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Motor skill learning is associated with diffusion characteristics of white matter in individuals with chronic stroke

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Abstract

Background and Purpose—Imaging advances allow investigation of white matter following stroke; a growing body of literature has shown links between diffusion-based measures of white matter microstructure and motor function. However, the relationship between these measures and motor skill learning has not been considered in individuals with stroke. The aim of this study was to investigate the relationships between post-training white matter microstructural status, as indexed by diffusion tensor imaging (DTI) within the ipsilesional posterior limb of the internal capsule (PLIC) and learning of a novel motor task in individuals with chronic stroke.

Methods—Thirteen participants with chronic stroke and nine healthy controls practiced a visuomotor pursuit task across five sessions. Change in motor behavior associated with learning was indexed by comparing baseline performance with a delayed retention test. Fractional anisotropy (FA) indexed at the retention test was the primary DTI-derived outcome measure.

Results—In individuals with chronic stroke, we discovered an association between post-training ipsilesional PLIC FA and the magnitude of change associated with motor learning; hierarchical multiple linear regression analyses revealed that the combination of age, time post stroke and ipsilesional PLIC FA post-training was associated with motor learning related change ($R^2=0.649$, $p=0.02$). Baseline motor performance was not related to post-training ipsilesional PLIC FA.

Discussion and Conclusions—Diffusion characteristics of post-training ipsilesional PLIC were linked to magnitude of change in skilled motor behavior. These results imply that the microstructural properties of regional white matter indexed by diffusion behavior may be an important factor to consider when determining potential response to rehabilitation in persons with stroke. **Video Abstract available** (See Video, Supplemental Digital Content 1.) for more insights from the authors.

Keywords

Motor behavior; Diffusion tensor imaging; Cerebrovascular accident; Posterior limb of the internal capsule; Rehabilitation

Background

Past work robustly demonstrates that the learning of new motor skills is not abolished by stroke.^{1–3} However, the magnitude of motor learning related change associated with a fixed amount of practice is highly variable across individuals with stroke, making it difficult to predict response to treatment and potential for recovery. In part, the degree of change that may occur in response to skilled motor practice depends on stroke severity. Boyd et al³ demonstrated lower slopes of change in individuals with moderate to severe stroke as compared to those with more mild damage. However, this work examined motor learning when individuals employed their less-affected, non-hemiparetic arm and did not examine the relationship between residual white matter status and learning-related change.

Consideration of how residual brain tissue microstructure impacts motor learning related change is key in advancing the understanding of which individuals with stroke may benefit from certain forms of rehabilitation aimed at restoration of motor function. A large body of work highlights the relationship between motor learning and changes in gray matter; developments in imaging technology now allow us to examine the relationship between white matter and learning. Diffusion tensor imaging (DTI) can provide a noninvasive characterization of white matter tissue status in both healthy individuals and individuals after stroke.⁴ Specifically, DTI-derived metrics (e.g. fractional anisotropy (FA)) can be used to determine the magnitude and direction of water diffusion, which are influenced by the microstructural properties of brain tissue.⁵ In particular, FA is the most commonly reported DTI-derived measure of white matter integrity and has been associated with function in neurologically intact individuals and persons with neurologic injury.^{6–8}

Past work examined white matter integrity in relation to training across different modalities. More specifically, training to improve knowledge of grammar rules, spelling, memory, or speech therapy in individuals with aphasia have all been linked to higher integrity (i.e., FA) of white matter in the tracts corresponding with cortical areas supporting these behaviors.^{9–12} However, limited work has linked motor training with change in diffusion behavior (i.e., increased FA) in regional white matter in healthy individuals. Past work has not considered whether DTI is sensitive to change in white matter microstructure associated with experience-dependent neuroplasticity in individuals with stroke or in older healthy adults. The few studies using DTI that show increased FA after training have employed very large doses of practice and been conducted in young healthy individuals. For example, after six weeks practicing juggling, healthy individuals demonstrate increased FA values in the right posterior intraparietalsulcus.¹³ Interestingly, these increases in FA values were not related to performance improvements, suggesting that the training time, rather than performance outcome is a key component to influencing white matter plasticity.¹³

