Chapter 4

Brain Reorganization in Late Adulthood: Rapid Left-to-Right Switch of Handedness Through Memory-Drawing Training

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Additional information is available at the end of the chapter

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Abstract

The neural correlates of hand preference are still debatable, and the very few studies on the mechanisms of enforced change of handedness from left to right are all restricted to early childhood. We were able to address the question of retraining handedness in late adulthood for the first time, well outside the accepted critical period for brain plasticity, through a unique training utilizing the complex motor task of blind memory-guided drawing, in a totally blind, congenitally left-handed man. Ten hours of this Cognitive-Kinesthetic Drawing Training, which the author initially developed to drive neuroplasticity in blindness rehabilitation, was sufficient to generate a profound switch in the cortical lateralization of motor control. This study provides new insights into the neuroplasticity of motor control architecture. The results are of high relevance to the long-standing debate about the sources of hemispheric asymmetry. The unprecedented effect on handedness of the rapid Cognitive-Kinesthetic Drawing Training implies a powerful potential of this training for further rehabilitation domains, such as the rehabilitation of stroke or trauma affecting hand control.

Keywords: neuroplasticity, drawing, training, learning, memory, neurorehabilitation, lateralization, left-handed, handedness, Cognitive-Kinesthetic training

1. Introduction

The neural correlates of hand preference are still debatable, and the very few studies on the mechanisms of enforced change of handedness are all restricted to handedness switching from left to right in early childhood [1]. The question of *retraining* handedness in *late adulthood,* well outside the accepted critical period for brain plasticity, has not been previously studied. The author was able to address this question for the first time by driving neuroplasticity through a unique training on the complex motor task of blind memory-guided drawing, in a congenitally left-handed man who had become totally blind 10 years before. The unprecedented effect on handedness of the rapid Cognitive-Kinesthetic Drawing Training—which the author initially developed for blindness rehabilitation [2–7], implies a powerful potential of this training for further rehabilitation domains, such as the rehabilitation of stroke or trauma affecting hand control.

Left-handers are often excluded from neuroscience study cohorts in order to focus on a more uniform population. However, left-handed individuals represent a substantial portion of the human population, and therefore, it is important to account for this aspect of neural coding in order to better understand brain functioning [8]. Most studies have found that, in both right- and left-handers, movements of the preferred hand activate mainly the contralateral hemisphere [9–18], whereas movements of the non-preferred hand tend to result in a more balanced pattern of activation in the two hemispheres, indicating greater involvement of ipsilateral cortex [1, 12]. For example, it has been found that right-handers had greater activation in the left premotor area for either hand [13], indicating a general dominance of the left hemisphere in motor function, whereas left-handers showed a symmetrical of activation in the premotor cortex contralateral to the moving hand (either left or right). A parallel pattern of such a contralaterality for either hand in the right-handed, but not in the left-handed, was found in another brain region—the sensorimotor cortex [19]. It should be noted, however, that there are still many discrepancies in the literature, which are often attributed to differences in experimental design, including the type of motor task.

Does forceful switching from left-to-right handedness in adulthood change the patterns of cortication activation in left-handers or not? How much of the observed inter-hemispheric patterns are entirely genetically predetermined or can be affected by experience, such as training? There are only a few studies addressing these questions, with divergent results (e.g., [1, 16, 20–24]).

2. The Cognitive-Kinesthetic Drawing Training

The Cognitive-Kinesthetic Drawing Training is a noninvasive approach to blindness rehabilitation that the author has developed based on a novel conceptual paradigm [3–6]. It utilizes a special protocol of *memory-guided drawing*. My previous studies show that this training affects a widely distributed brain network, including both lower-level regions, such as the primary visual cortex (even in the blind), and higher level regions as the hippocampus or a swath of temporal cortex regions [6]. It also enhances top-down connectivity from the hippocampus and other memory-related regions such as the perirhinal cortex [25–26] to early visual areas.

The results from my previous study [6] also revealed the remarkable learning dynamics of functional reorganization in the hippocampal complex and the temporal-lobe object processing hierarchy over a two-month-long consolidation period. In particular, the hippocampal pattern of profound *learning-based transformations* was strongly reflected in the primary visual cortex (V1), with the memory retrieval function showing massive growth as a result of the Cognitive-Kinesthetic memory training and consolidation, while the initially strong hippocampal response during tactile exploration and encoding became almost nonexistent. Furthermore, the inferior temporal cortex manifested a striking *alternating patch structure* [6] (**Figure 1**, bottom panel) reminiscent of the face and object patches reported along the temporal lobe [27]. However, in my study, the differentiation was a function of the *temporal evolution of learning* changes, that is, it was reflecting the effect of training *over time* (instead being a function of face/object category). This cascade of alternating discrete regions also underwent a radical *sequence of transformations* as a

