Diffusion Tensor and Volumetric Magnetic Resonance Imaging using an MR Compatible Rehabilitation Hand Device suggests Training-Induced Neuroplasticity in Chronic Stroke

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Target audience- MR Scientists, Radiologists, Neuroradiologists, Neurologists, Neurosurgeons, Physicians, Rehabilitation therapists

Purpose– Stroke is the most frequent cause of adult-onset disability among people in the United States, and the cost of their care is among the fastest-growing expenses for Medicare (1). Post-stroke therapy may improve recovery and reduce long-term disability (2), but objective methods for evaluating the specific effects of rehabilitation are needed. Brain imaging studies in chronic stroke patients have shown evidence for plastic changes co-localization of areas showing functional plasticity after a stroke. Here, our purpose was to: a) to present combined MRI volumetric and DTI data using a novel MR-compatible hand-induced robotic device (MR_CHIROD), (3-5) and b) to investigate reorganization of motor systems by probing alterations in diffusion-based tractography and consequently to demonstrate changes in anatomical and structural plasticity in addition to the functional changes we have already observed in the brains of chronic stroke patients produced by hand training (5). We are thus attempting to fill the current gap in stroke recovery knowledge regarding brain reorganization in conjunction with MR-compatible robotic devices in chronic stroke.

Materials and Methods– We studied 15 healthy controls with DTI as part of an overall patient MR session, which included 3D high-resolution T1-weighted MRI, fMRI and DTI; we also studied 4 patients serially. Patients had first-ever left-sided ischemic subcortical middle cerebral artery (MCA) stroke ≥ 6 months prior, with no spasticity or joint stiffness. Patients trained at home and underwent serial MR evaluation at baseline (before training), during and after 8 weeks of training. Training at home consisted of squeezing a gel exercise ball with the paretic hand at approximately 75% of maximum strength for 1 hour/day, 3 days/week. For each patient, reference (100%) was own maximum force, defined as the force at which subjects could just completely squeeze the MR_CHIROD [group max force: 128 N ± 13 N (n = 5, male)]. All studies were performed on a Siemens Tim Trio (3T). DTI images were acquired as part of an MR session for each patient, which included, 3D high-resolution T1-weighted MRI, fMRI and DTI. Also a very fast, low resolution fully-sampled T1 MP-RAGE or fast spin-density weighted 3D fast low-angle shot (FLASH) gradient echo sequence was acquired (typical acquisition time: 6 s) in order to guide the calculation of the GRAPPA reconstruction parameters. Imaging parameters were as follows: sagittal orientation; 7° flip angle; TE = 4.73 ms; TR = 2,530 ms; inversion time (TI) = 1,100 ms; 1-mm slice thickness; 352 x 352 x 192 matrix; GRAPPA factor = 3-6 to achieve the shortest acquisition time. Each volunteer performed the paradigm at 45%, 60%, and 75% of their maximum grip strength and could fully squeeze the device at all levels. The percent levels compensate for performance confounds. Care was taken to minimize elbow flexion and/or reflexive motion, and head motion (typically 0.1 to 0.4 mm). Typical imaging parameters for DTI were: 2mm × 2mm × 2mm voxel size, 64 slices, two diffusion weightings (b = 0 s ⁄mm2, b=1000 s⁄ mm2), TR/TE=8600ms/100ms, 12 diffusion directions, 4 dummy scans, 10 T2 weighted images, 2 averages. The imaging sequence employs the twice-refocused spin-echo method for reduction of eddy current. To assess the thickness of cortical gray matter, we used FreeSurfer (http://surfer.nmr.mgh.harvard.edu) and Voxel based morphometry (VBM) conducted with SPM8 calculated deviations of brain volume of this patient from 11 age- and sex-matched controls. Total acquisition time for DTI was 10 min. DTI fiber tract reconstruction was performed with Diffusion Toolkit and visualized with Trackvis (Diffusion Toolkit 0.4.3 and Trackvis 0.4.3, http://www.trackvis.org/). Deterministic tractography was performed using the FACT algorithm (6) implemented in Diffusion Toolkit. All tracts were visualized and were subsequently visually inspected for directionality and location. ROIs (balls of 3mm diameter) were placed on the tracts to select the reconstructed corticospinal tracts (CST) choosing as seeding areas the pons, the posterior limb of the internal capsule, and the motor cortex.

Results: Table 1 shows that fiber number and average tract length is significantly affected by hand training. Figure 1 shows DTI images from a representative patient who suffered a single left-sided ischemic subcortical MCA stroke ≥6 mos. prior and did not have spasticity or joint stiffness. New CST fiber tracts (arrows) projecting progressively closer to motor cortex appeared during training. New DTI fibers may be indicative of structural neuroplasticity. In addition, our volumetric data analysis showed a statistically significant increase in the cortical thickness of the ventral postcentral gyrus areas of patients after training relative to pre-training cortical thickness (Fig. 2), thus exhibiting evidence of structural plasticity.

Affected Fibers	Average Number ± SD	Average Length ± SD (mm)	T-test *P value*
Before training	46 ± 8.1	43.6 ± 3.6	<0.001
After training	96.8 ± 7.1	71.4 ± 4.5	<0.001

Table 1. *Comparison of CST fibers of the affected hemisphere before and after 2 mos. of training*

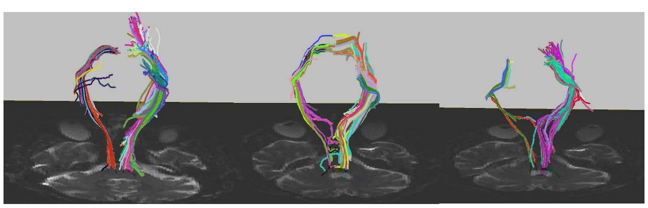

Figure 1. *Reconstructed CST tracts before (firsts) and after training after 4 wks of training (middle and after 8 wks of training (last)*

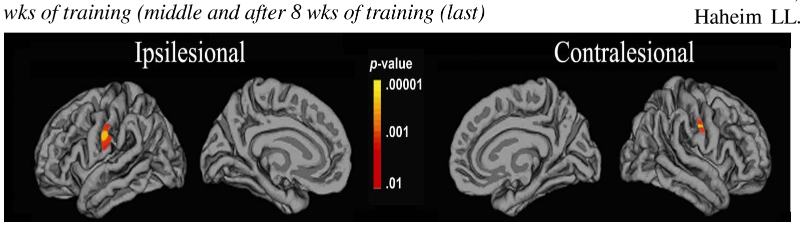

Figure 2. *Increase of cortical increase induced by robotized training in 6 patients*

Discussion: These results show alterations in fiber density and cortical thickness and suggest neuroplasticity. CST fiber tract (blue fibers) density is altered through exercise, and SMA recruitment is possibly indicated from a bundle (Fig. 1). These results are in agreement with reports of structural DTI fiber tract alterations and are consistent with the possibility that functional neuroplasticity in chronic stroke patients may be concomitant with connectivity alterations (7-9). Multimodal MRI methods attempt to take advantage of anatomical and structural information provided by different imaging modalities. Additionally, DTI has the advantage to address brain plasticity directly by depicting structural changes.

Conclusion: Nowadays studies using robotic neuroimaging to predict motor recovery as well as studies of novel therapies and techniques might influence stroke practice and policy in the future. Our finding also address the longstanding view that neuroplasticity was not possible beyond 6 mos. post-stroke has been a critical barrier of progress in the field of rehabilitation in chronic stroke.

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