A growing body of literature has examined white matter integrity using single time point diffusion scans in stroke populations. Hemispheric asymmetry of FA values within the posterior limb of the internal capsule (PLIC) and the corticospinal tract have been shown to predict change in Fugl-Meyer score following increased use of the hemiparetic arm to move a series of wooden blocks.¹⁴ Further, the degree of impairment in function of the upper limb is closely linked to FA values in the PLIC, even more so than the blood-oxygen-level-dependent signal in motor regions during training.¹⁵ The contralesional and ipsilesional corticospinal tracts have also been linked to motor function on measures such as grip strength, hand dexterity, pegboard, and index finger tapping.^{16,17} Similar trends have been shown with a varying array of functional measures and the corresponding white matter tracts.^{18,19} Short-term practice effects also appear to be related to baseline FA values in the PLIC bilaterally.²⁰ However, it remains unclear if long-term practice effects are also mediated by white matter status in individuals with chronic stroke.

The purpose of the current study was to evaluate how post-training white matter status is linked to the magnitude of motor skill learning in individuals with chronic stroke. We hypothesized that ipsilesional white matter microstructural status at retention testing would be linked to motor learning related change such that higher ipsilesional FA values would be associated with larger change in motor performance after training. Evaluation of these relationships is of interest for both neuroscientists and clinicians alike, and should inform our collective understanding of how white matter tissue status within the stroke-affected brain may affect the capacity for motor learning. Further, a refined understanding of the relationships between microstructural status in the stroke-damaged brain and potential for motor learning related change may enable clinicians to better predict response to, and evaluation of, rehabilitation interventions.

Methods

Participants

Thirteen well-recovered individuals with a single, clinically diagnosed chronic (>6 months post-stroke)²¹ ischaemic stroke affecting the middle cerebral artery distribution (mean age $63.8 \pm \text{SD: } 1.8$) and nine healthy control participants (mean age $66.0 \pm \text{SD: } 8.0$) were recruited from the community (Table 1). The two groups had similar distributions of age, gender, and handedness. Informed consent was obtained from each participant in accordance with the Declaration of Helsinki. The University of British Columbia (UBC) research ethics boards approved all aspects of the study protocol.

Inclusion/Exclusion Criteria

Individuals with a single middle cerebral artery ischaemic stroke occurring more than 6 months prior to participation were included in this study. Individuals were excluded from participation if they had any other known neurological impairments, scored below the 25th percentile on the Mini-Mental Status Exam,²² scored below 15 on the Fugl-Meyer Upper Extremity Motor Scale,²³ or had any contraindications to magnetic resonance imaging (MRI). Additionally, participants required sufficient strength and motor control in order to grasp and manipulate a joystick to complete the skilled movements associated with our

training task. Controls were excluded if they had known neurological impairments or contraindications to MRI.

Research Design

Each participant completed seven experimental sessions. The first session indexed baseline motor performance. Next, five practice sessions were completed on separate days, followed by a delayed retention test, which was performed on day 7. The data reported here were a part of a larger study that included multiple functional (f)MRI sessions. DTI data for this research were collected as a part of a single structural scanning battery that took place on day 7.

Visuomotor Pursuit Task

Participants sat in front of a computer monitor that displayed a white circle indicating the target and a red dot representing movement by the participant. Participants practiced tracking a moving target continuously using a joystick controlled by the hemiparetic arm (stroke group); healthy controls were matched for arm use (ie, right vs left) (Table 1). The participants' forearms were fixed into foam-lined trays throughout the task, which necessitated movements into radial and ulnar deviation to control the joystick. On each training day, five tracking task blocks, composed of 10 tracking trials (20s each), were completed. Although the target and movement were visible, visual feed forward and feedback information regarding the upcoming movement pattern or previous tracking performance was not available (i.e., no pattern or trace was displayed on the computer screen). Each day participants were instructed to track the target as accurately as possible by controlling the position of the cursor with the joystick. At the completion of practice sessions, each participant completed 83.3 minutes of tracking training in total. The retention test consisted of a single block of the task (ten 20s tracking trials) completed in the functional (f)MRI scanner. This test was performed in order to assess improvement that had occurred as a result of previous training (as opposed to improvement within a single session). The time elapsed between each training session and between the final training session and retention test varied between 2–5 days.