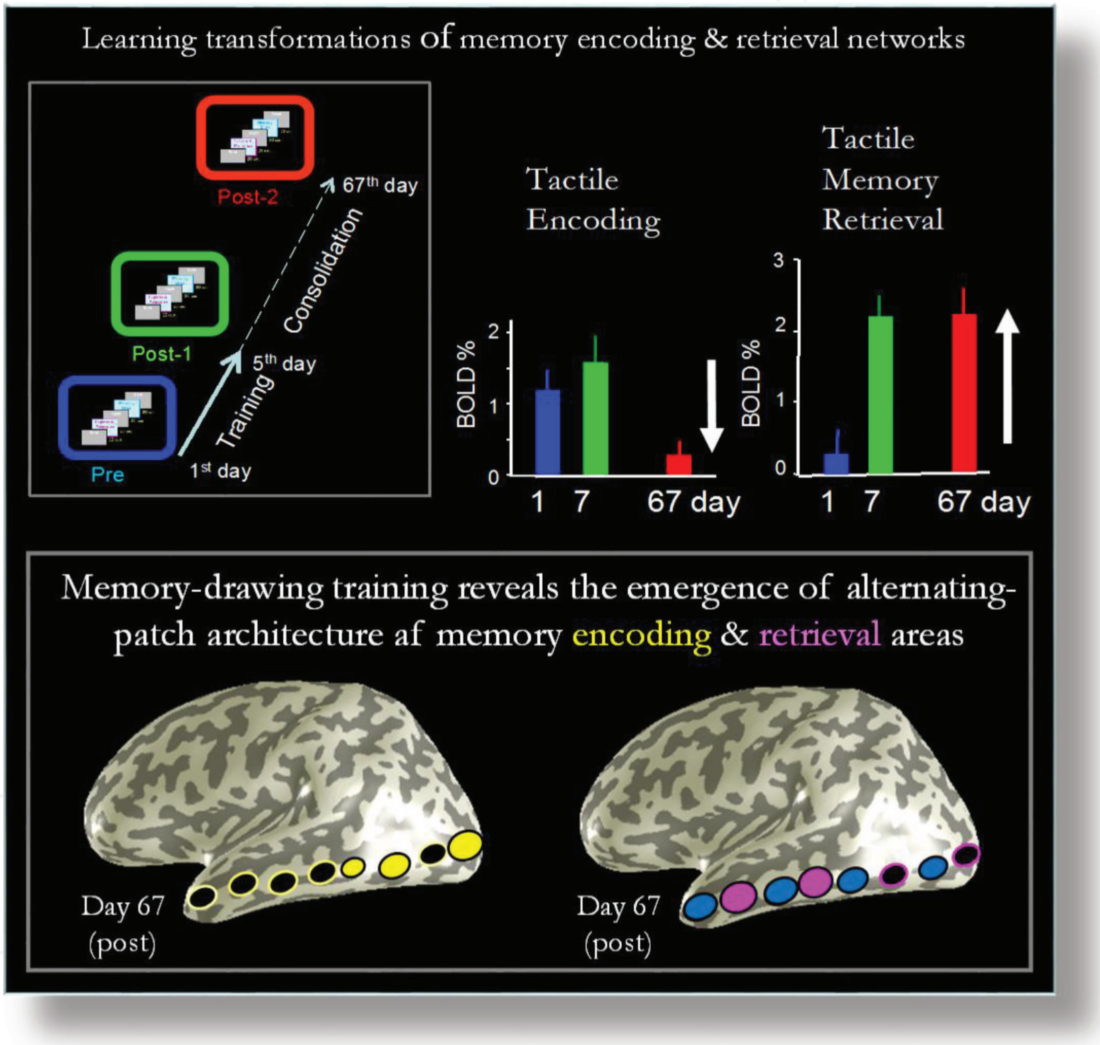

Figure 1. Learning evolution along IT driven by the Cognitive-Kinesthetic memory-drawing training. **Upper panel:** Left: Experimental design, including 3 fMRI assessments: i) a pre-training (*pre/blue*), ii) an immediate after training (*post1/green*), and iii) two months after consolidation period with no training (*post2/red*) assessments. Right: Example of the dramatic reorganization of BOLD responses in an IT region for the *tactile encoding*, and the *tactile memory retrieval tasks* from Day1 (pre-training), to day 7 (immediately post-training) to day 67 (2 months after training). **Bottom panel:** Alternating-patch structure of dissociated, largely non-overlapping encoding and retrieval regions after consolidation (day 67; after training). Left: Memory-encoding task. Yellow—areas still active after consolidation; black—areas not activated anymore. Right: Memory-retrieval task: Purple—areas that become active; blue—suppressed areas; black—areas not involved anymore (after Likova [6]).

function of the *stage of learning*, toward a *complete functional specialization* in terms of either *encoding* or *retrieval* after consolidation. Several distinct patterns of this learning evolution *within* each of the patches (see, e.g., in **Figure 1**, top panel) implied a complex reorganization of the object processing sub-networks throughout both the *training* and the following *consolidation* period.

3. Generalization of drawing-learning effects

While there have been many cross-sectional comparisons of blind and sighted capabilities, the only research focused on *interventions* to enhance basic spatial-cognition abilities in people with blindness has been that based on my Cognitive-Kinesthetic drawing training. This intervention has been shown to improve *spatial memory* and *memory-guided spatiomotor coordination* to a dramatic extent. Although it is typically assumed that drawing is dependent on vision, previous work indicates that individuals with congenital blindness are able to learn to draw over some unspecified time period that often may take years [28–30]. My studies have shown, however, that everyone—blind, sighted, or visually impaired—can learn this skill in only a few hours through an appropriate training, such as the Cognitive-Kinesthetic methodology [3–4, 31–33].

I have further hypothesized that the improvements from the Cognitive-Kinesthetic training would *transfer*, or—*generalize,* to a wide range of *untrained* basic spatial-cognition abilities that extend well beyond the drawing task *per se* [6]. "Basic" abilities were conceptualized as those that are foundational to other tasks, such as the ability to perceive, and remember object features, textures, spatial configurations, and patterns, together with abilities for spatial analysis and new concept learning. My rationale for this *transfer of learning*, or *Generalization of Learning,* hypothesis derived from the fact that the act of drawing complex images from memory "orchestrates" multiple spatial-cognition abilities [2–3, 31–33]. A recent study confirmed my Generalization of Learning Hypothesis [34] by showing significant improvements in a large standardized battery of untrained cognitive tests [35–36] for the blind and low vision following the 10 hours of Cognitive-Kinesthetic training in a cohort of congenitally blind and severe low-vision participants.

4. Switching of handedness as a form of learning effect?

In the earlier cited studies, the Cognitive-Kinesthetic Drawing Training was designed and applied as a noninvasive intervention for a rapid enhancement of *spatial memory*, *spatial cognition* in general, and precise *memory-guided motor control* in both the blind and the sighted. The memory drawing protocol in the form developed for this training, fully engages the whole *perception-cognition-action loop* [3–4], which was a key element of my *conceptual framework* underlying the training. (Note here the expansion of the traditional "perception-action" loop to include the central component of "cognition" (**Figure 2**), as I believe it is critical to its generalization to the gamut of spatial-cognition abilities.)

