellipse areas for the preferred and non-preferred arms for each subject. Points laying along the dashed grey line have of unit slope would have equal variability across limbs. All NI subjects fell below the line whereas all but one (moderately impaired) stroke survivor fell above the line. The different symbols indicate impairment group membership. Subjects whose proprioceptive sense was measured to be impaired are indicated by the encircled symbols. Note the unequal scaling of the abscissa and ordinate.

**Figure 8:** Comparison final position regulation (the inter-limb difference in confidence interval ellipse areas $\Delta$) against measures of trajectory adaptation in the non-preferred arm (adaptation model coefficient $a_1$, panel A and the ratio $-b_1/b_0$, panel B). In both panels, the solid line is the least-squares linear regression of $\Delta$ onto the model parameters, including the data from all subjects. The dashed line is the regression of $\Delta$ onto the model parameters, after excluding those subjects with obviously-impaired proprioception. Symbols indicate impairment group membership. Subjects whose proprioceptive sense was measured to be impaired are indicated by the encircled symbols.
References


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Figure 1: Description of the environmental perturbations and identification of kinematic performance features. A) Viscous curl force field perturbation applied to the subject’s hand during reaching. The hand force was directed perpendicular to the instantaneous hand speed, with a magnitude proportional to that speed. B) Sequence of gains used to scale perturbation of panel A on a trial-by-trial basis. C) Distribution of perturbation gains in panel B. Shading indicates those trials used in subsequent analyses to compute average performance in the weakest (blue), strongest (red) and average (purple) force field perturbations. D) Sample hand path with the locations indicated for starting point (red), peak velocity point (green), penultimate position point (blue) and final position point (yellow). E) Sample hand speed profile with vertical markers indicating the time of kinematic fiducial points indicated for panel D. The horizontal dashed line indicates the threshold value (0.1 m/sec) used to identify movement onset.
Figure 2: Average hand trajectories for the non-preferred and preferred limbs (left and right panels, respectively) for representative subjects from the neurologically intact (NI), mildly-impaired, moderately-impaired, and severely-impaired subject groups. Within each panel, the left-most trace displays the average hand paths during baseline (BL) training without perturbation. The middle traces display average trajectories from those training block movements in the weakest (blue), strongest (red) and average fields (purple). Shading represents 95% confidence intervals about the mean trajectory. The right-most trace displays the average hand paths obtained during the last 30 null-field trials after training. Scale bars indicate 5 cm displacements in both the x (lateral) and y (forward) directions.
Figure 3: Average difference $d\theta$ between the initial direction errors observed in the weakest force field trials compared to those observed during baseline practice for the non-preferred and preferred limbs (left and right bar clusters, respectively). Deflections in the direction opposed to the imposed perturbations (consistent with overcompensation in the weakest force field trials) are indicated by positive $d\theta$ values. Asterisks indicate those limbs and subject groups demonstrating significant over-compensation ($p<0.05$), consistent with adaptation to the approximate mean of the perturbation sequence. Error bars indicate ±1 standard deviation.
Figure 4: Analysis of memory-based motor adaptation model coefficients during reaching as a function of limb type (neurologically intact, ipsilesional, and contralesional). A) Regression analysis demonstrating that the imposed perturbations were reasonably effective in eliciting proportional errors in hand trajectories. Solid lines indicate separate regressions for the average responses from neurologically intact limbs (black, 78% VAF), ipsilesional limbs (blue, 81% VAF), and contralesional limbs (red, 75%). B) Time series plot and best-fit exponential model of average responses from neurologically intact limbs (black), ipsilesional limbs (blue), and contralesional limbs (red). An adaptive reduction in error was observed in each average response. C) Coefficient analysis for adaptation model term $a_1$. D) Coefficient analysis for the ratio $-b_1/b_0$. E) Coefficient analysis for adaptation model term $b_0$. 
Figure 5: Analysis of adaptation model coefficients as a function of impairment level (neurologically intact, mildly-, moderately-, and severely-impaired) and limb (non-preferred and preferred). A) Coefficient analysis for adaptation model term $a_1$. B) Coefficient analysis for the ratio $-b_1/b_0$. C) Simulations demonstrating the varying effectiveness of selected models to a hypothetical step change in perturbation strength. Prior to simulation, and to facilitate direct comparison of responses across subjects, we normalized $b_0$ to -1.0 in each case, and then re-computed the $b_1$ coefficients ensuring that the ratio $-b_1/b_0$, which remained unchanged. For the simulated intact subject, the perturbation causes an initial increase in error which is reduced greatly within 3 to 5 trials. Simulated subjects from the mildly- and moderately-impaired groups show some reduction in error, but much less than the intact subject. The simulated subject from the severely-impaired group predicts adaptive performance that is worse than if the subject had not employed a memory-based adaptation strategy (the grey trace labeled NONE). D) Steady-state errors were also predicted in response to random perturbations. Here we show simulated responses of a neurologically-intact (light thin line) and severely-impaired (dark thick line) limb to the random perturbation sequence used experimentally. Only the second half of the experiment was simulated so that the model responses could be compared directly to the steady-state errors actually observed in these limbs (horizontal dashed lines).
Figure 6: Analysis of adaptation model coefficients as a function of non-preferred limb proprioceptive status (intact or impaired). A) Coefficient analysis for adaptation model term $a_1$. B) Coefficient analysis for the ratio $-b_1/b_0$. 
Figure 7: Final hand position analysis. 

A) Final hand position plots for the non-preferred (left panel) and preferred limbs (right panel) from representative subjects from each group relative to the final target position (red square). Yellow ellipses indicate the 95% confidence boundaries of the distribution of final positions. Bars provide 2.5 cm scales in both the x and y directions.

B) Comparison of the 95% confidence ellipse areas for the preferred and non-preferred arms for each subject. Points laying along the dashed grey line have of unit slope would have equal variability across limbs. All NI subjects fell below the line whereas all but one (moderately impaired) stroke survivor fell above the line. The different symbols indicate impairment group membership. Subjects whose proprioceptive sense was measured to be impaired are indicated by the encircled symbols. Note the unequal scaling of the abscissa and ordinate.
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