Skill performance was quantified by root mean square error (RMSE) between target and response over time of each trial individually. RMSE was averaged across the first block of 10 (20s) trials for day 1 and day 7 assessments. A change score was calculated (Day 7 – Day 1) separately to assess improvement in tracking error associated with practice. Larger negative change scores represented greater *reductions* in visuomotor pursuit RMSE indicative of training-associated *improvements* in tracking skill.

MRI Data Acquisition

MR acquisition was conducted at the UBC MRI Research Centre on a Philips Achieva 3.0T whole body MRI scanner (Phillips Healthcare, Andover, MD) using an eight-channel sensitivity encoding head coil (SENSE factor=2.4) and parallel imaging. A high-resolution anatomical scan (TR = 12.4 ms, TE = 5.4 ms, flip angle $\theta = 8^\circ$, FOV = 256 mm, 170 slices, 1 mm thickness) was collected. A diffusion weighted scan was conducted with a single shot echo-planar imaging (EPI) sequence (TR = 7465 ms, TE = 75 ms, FOV = 212 × 212mm, 60

slices, 2.2 mm slice thickness, voxel dimension = 2.2³mm). Diffusion weighting was applied across 15 independent non-collinear orientations ($b = 1000 \text{ s/mm}^2$) along with a non-weighted diffusion weighted image acquired ($b=0$). A gradient table was used for subsequent data analysis, computed using parameters of the diffusion-weighted images.²⁴

MR Data Processing

Diffusion-weighted images (Fig. 1A) were visually inspected for excessive motion artifact or instrumental noise; if an image was deemed corrupt, it was removed prior to tensor calculation.²⁵ Less than 1% of images were removed across all subjects. After tensor calculation, FA maps were produced based on the magnitude of diffusivity in three defined orientations and the mean diffusivity of each within a given tensor.⁵ Color-coded orientation maps were used to visualize the principal fiber orientation within each pixel (red: right-left, blue: superior-inferior, green: anterior-posterior).

The ROEditor software program (www.MRISStudio.org) was used to perform manual quantification of PLIC for each participant in subject-space. The PLIC was delineated bilaterally, beginning at the level of the anterior commissure and terminating at the inferior border of the corona radiata²⁶ (Fig. 1B, C). The regions of interest (ROIs) were delineated using the FA and color maps and a white matter atlas.²⁷ Lesions penetrating the PLIC were not excluded from the drawing procedure. Complete disruption of the affected PLIC was not observed for any participant. Mean FA values for the delineated region were computed by removing pixels with zero or negative FA values; the mean FA from the remaining voxels within the manually defined ROI mask was used for statistical analyses. We have previously shown that this approach has good reproducibility in individuals with stroke and healthy participants.^{7,16}

Statistical Analyses

A two-way (Group $\times$ Day) repeated-measures analysis of variance (RM-ANOVA) was conducted to evaluate the differences in motor skill performance (i.e., RMSE) between the participants with stroke and healthy participants. The groups were then evaluated separately to measure the relationship between skill performance change and post-training FA values within the PLIC bilaterally. A one-way (Group) multiple analysis of variance (MANOVA) was conducted to assess differences in ipsilesional and contralesional post-training PLIC FA values in the stroke group compared to the non-dominant and dominant PLIC in the control group.

Hierarchical multiple linear regression analyses were performed to assess the amount of variance in RMSE change scores explained by PLIC FA values and demographic information. In the stroke group, post-stroke duration and age were entered together first into the model to account for stroke chronicity^{28–30} and age-related changes in learning capacity³¹ and white matter status.³² Post-training ipsilesional PLIC FA was the next predictor entered into the model, based on findings suggesting ipsilesional tract integrity is related to upper limb function,²⁶ followed by contralesional post-training PLIC FA. In the healthy group, the same order of entry was used with age entered first into the model followed by non-dominant (trained) post-training PLIC FA and then dominant (untrained)

post-training PLIC FA. We conducted the same analyses using hemispheric post-training PLIC FA asymmetry $[(FA_{\text{contra}} - FA_{\text{ipsi}})/(FA_{\text{contra}} + FA_{\text{ipsi}})]$ as a single predictor where larger positive asymmetry values represented greater within-subject differences in post-training PLIC microstructural integrity. The analyses were also conducted to evaluate the relationship between naïve skill performance (day 1) and post-training FA values.