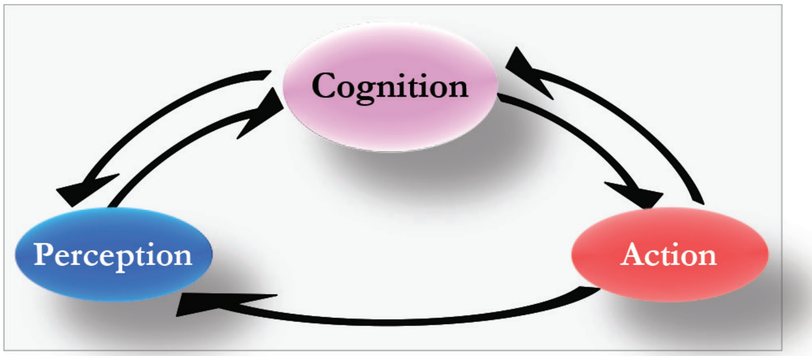

Figure 2. Perception-Cognition-Action Loop. Note the inclusion of the *cognition* module as a central mediator into the traditional perception-action loop [4].

In this chapter, we ask whether the learning effect of this training could extend to the ***action*** component of the processing *loop* involved. Specifically, can it drive reorganization of motor-architecture for *switching handedness*?

5. Methods and procedures

5.1. Participant and the Cognitive-Kinesthetic Training

The participant was a 57-year-old male who had full vision until age of 47, when his vision began declining in one eye and then the other, and he was diagnosed with Leber's hereditary optic neuropathy. Within a year, he was blind, seeing only some light in the far periphery. He had been left-handed since birth. The participant gave informed consent for the experimental protocol, which was approved by the Smith-Kettlewell Institutional Review Board as in full conformance with the Declaration of Helsinki.

After only a total of 10 hours of the Cognitive-Kinesthetic Drawing Training (2 hours/day for 5 days [3]), this left-handed blind participant learned to develop detailed and robust *memory representations* of *haptically* explored (with the ***preferred/left*** hand) raised-line depictions of complex images, such as human faces and objects, in order to draw them with his ***non-preferred/right*** hand. Thus, in order to generate the structured motor output of the drawing, he had to learn how to use these enhanced haptic memory representations to *replace* his *lost "eye-hand coordination"* by a *"memory-hand coordination"* mechanism now that he was blind.

In the process, this blind participant learned to *draw freely* with his *non-preferred/right* hand, guided *solely* by the haptic memory acquired with the other hand. This man had never been able to draw well even with his preferred/left hand while still sighted, so he and his family were greatly surprised by this successful outcome.

> *I never could draw very well … That's why it's very interesting to me that I would've been the person that did not have drawing skills before, and to be able to do something like this now .., wow, it is exciting - you have thought me drawing better than I could when I could see … and - to do this with my right hand …!.*

In an additional session, he subsequently practiced drawing the *already* memorized images with his preferred/left hand.

5.2. Experimental design

A key component of the study was measuring whole-brain functional MRI (fMRI) activation before and after applying the Cognitive-Kinesthetic Drawing Training, allowing us to determine the neuroplastic changes in a *causal* framework (**Figure 3**).

As in previous studies with the Likova Cognitive-Kinesthetic training method, fMRI was run *before* and *after* the training for a battery of *raised-line* models of faces and objects as the drawing targets in a three-task block fMRI design [3–4]. The three tasks were as follows: *Haptic Exploration* (*HE*) involving perceptual exploration and encoding in memory of the raised-line model to be drawn; *Memory Draw* (*MD*)—the task to draw this model freehand, guided solely by the encoded haptic memory; *Scribble* (*S*) was a negative memory-control and motor-control task for the hand movements alone. Each task duration was 20 s, with a 20-s baseline condition (*Rest*, *R*) intervening between tasks. Importantly, as opposed to the usual null periods, the participant not only rested motionless but was also instructed and practiced to clear any memory or imagery from awareness ("*blank-mind*"). The start of each task or rest interval was prompted by an auditory cue. The whole task sequence with interleaved rest intervals (*R, HE, R, MD, R, S, R*) was repeated 12 times in each 1.5-hour fMRI session using a new face or object image for each repeat. The *HE* task was always performed with the preferred/left hand. The *MD* and *S* tasks were performed with the non-preferred/right, and additionally, with the preferred/left hand in separate scans.

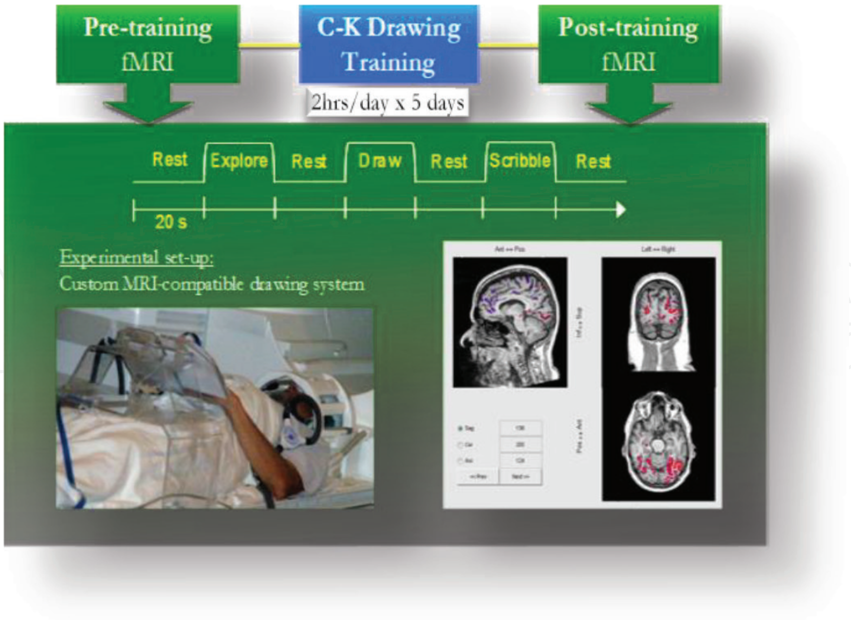

Figure 3. Experimental design. The rapid Cognitive-Kinesthetic drawing training (2 hours/day × 5 days) was preceded and followed by fMRI scans. In the scanner, three tasks were performed in a block paradigm: *Haptic Exploration, Memory Draw*, and *Scribble.* Each task and interleaved rest period were 20 s in duration. An innovative MRI-compatible lectern (lower left) provided for tactile stimulus presentation and both nonvisual and visual drawing. Functional brain activation is color coded in red (lower right).