Zero-order, part and partial correlations were produced for each model. Colinearity between multiple predictors was evaluated using Variance Inflation Factor (VIF) and Tolerance levels. Values under 10 for VIF and above 0.1 for Tolerance were critical levels for acceptable colinearity.³³ Residual statistics and plots were produced to ensure normality and homoscedasticity of the data.^{33,34} Durbin-Watson diagnostics were provided to ensure independence of the residuals. Influential cases and extreme outliers were determined using Cook's distance (>1), studentized residuals (>3) and Mahalanobis distance (>10).³³ No extreme outliers were detected. For each statistical test, significance level was set at $p < 0.05$. All statistical procedures were conducted using SPSS software (SPSS 19.0).

Results

Comparisons between healthy and chronic stroke individuals

Across sessions, healthy participants demonstrated superior skill performance (indicated by lower RMSE values) compared to participants with stroke (Main effect of Group; $F_{(1, 20)} = 6.09$, $p = 0.023$). Examining the change in skill across training, a group by time interaction was not observed ($F_{(1, 20)} = 0.38$, $p = 0.545$). Both groups benefitted significantly from practice as shown by reduced RMSE values from day 1 to the retention test on day 7 (Main effect of Time; $F_{(1, 20)} = 33.60$, $p < 0.0005$) (Fig. 2). Results from the MANOVA demonstrated differences in post-training FA between groups (Pillai's Trace: $F_{(2, 19)} = 4.34$, $p = 0.028$). This was attributed to difference in post-training FA in the ipsilesional PLIC. Post-training mean FA values in the contralesional PLIC did not differ between groups ($F_{(1, 20)} = 2.24$, $p = 0.151$); however, post-training mean FA values for the ipsilesional PLIC were lower in the stroke group than in healthy controls ($F_{(1, 20)} = 7.85$, $p = 0.011$) (Fig. 3).

Associations between visuomotor skill performance and diffusion measures

Results of the regression analyses conducted for both groups is summarized in Table 2. In the stroke group, the initial model (post-stroke duration, age) did not alone explain a significant amount of variance in change in RMSE associated with skill training or baseline skill performance. Adding post-training ipsilesional PLIC FA values produced a model that explained a unique amount of variance in response to skill training ($R^2 = 0.649$, $F_{(3, 9)} = 5.55$, $p = 0.020$, $\beta_{\text{ipsiFA}} = -1.073$) but was not associated with baseline performance. Individuals that demonstrated greater improvements associated with practice (indicated by larger negative RMSE change scores) had higher post-training ipsilesional PLIC FA values. The bivariate relationship between change in RMSE and post-training ipsilesional PLIC FA is illustrated in Figure 4A. Note that when the amount of variance in change in RMSE explained by age and post-stroke duration are accounted for, post-training ipsilesional PLIC mean FA explains a larger proportion of variance in performance improvement (reduced RMSE) following training (Fig. 4B). Adding post-training contralesional PLIC FA to the model did

not explain an additional amount of unique variance in change in performance, however the overall model remained significant ($R^2=0.746$, $F_{(4,8)}=5.89$, $p=0.016$).

In a separate model, adding post-training FA asymmetry as a predictor of change in motor skill learning produced a significant model ($R^2=0.573$, $F_{(3,9)}=4.03$, $p=0.045$, $\beta_{FA \text{ asymmetry}}: 0.984$) (Fig. 5A and B) where less asymmetry in post-training PLIC FA was associated with greater change in motor skill following training. No association was observed with baseline tracking performance for post-training FA asymmetry ($p>0.05$).

In the healthy group, regression analyses did not demonstrate a significant association between post-training FA values with change in skill or baseline performance ($p>0.05$) (Table 2) (Figure 6).

Discussion

Consistent with past work, our results demonstrate that both individuals with stroke and age-matched healthy controls benefit from skilled practice and can demonstrate motor learning of a novel motor task.^{2,35} However, our data extend past work showing that magnitude of motor learning related change in the performance of a complex visuomotor task is associated with post-training ipsilesional PLIC status, indexed by FA, in individuals with chronic stroke. Interestingly, baseline motor performance was not related to post-training ipsilesional PLIC FA values, suggesting that white matter status within this region is linked to change in skilled motor behavior rather than naïve motor skill performance.

Numerous studies have shown that given adequate doses of practice individuals with stroke can learn new motor skills using either their hemiparetic^{1,2,36} or non-hemiparetic arm.^{3,37–40} Yet, the magnitude of change associated with motor learning after stroke is highly variable, and motor performance after stroke is rarely as accurate or as fast as that of age-matched healthy controls. Our findings suggest that post-training FA within the ipsilesional PLIC may be an important marker of motor learning related change in chronic stroke. It has begun to be considered in motor learning studies in healthy controls. When healthy individuals practice a new motor task, a strong relationship exists between skill development and baseline, pre-training FA within the corticospinal tract.⁴¹ Thus, future work may need to account for ipsilesional PLIC FA to individualize and optimize motor learning after stroke.

Taken together with other work^{26,42,43} our data show the necessity for a certain level of residual white matter tissue to demonstrate motor learning related behavioral change after stroke. In fact, our data suggest that after stroke behavioral capacity for learning related change scales with post-training FA. Although it is possible that training altered FA values, our results show that individuals with higher post-training FA in the ipsilesional PLIC demonstrated greater magnitude of motor learning related change (Fig. 4A). \

Importantly, age and time post stroke *alone* were not significantly associated with motor learning related change in behavior; only when these factors were combined with post-training ipsilesional PLIC FA did the model explain a significant amount of variance in change in skill. This finding indicates that age and post stroke duration should not be used in isolation, to determine potential for motor learning related change. This is important

information for individuals who design the content and course of rehabilitation interventions. A recent systematic review supports this contention and determined there is inconclusive evidence that time since stroke influences upper limb motor recovery.⁴⁴ It has also been suggested that motor outcomes after stroke may be best predicted with diffusion-based information.⁶ Further we propose that altered white matter microstructural integrity within the ipsilesional PLIC may be one source of variability that could account for some degree of between-participant differences in outcomes across motor learning studies. This factor may need to be accounted for in the design and interpretation of experiments intended to ascertain the optimal choice of rehabilitation intervention, dose of practice, and feedback schedule to stimulate motor learning after stroke.

Our data confirm and extend those of Stinear et al²⁶ showing that motor learning related change is associated with FA asymmetry between ipsi- and contralesional PLIC where an asymmetry greater than 0.25 was associated with lower potential for functional recovery and reduced response to an experimental block moving task. Given that even after a unilateral stroke white matter in both PLIC's and motor function in both arms may be disrupted, indexing FA asymmetry provides a measure of white matter status that more fully characterizes upper extremity motor function. Interestingly, examination of our results shows that individuals with asymmetry of 0.20 or higher failed to demonstrate motor learning related change (Fig. 5A). It may be that the greater complexity and motor control requirements of our visuomotor pursuit motor learning task necessitated more symmetry between ipsi- and contralesional post-training PLIC FA values as compared to the relatively simple block moving task employed in past work. Importantly, it is consistently clear in the literature that greater asymmetry in PLIC FA after stroke contributes to both increased level of physical impairment (reduced FM scores)^{15,26} and reduced motor learning capacity.