5.3. Innovative experimental platform

The overall experimental platform integrated a number of innovations, such as, a *multisensory magnetic resonance (MR)-Compatible Tablet system*, and a novel type of parametric brain mapping—*Categorical-Change Maps* [37] that we developed especially for the purpose of assessing *brain plasticity changes* as a result of a causal intervention, and the *Cognitive-Kinesthetic Training*.

The custom MR-Compatible Tablet system (**Figure 3**) allows for participant-controlled tactile-stimulus presentation for haptic exploration and drawing in the scanner. This system consists of a plexiglass lectern extending across the participant's lap, topped with a dual-slot height-adjustable surface [3]. In the left slot was the raised-line drawing stimulus to be haptically explored during the *HE* task, and in the right slot was an MR-compatible electronic drawing tablet (EMS Medical Systems, Bologna, Italy) to be used during the *MD* and *S* tasks. Between scans, the participant was instructed how to remove the topmost raised-line drawing stimulus (which was just explored and drawn) from the left slot and place it by their side, exposing the next stimulus in the prescribed sequence. Participants used a plastic stylus to draw and scribble, with the movement of the stylus across the drawing tablet being recorded and presented in real time to the experimenters on a display in the control room. Auditory cues were presented through MR-compatible headphones (Resonance Technologies, Salem, MA). Our custom MR-compatible tablet system allowed participants to draw comfortably on the plastic lectern across their torso/lap without moving their head. Additionally, during scanning, the participant's head was stabilized in the head coil with firm but comfortable padding around all sides to minimize movement.

5.4. Brain imaging data acquisition and preprocessing

Functional MRI data were collected on a Siemens Trio 3 T magnet equipped with a 12-channel head coil (Siemens Healthcare, Erlangen, Germany). BOLD responses were obtained using an echo-planar (EPI) acquisition (TR = 2 s, TE = 28 ms, flip angle = 80^o, voxel size = 3.0 × 3.0 × 3.5 mm) consisting of 35 axial slices extending across the whole brain. Preprocessing was conducted using FSL (FMRIB Analysis Group, Oxford, UK) and included slice-time correction and two-phase motion correction, consisting of both within-scan and between-scan six-parameter rigid-body corrections. To facilitate segmentation and registration, a whole-brain high-resolution T1-weighted anatomical scan was also obtained for each participant (voxel size = 0.8 × 0.8 × 0.8 mm). White matter segmentation in this T1 scan was conducted using FreeSurfer (Martinos Center for Biomedical Imaging, Massachusetts General Hospital) and gray matter was generated with the mrGray function in the mrVISTA software package (Stanford Vision and Imaging Science and Technology, Palo Alto, USA). The Stanford package mrVISTA allows us to estimate the neural activation amplitudes for each task within respective regions of interest (ROIs) using a standard general linear model (GLM) procedure for each task regressor applied to the average signal across all voxels within each ROI.

5.5. Categorical-Change parametric mapping: a novel concept and methodology for the assessment of brain plasticity changes

In studies on brain plasticity, it is critical to be able to fully assess functional brain *changes* due to either an intervention, a natural development, or other causes, such as loss of vision.

Figure 4. Color coding for Categorical-Change mapping in the case of *positive baseline* activation. *Orange*: No significant change; *Red*: Reduced but still positive activation; *Yellow*: Increased positive activation; *Black*: Lost activation; *Blue*: BOLD signal inverted from positive into negative.

We have conceptualized a system of ***brain-change categories*** and developed a novel type of voxel-wise parametric mapping that can provide the needed *multifaceted assessment of neuroplasticity* [37], and thus, bridge a major gap in this field. This is based on (1) assessing the activation (in each voxel of the brain) during an initial state (e.g., *before* training; *baseline*) and (2) the change in activation (e.g., *after* training) ***relative*** to that baseline.

In the current study, we employed a subset of the categorical-change mapping to visualize **at once** *all five possible categories* of post-training change (or lack thereof) of any ***positive baseline*** activation prior to the state change or intervention.

The color coding for novel type of maps is shown in **Figure 4**. If an activated region did not undergo any significant change relative to the initial state, it is visualized in orange; if its positive activation was increased—in yellow; if it was reduced but still positive—in red; if the activation was lost—in black; while if the sign of the BOLD signal was inverted from positive into negative reflecting a changed in the nature of processing, it is shown in blue.

Note that we have developed the categorical-change mapping to assess the ***full spectrum of possible changes***, relative to a given pre-intervention state. In other words, this mapping tool can also be applied to brain regions that in the ***baseline*** state have ***negative*** BOLD signal, or have ***no activation*** at all. These two options are beyond the scope of the present analysis, however.

6. Results

6.1. Drawing qualities

A total of only 10 hours of the Cognitive-Kinesthetic Drawing, spread out over 5 days, led to dramatic motor control changes in this *congenitally left-handed* blind participant, who was able for the first time to obtain a highly precise control of his *non-preferred right* hand.