There are limitations to this study. The sample of participants with stroke was relatively small and homogenous. Although this homogeneity may improve sensitivity to observing effects by reducing inter-subject variability, it could also limit its generalizability to all stroke populations. Sample size may have also reduced statistical power required to detect associations between white matter integrity and baseline skill performance. The sample size studied may also limit generalizability of the results from the multiple regression analyses. Future work should evaluate our preliminary findings in a larger participant cohort. Further, we were not powered to detect relationships between our variables within the healthy control group. Diffusion imaging was limited to one scan with a limited number of orientations, yet this is comparable to related investigations.^{14,15,45} However, our scan parameters may have decreased the signal-to-noise ratio and resolution, thus decreasing sensitivity to detecting small changes in diffusion behavior, especially at tissue boundaries and brain regions with crossing fibers. We focused on evaluating one DTI-based metric of white matter in the PLIC in an effort to minimize these potential limitations. We also limited our investigation to the PLIC because it was a region previously shown to have reduced integrity following stroke.^{14,15} Other investigations have used alternative analysis techniques to evaluate this subsection of tract and also other white matter regions within the brain.⁴⁵⁻⁴⁷ Currently there is no gold standard for DTI analysis techniques and all approaches have potential limitations and pitfalls⁴⁸ that need to be considered when determine optimal imaging and analysis parameters in stroke.

Another limitation of this study was that diffusion imaging was performed following training. Currently, the time period required to observe training-induced white matter plasticity in healthy individuals is unclear. Studies showing change in white matter diffusion behavior following training generally occur over 5–8 weeks.^{9,10,13} Further, in a study specifically related to motor-based training, healthy individuals were trained on a serial reaction time motor skill task for 10 days within only a 2-week period and showed no FA differences following training.⁴⁹ However, a recent investigation showed only two hours of training on a spatial memory and learning motor task produced short-term changes in hippocampal and parahippocampal white matter.⁵⁰ Only one research report has documented white matter change in individuals with stroke; this work considered the impact of a functional electrical stimulation intervention on mean FA values.⁵¹ This work included only 3 participants and has yet to be replicated. Finally, DTI has not shown sensitivity to detect small, positive changes in white matter microstructure (i.e., increases in FA) that are likely associated with laboratory-based motor learning studies in older individuals or in people with chronic stroke; this result may stem in part from the relatively low doses of practice delivered in most motor learning studies.^{2,3,35,52} A newer imaging modality called multi-component T₂ relaxation imaging (MCRI) has recently been shown to index a specific element of white matter microstructure, myelin, in individuals with chronic stroke.⁵³ Although MCRI may allow the quantification of motor learning related change in white matter microstructure after stroke, it has yet to be fully investigated in this context. Thus, given the issues outlined above, for the present study, we chose not to attempt to index change in FA but instead focused on understanding if post-training white matter tissue status might be associated with motor learning related change in behavior. Further work including longitudinal studies of training and white matter plasticity, that employ imaging techniques that are both sensitive to change and specific to brain structure such as MCRI, will be required to determine whether it is possible that training-induced white matter plasticity supports the acquisition of new motor skills.

Lastly, this investigation focused on one type of skill learning and a single training paradigm. Repeated daily practice sessions performing continuous tracking with the affected extremity have previously demonstrated implicit motor skill learning in individuals with stroke¹ and have important implications for rehabilitation.^{54,55} Future inquiry should evaluate relationships between adaptive brain structure and function with response to different motor learning task paradigms using multimodal neuroimaging approaches.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Clinical Implications

Our findings indicate that post-training diffusion-based measures of white matter microstructural integrity of ipsilesional primary motor output tracts are closely associated with response to motor skill training in well-recovered individuals with stroke in the chronic phase of recovery. Importantly, demographic information in isolation did not predict motor learning related change. These results imply that regional white matter diffusion characteristics may be an important factor to consider when interpreting or predicting response to rehabilitation or when designing studies that consider motor learning related change.

Figure 1.

A) Axial slice of a raw diffusion weighted image. B) fractional anisotropy and C) color-coded orientation maps from a representative subject in the stroke group. Right (pink) and left (orange) posterior limb of the internal capsule regions of interest are overlaid in each image.

Figure 2.

Difference in root mean square error (RMSE) for the visuomotor pursuit task from day 1 to the delayed retention test, which took place on day 7. Lower scores reflect more accurate visuomotor tracking and less error. Both groups demonstrated improved performance after completing the five training sessions. Error bars are standard deviation of the mean (SD).

Figure 3.

Mean post-training FA values from for dominant and non-dominant PLICs for healthy controls and ipsi- and contralateral PLICs for individuals with stroke. Reduced post-training mean FA was observed in the ipsilesional PLIC in the stroke group compared to the non-dominant PLIC in the healthy control group (* $p < 0.05$). Error bars are standard deviation of the mean (SD).

Figure 4.

A) Scatterplot depicting the bivariate relationship between change in tracking performance (root mean square error, RMSE) and post-training ipsilesional PLIC FA values. Tracking performance improvements (more negative RMSE change scores) were correlated with higher post-training ipsilesional PLIC mean FA values. B) Partial residual plot illustrating the relationship between change RMSE and post-training ipsilesional PLIC FA after regressing each separately on age and post-stroke duration. The amount of variance in change in RMSE explained by post-training ipsilesional PLIC FA was increased after accounting for the variance in RMSE change explained by age and post-stroke duration.

Figure 5.

A) Scatterplot depicting the bivariate relationship between change in RMSE and post-training hemispheric PLIC FA asymmetry values. Performance improvements were associated with reduced post-training hemispheric PLIC FA asymmetry. B) Partial residual plot illustrating the relationship between change in RMSE and post-training hemispheric PLIC FA asymmetry after regressing each separately on age and post-stroke duration.

Figure 6.

Scatterplot demonstrating the relationship between post-training FA values in the ipsilesional (stroke group) and non-dominant (healthy group) PLIC with change in RMSE following training. These data reiterate the significant relationship observed between post-training FA values in the ipsilesional PLIC and change in performance with increasing post-training FA associated with greater skill improvement (reduced RMSE values) in the stroke group. No significant relationship was observed in the healthy group of individuals.

Table 1

Participant demographic information

Subject ID	Age (y)	Gender	Affected/Trained Hand	Dominant Hand	Post-Stroke Duration (mo)	FA		RMSE		Lesion Location	
						Contra	Ipsi	Day 1	Day7		
S50	65	M	L	R	20	0.62	0.56	7.94	6.17	Putamen, lentiform nucleus	
S51	72	M	L	R	169	0.58	0.47	16.41	11.93	Putamen, thalamus	
S52	59	F	L	R	42	0.63	0.65	12.21	8.54	Middle frontal gyrus, precentral gyrus	
S55	72	M	L	L	101	0.63	0.45	22.76	18.57	Inferior, middle frontal gyri	
S57	74	M	L	R	65	0.60	0.59	17.65	15.16	Putamen	
S58	55	F	L	R	19	0.61	0.57	13.68	10.05	Cingulate gyrus	
S62	59	M	R	L	38	0.65	0.67	15.48	6.21	Insula, inferior parietal lobe	
S65	55	M	R	L	101	0.65	0.26	12.42	11.75	Insula, putamen, precentral gyrus	
S66	64	M	L	R	29	0.63	0.52	10.79	6.95	Thalamus	
S67	65	F	L	R	90	0.61	0.35	15.18	15.46	Caudate, putamen, lentiform nucleus, ins	
S68	68	F	L	L	136	0.60	0.47	27.09	20.56	Superior temporal gyrus, insula	
S69	58	M	L	R	17	0.63	0.67	16.29	8.90	Pons	
S70	63	M	L	R	28	0.63	0.54	14.69	11.67	Cingulate gyrus	
Mean ± SD:					63.77 ± 6.42	0.62 ± 0.02	0.52 ± 0.12	15.58 ± 4.97	11.68 ± 4.62		
H05	64	F	L	R		0.58	0.6	9.07	6.43		
H06	72	F	L	R		0.64	0.63	14.60	9.56		
H07	67	F	L	R		0.68	0.66	12.98	10.13		
H08	63	M	L	R		0.61	0.6	7.24	6.10		
H09	60	F	L	R		0.67	0.67	7.98	7.49		
H10	51	M	L	R		0.64	0.64	17.94	7.54		
H11	68	M	L	R		0.65	0.63	11.45	10.05		
H13	80	F	L	R		0.65	0.64	8.38	6.26		
H14	69	M	L	R		0.62	0.64	9.97	7.78		