The scope and quality of this unexpected new ability of the *non-preferred* hand is illustrated in **Figure 5**. The *central panel* shows a comparison of his pre-training versus post-training drawing

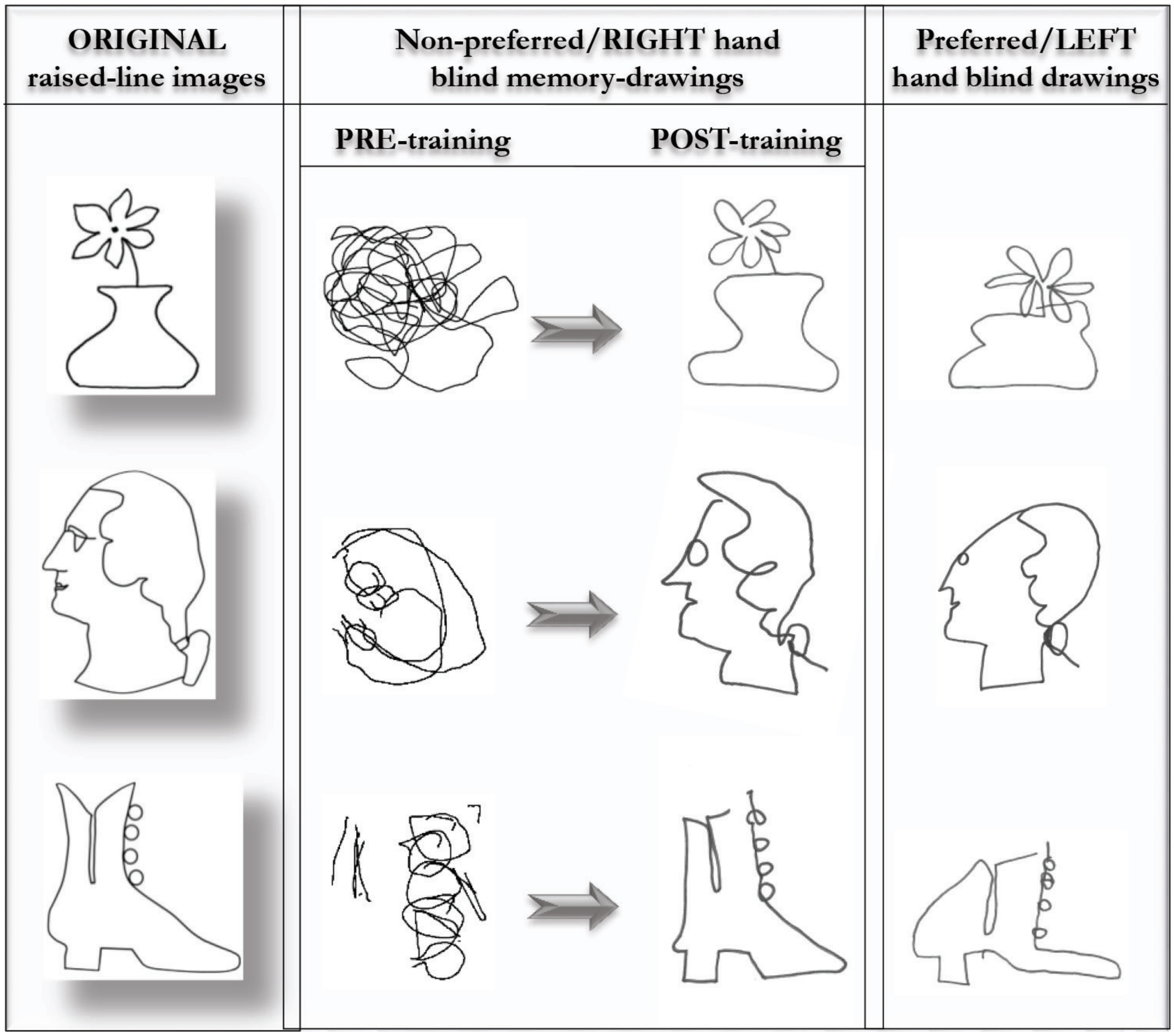

Figure 5. Examples of drawings made by the left-handed blind participant, who underwent the Cognitive-Kinesthetic drawing training. **Left panel:** Raised-line originals used in the haptic exploration and memorization phase. The exploration was always done with the preferred/left hand. **Middle panel:** Drawing from memory with the ***non-preferred/right*** hand, showing the dramatic improvement *from pre-training to post-training*, despite the fact that this hand has never been used before for drawing, writing, or any other habitual motor activity. **Right panel:** Drawings with the ***preferred/left*** hand. These drawings are guided by the same memory that was guiding the other hand; the memory per se, however, was based always on the haptic exploration of the originals with the preferred/left hand. Note that the two hands seem to express two different personalities.

done with the right (non-preferred) hand. Note, these are performed entirely *non-visually*, guided solely by the *memory from the haptic* exploration of the raised-line originals shown in the *left panel*. Note that the exploration was always done with the *preferred/left* hand.

After completing the training of the non-preferred/right hand, the participant had a session of practicing drawing with his all-life preferred (but untrained on the blind memory drawing) left hand. He was then asked to use the untrained left hand to draw the same images guided by the *already* acquired memory (**Figure 3**, *right panel*). Because the left hand had been the dominant one for almost six decades, and moreover, as the haptic exploration and memorization phase

(*HE*) was always done with this hand, the expectation would be for these to provide definitive advantages for *left*-handed drawing.

Conversely, in the main study (drawing with the non-preferred/right hand), the fact that the image information was gathered through exploration with the opposite (left) hand, sets the expectation that the *right*-hand drawing would be at a disadvantage. However, this seems to be the case only *before* the training. Note the rapidly achieved dramatic improvement ***from pre-training to post-training*** for the right hand (**Figure 3**, *middle panel*) despite this disadvantage, and despite the fact that his right hand had never been used before for drawing, writing, or any other habitual motor activity. It is thus surprising, that the *post-training* reproductions with the right hand resembled the originals better than those done with the whole-life-preferred left hand (**Figure 5**, *right panel*). Note again that both phases of the process—*haptic memory encoding* and *retrieval for memory drawing*—were done without the involvement of any vision in this blind participant.

Although the drawing quality and similarity are evident to the human eye, we further assessed the drawing quality by *bi-dimensional regression analysis* [38]. First, for each original image, landmarks were set at unique points that could be easily identified by the naked eye in the original figures and the resulting drawings. Second, bi-dimensional analysis was run for the correspondence between landmarks on the original images and those available on their reproduction by drawing. The specific measure for analyzing the quality of drawings was the fit of an affine bi-dimensional regression (expressed as Fisher-Z values of the respective Rs). The number of landmarks depended on the complexity for each template image.

The bi-dimensional regression scores indicated an improvement averaging about a factor of six *from pre- to post-training* accuracy with the trained hand. Consistent with the perceptual evaluation done earlier, the *post-training* bi-dimensional regression values were significantly higher overall for the non-preferred (but Cognitive-Kinesthetically trained) right hand versus the preferred but untrained left hand, even though the left hand was the one used in acquiring the spatial memory that guided each of the hands along the drawing trajectories.