Subject ID	Age (y)	Gender	Affected/Trained Hand	Dominant Hand	Post-Stroke Duration (mo)	FA		RMSE		Lesion Location	
						Contra	Ipsi	Day 1	Day7		

Mean ± SD: 66 ± 8.06 0.64 ± 0.03 0.63 ± 0.02 11.07 ± 3.54 7.93 ± 1.61

FA: fractional anisotropy, RMSE: root mean square error, Asym: asymmetry, Contra: contralesional, Ipsi: ipsilesional, M: male, F: female, L: left, R: right, SD: standard deviation, y: years, mo: months, S: stroke, H: healthy

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Summary of regression modeling of post-stroke duration and post-training PLIC integrity for baseline performance and motor learning

Table 2a

<i>Stroke Group</i>	<i>Predictors</i>	<i>R²</i>	<i>F statistic</i>	<i>Significance</i>	<i>β_{PSD}</i>	<i>β_{age}</i>	<i>β_{ipsi}</i>	<i>β_{contra}</i>
Baseline Performance								
Model 1	PSD, age	0.379	3.050	0.092	0.459	0.231		
Model 2	PSD, age, FAIpsi	0.446	2.415	0.134	0.730	0.122	0.347	
Model 3	PSD, age, FAIpsi, FAContra	0.458	1.692	0.244	0.787	0.199	0.381	0.157
Day 7 - Day 1 Change								
Model 1	PSD, age	0.008	0.041	0.960	0.049	0.053		
Model 2	PSD, age, FAIpsi	0.649	5.545	0.020*	-0.788*	0.393	-1.073*	
Model 3	PSD, age, FAIpsi, FAContra	0.746	5.885	0.016*	-0.948*	0.175	-1.167*	-0.441
<i>Healthy Group</i>	<i>Predictors</i>	<i>R²</i>	<i>F statistic</i>	<i>Significance</i>	<i>β_{age}</i>	<i>β_{ipsi}</i>	<i>β_{contra}</i>	
Baseline Performance								
Model 1	Age	0.142	1.163	0.317	-0.377			
Model 2	Age, FAIpsi	0.190	0.705	0.531	-0.366	0.219		
Model 3	Age, FAIpsi, FAContra	0.226	0.487	0.706	-0.443	-0.121	0.394	
Day 7 - Day 1 Change								
Model 1	Age	0.241	2.226	0.179	0.491			
sdModel 2	Age, FAIpsi	0.241	0.954	0.437	0.491	-0.003		
Model 3	Age, FAIpsi, FAContra	0.244	0.537	0.677	0.511	0.082	-0.099	

Summary of regression modeling of post-stroke duration and FA asymmetry for baseline performance and motor learning

Table 2b

<i>Stroke Group</i>	<i>Predictors</i>	<i>R²</i>	<i>F statistic</i>	<i>Significance</i>	<i>β_{PSD}</i>	<i>β_{age}</i>	<i>β_{asym}</i>
Baseline Performance							
Model 1	PSD, age	0.379	3.050	0.092	0.459	0.231	
Model 2	PSD, age, FA asym	0.440	2.362	0.139	0.707	0.077	-0.325
Day 7 - Day 1 Change							
Model 1	PSD, age	0.008	0.041	0.960	0.049	0.053	
Model 2	PSD, age, FA _{asym}	0.573	4.025	0.045*	-0.701	0.519	0.984*

<i>Healthy Group</i>	<i>Predictors</i>	<i>R²</i>	<i>F statistic</i>	<i>Significance</i>	<i>β_{age}</i>	<i>β_{asym}</i>
Baseline Performance						
Model 1	Age	0.142	1.163	0.317	-0.377	
Model 2	Age, FA _{asym}	0.201	0.756	0.510	-0.467	0.258
Day 7 - Day 1 Change						
Model 1	Age	0.241	2.226	0.179	0.491	
Model 2	Age, FA _{asym}	0.243	0.965	0.433	0.508	-0.05

PLIC: posterior limb internal capsule, PSD: post-stroke duration, ipsi: ipsilateral, contra: contralateral, asym: asymmetry