Interestingly, although the line stability, and image completeness produced by the preferred/left hand were very good, the accuracy of reproduction with this preferred but untrained hand was lower by about a factor of two relative to the strong improvement with the training of the non-preferred/right hand. What was even more surprising was that, stylistically, it could be said that the two hands seemed to express two different personalities.

6.2. Brain plasticity driven by the Cognitive-Kinesthetic Drawing Training

6.2.1. Baseline A: the activation in the brain network engaged by the left hand in memory drawing as baseline

The fMRI recordings run *before* and *after* the training provided a measure of the neuroplastic functional changes underlying the behavioral improvements. To assess not simply *what* has been changed, but ***how*** was it changed and what specific *categories of change* had occurred in the cortex, we used our novel approach of Categorical-Change parametric brain mapping described earlier.

Using the categorical-change parametric mapping, **Figure 6** shows the types of changes that happened in the cortical network activated during memory drawing with the preferred/left hand (*baseline*), when the non-preferred/right hand instead performed the same memory drawing task either *before* training (*top panel*) or *after* training (*bottom panel*).

6.2.1.1. Pre-training (top panel)

The architecture of the *baseline network* (used as a mask) indicates that the movements of the *preferred/left* hand activated predominantly its *contralateral*/right hemisphere, as expected.

As also expected, the categorical-change mapping shows that *before* training, the drawing movements of the *non-preferred/right* hand resulted in a more ***balanced inter-hemispheric*** pattern of activation, indicating preservation of the greater involvement of the ipsilateral (right) hemisphere, consistent with previous studies on switching handedness (see Introduction). This result demonstrates that in its attempt to perform such a complex and precision-demanding motor task *before* training, the non-preferred/right hand continued to depend on the functional architecture of the preferred/left hand. Third, the figure shows that all motor, premotor, and sensorimotor regions in *both* hemispheres that were engaged by the preferred left hand were engaged to an even higher degree by the non-preferred hand.

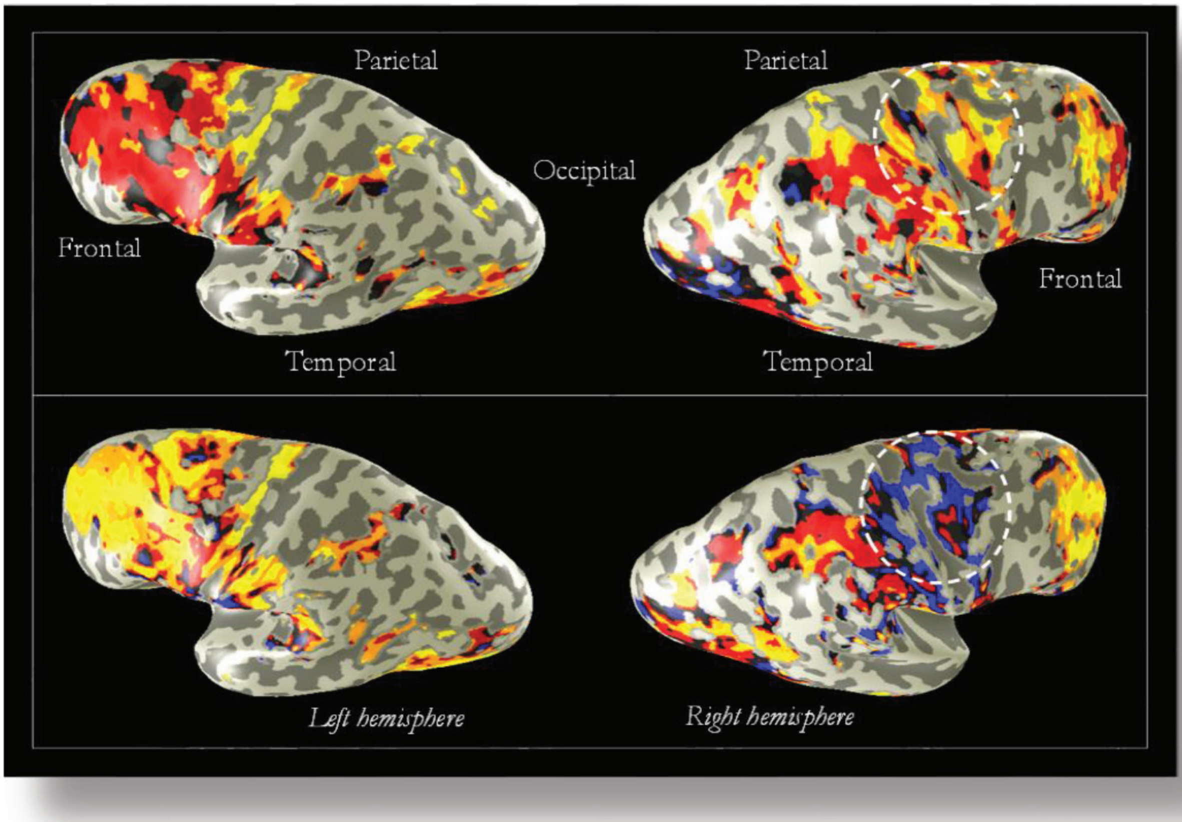

Figure 6. Categorical changes in cortical activation relative to that for memory-guided drawing with the untrained left hand *(baseline)*. The *positive* activation in the brain network engaged by memory drawing with the *left hand* was used as the ***baseline*** for the comparisons in both panels. The differences from that *baseline* for the non-preferred/right-hand activation *before training* are shown in the top panel; *after training*, they are shown in the bottom panel. The voxel-wise changes are presented on inflated views of the lateral surfaces of the left and right hemispheres. Color coding as in **Figure 4**: *Orange*—No change relative to baseline; *Yellow*—Increased positive signal; *Red*—Decreased positive signal; *Black*—Reduction to no significant signal; *Blue*—Negative signal.

6.2.1.2. Post-training (bottom panel)

Remarkably, after the Cognitive-Kinesthetic training, we observed a dramatic reorganization of motor architecture of the *non-preferred/right* hand toward a strongly expressed *contralateral* (left hemisphere) dominance. This previously unobserved reorganization is also clearly confirmed by the categorical-change map analysis in Section 6.2.2. below, where the *pre-training right-hand* network was used as baseline.

6.2.2. Baseline B: the activation in the brain network engaged by the non-preferred/right in memory drawing before training as a baseline

In this section, the network activated by the non-preffered/right hand during MD was used as the basline in the analysis. Consistent with findings from Section 6.2.1. above (see **Figure 6**), the categorical-maps shown in **Figure 7** confirm both the *bilateral* pattern of (positive) activation of the *non-preferred* hand *before* training (used as the baseline mask) and the ***transformation*** of this *bilaterality* into a *strong contralaterality* as a result of training. Another striking finding from the categorical comparison in **Figure 7** was the *massive suppression* (blue) of the BOLD responses in the motor and premotor cortex of the *ipsilateral*/right hemisphere. Furthermore, contrary to what may be expected, this happened in conjunction not with an increase but with an almost *unchanged (orange) or even reduced (red)* activation in these motor control regions of the *contralateral*/left hemisphere relative to pre-training. In other words, the increased contralaterality (left hemisphere greater than right) was *not* caused by increased contralateral/left activation but by an *ipsilateral suppression*, in spite of the fact that this right hemisphere has been the dominant one for the *entire life* of this participant.

It is noteworthy that drawing, particularly if it is solely guided by memory as in the Cognitive-Kinesthetic training applied here, is a highly complex task *orchestrating* a wide

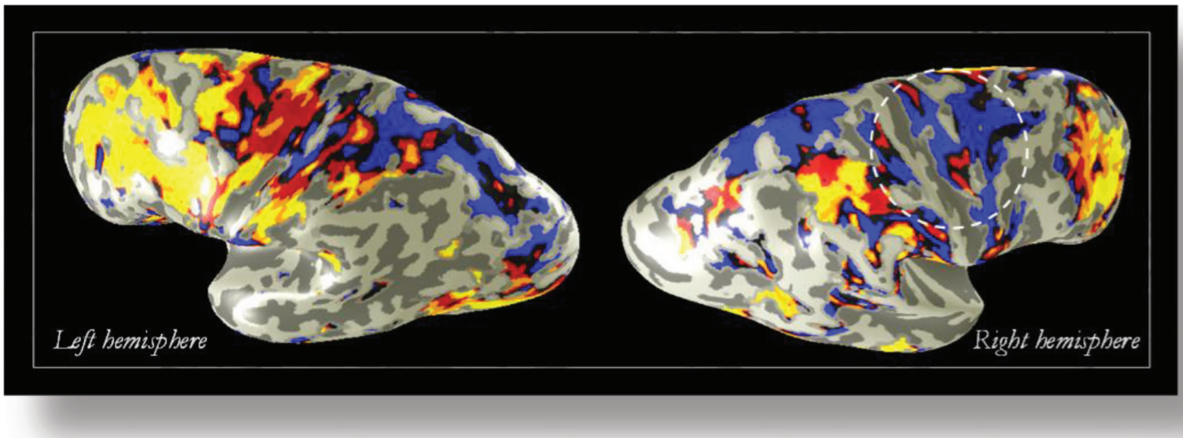

Figure 7. Rapid switch of handedness. To establish the categories of ***training-induced*** changes in the cortical network controlling the ***non-preferred/right*** hand during *MemoryDraw*, our categorical-change mapping was used with the *pre-training* activation pattern of the ***right*** hand as a ***baseline*** in a comparison with its activation ***after*** the right hand underwent the 10 hours of ***training***. The ***training-induced*** categorical changes in the ***functional architecture of the non-preferred right*** are shown on the lateral surfaces of the left and right hemisphere. Color coding as in **Figure 4**: *Orange* — No change relative to baseline; *Yellow* — Increased positive signal; *Red* — Decreased positive signal; *Black* — Reduction to no significant signal; *Blue* — Negative signal

range of perceptual, cognitive, and precise motor functions, thus engaging widely *distributed networks* throughout the brain; their detailed analysis, however, is beyond the scope of this chapter.

6.3. Patterns of hemispheric asymmetry

To quantitatively assess and compare the hemispheric patterns of activation across conditions, we applied the approach used in [1] of comparing the number of voxels, or—volume, activated in each condition. We, however, significantly expanded this approach by taking both positive and negative voxel activations and considering them separately. The voxel numbers were calculated for the conjunction of the motor, premotor, supplementary motor, and somatosensory cortices. The respective FreeSurfer ROIs were used to define the respective cortical regions for quantitative analysis.

Figure 8 shows that both the preferred/left hand (*left panel*) and the non-preferred/right hand pre-training (*middle panel*) conformed to pre-existing models: (1) the activation for the left hand was *predominantly contralateral* (right > left; see *left panel*), whereas (2) a more *balanced, bilateral* pattern of activation was observed for the drawing movements of the *right hand (middle panel)*, indicating a greater ipsilateral involvement.

The *right panel* of **Figure 8**, on the other hand, reveals a radical reorganization in the motor control architecture of the right (non-preferred*)* hand as a result of the Cognitive-Kinesthetic drawing training. The bilateral pattern of (strongly positive) activation *before* training (*middle panel*) rapidly changed into a strongly contralateral (left hemispheric) pattern *after* training (*right panel*).

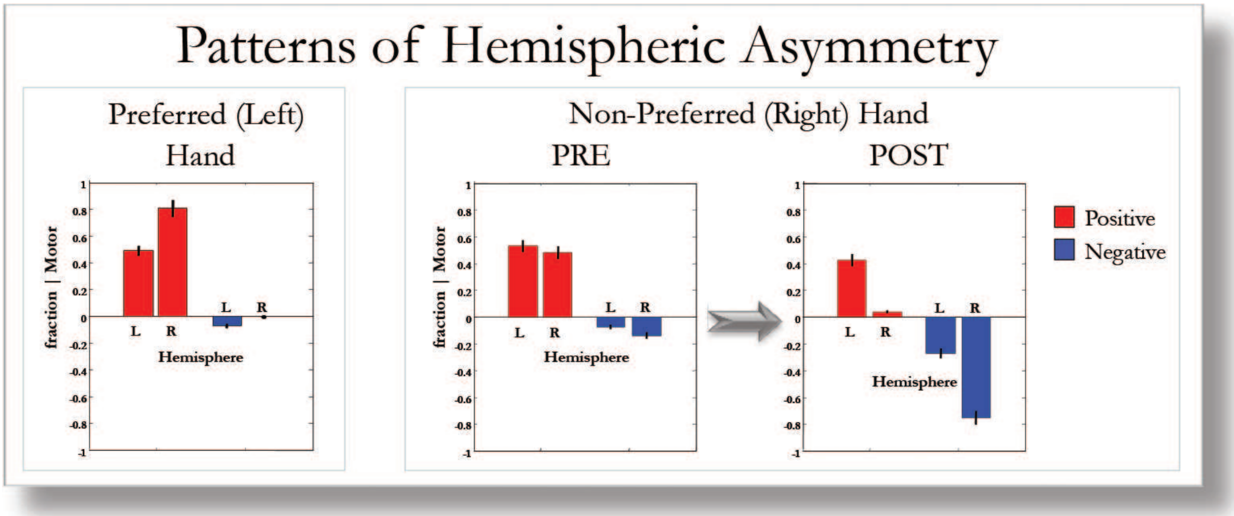

Figure 8. Cognitive-Kinesthetic training effects on the pattern of inter-hemispheric interactions. Three distinct patterns of inter-hemispheric interaction were observed. The distributions of positive (*red*) and negative (*blue*) voxels per hemisphere (*L, left; R, right*) in the conjunction of the motor, premotor, supramotor, and somatosensory cortices during memory-guided drawing is shown for the preferred/left hand (*left panel*), the non-preferred/right hand *pre*-training (*middle panel*), and the non-preferred/right hand *post*-training (*right panel*).

7. General discussion

It is generally accepted that, in both *left- and right-handed* subjects, the preferred hand is controlled mainly by the hemisphere *contralateral* to that hand, whereas the *non-preferred* hand is controlled by *both hemispheres*. In relation to *left-to-right switches* in handedness, the switched individuals have been found to share features of both left-handers and right-handers regarding their motor control architectures. ([1], see Introduction).

Before training, the results for both the *preferred*/left and the *non-preferred*/right hand conformed to these preexisting models: the *preferred*/left hand produced predominantly *contralateral* activation, whereas the *non-preferred*/right hand produced a more balanced *bilateral* activation, indicating control by both hemispheres.

After training, however, the bilateral pattern expected in switchers was not observed any more. Instead, the non-preferred/right hand underwent a strong training-based reorganization of its motor control architecture, so as its bilateral activation pattern radically changed post-training into a contralateral one. Remarkably, this *contralaterality* (left hemisphere > right hemisphere) was caused not by increased contralateral (left) activation but by a massive suppression in the ipsilateral (right) hemisphere; it is particularly surprising that this happened despite the fact that the right hemisphere has been the dominant one since birth.

These findings show for the first time that the dominance of the preferred hemisphere can be rapidly overturned, and that this can happen even in late adulthood after decades of established dominance. Note that, until now, despite long-standing efforts across many disciplines to achieve a fully-fledged hand switching in left-handers, the best that has been achieved has been to engage the contralateral left hemisphere without being able to overturn the ipsilateral right hemisphere control [1, 12]. The fact that the Cognitive-Kinesthetic Drawing Training was able to transform the bilateral into a definitive contralateral pattern, and to do so effectively and efficiently, implies a serious deficiency in the current knowledge on motor control plasticity, and the need for enhanced investigation into this process. Moreover, the power of this memory-driven motor training to rapidly drive motor-control plasticity, in addition to the previously shown effects on memory and spatial cognition, for example [2–5, 39–41], suggests strong involvement of cognitive mechanisms in this process, as codified earlier by the introduction of the "perception-cognition-action loop" concept.

The resulting neural reorganization in this congenitally left-handed individual was correlated with similarly remarkable enhancement in the memory-drawing performance of the non-preferred hand, which post-training resembled the original much better than pre-training, and moreover, significantly better than the experienced preferred hand. This was particularly unexpected because the left hand had several additional advantages. First, the *haptic exploration* of the originals was *always* done with the *left* hand, thus providing a direct perception and encoding of this hand's movements along the lines of that image. In contrast, the non-preferred right hand *never* received any direct encoding of the trajectory but for planning and execution of the drawing trajectory it had to use the memory image developed through the other hand. Second, the nature of the left-hand exploration phase represents a strong form of *dual* memory encoding for that hand. There was no difficulty or delay, however, to successfully use thus acquired memory for guiding drawing with the right hand. It should be noted that, in the drawing phase, the hand under training receives multifaceted, Cognitive-Kinesthetic feedback, which affects the initial haptic memory, corrects and sharpens it, thus adding another layer of enhancement and embodiment to the overall encoding.

An important practical implication of these findings is that the effects of the Cognitive-Kinesthetic Training can generalize over the full "perception-cognition-action loop" involved throughout the process, which suggests its usefulness not only in the domains of spatial cognition and memory rehabilitation but also in motor control rehabilitation as well.

8. Conclusions

This study is the first to show results that contradict the models of the nondominant hand always being controlled by both hemispheres, as had been previously thought. It is particularly remarkable that this brief memory-guided drawing training was able to switch lifelong handedness, overturning almost six decades of dominance of the right hemisphere by inducing profound suppression in the previously dominant hemisphere. In terms of handedness research as a whole, the study suggests a critical role for functional mechanisms, such as inter-hemispheric competition, as opposed to an inherent structural predetermination in hand dominance. The results are consequently of high relevance to the long-standing debate about the sources of hemispheric asymmetry. The unprecedented effect on handedness of the rapid Cognitive-Kinesthetic Drawing Training also implies the powerful potential of this training for further rehabilitation domains, such as the rehabilitation of stroke or trauma affecting hand control.

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