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Training-Induced Reorganization of the Cross-Modal Connectivity of the Human Motion Area in Severe Low Vision

Lora T Likova, Kristyo N Mineff, Zhangziyi Zhou, Michael Liang, Christopher W Tyler
The Smith-Kettlewell Eye Research Institute, San Francisco, CA

Abstract

Does the functional organization of the brain connectivity of the visual motion areas depend on the loss of form vision? We report large-scale reorganization in low vision individuals following a unique form of non-visual spatial navigation training. Participants completed five sessions of the haptic Cognitive-Kinesthetic Memory-Drawing Training with raised-line tactile navigational maps. Pre- and post-training, whole-brain fMRI scans were conducted while participants (i) haptically explored and memorized raised-line maps and then (ii) drew the maps from haptic memory while blindfolded. Granger Causal connectivity was assessed across the network of brain areas activated during these tasks.

Before training, the participants' hMT+ connectivity in low vision was predominantly top-down from the sensorimotor pre- and post-central cortices, supplementary motor areas, and insular cortices, with only weak outputs to occipital and cingulate cortex. Large-scale reorganization of the connectivity strengthen the pre-top-down inputs to hMT+, but also dramatically extended its outputs throughout the occipital and parietal cortices, especially from right hMT+.

These results are consistent with the fact that low vision individuals have a lifetime of visual inputs to hMT+, and it may become one of the principal perceptual inputs as their form vision is reduced, making it a key source of navigational information during the unfolding of the drawing trajectory. When forced to perform the spatiomotor task of haptic drawing without vision, however, hMT+ becomes a key conduit for signals from the executive control regions of prefrontal cortex to the medial navigational network and occipito-parieto-temporal spatial representation regions. These findings uncover novel forms of brain reorganization that have strong implications for the principles of rapid learning-driven neuroplasticity.

INTRODUCTION

This study is based on the core concept (Likova, 2012) that when vision, with its built-in spatial functionality, is greatly impaired or lost, particular reliance must be placed on the development of the *mental maps*, and on the ability to use them effectively *for (non-visual) spatiomotor control*. Under such circumstances, these spatial mental/cognitive maps (or spatial memory representations) can be supported only by tactile and auditory sensory inputs. The Likova *Cognitive-Kinesthetic (C-K) Memory-Drawing Rehabilitation Training* (e.g., Likova, 2012, 2013; Likova et al., 2017, etc.) utilizes a unique form of blind memory-guided drawing that rapidly and sustainably develops cognitive mapping to a high level of proficiency in the blind, visually impaired and the sighted. To train the spatial cognition and memory functions underlying successful navigation, we used the power of the Cognitive-Kinesthetic Rehabilitation Training, in the task of memory-guided drawing along complex navigational trajectories. The present analysis focuses on a sub-population of the visually impaired – those falling between the sighted and the totally blind, with *severe low vision* specified as having visual acuity of less than 20/500.

Neuroplasticity Driven by the C-K Training

Although there are numerous brain imaging studies in the blind, and many studies on navigation in particular, typically brain data in blind or low-vision individuals are simply compared to those in the sighted on the same experimental task, or a cross-sectional comparisons between categories of blindness. The few studies implementing a longitudinal training paradigm are focused on a specific sensory substitution device, such as the tongue display unit (TDU) (Ptito et al., 2012), or sighted adults under temporal blindfolding (e.g., Merabet et al., 2008). Only the rapid and highly efficient *Cognitive-Kinesthetic* training has made it possible to gain knowledge on the cross-modal learning and neuroplasticity mechanisms involved in the spatial memory and spatiomotor enhancements (Likova 2012; 2013; 2014; 2015; 2017, 2018, 2019, 2021; Cacciamani & Likova, 2016a,b; 2017; Karim et al., 2022).

To establish the role of the motion area hMT+ in the visually impaired brain, we highlight the study by Burton et al. (2004) of cortical activation during a vibrotactile frequency discrimination task in three types of blindness (Fig. 1, left panel). In early blind participants, the predominant activation was in the bilateral anterior parietal ("kinesthetic") area and the supplementary motor area (SMA), with surprisingly weak activation in the hand area of S1 and surprisingly strong activation in the mouth area of S1 and PMC. There was also bilateral activation in hMT+, which is anomalous because there was no motion in the vibrotactile stimulation. Conversely, there was no activation of the established navigation loci in the brain for this discrimination task, emphasizing the task-related specialization of these networks, as opposed to a general attentional-task-related activation. Late blind participants showed a similar pattern of activation in the same study, though now focused on the parietal operculum together with dorsolateral prefrontal cortex (DLPFC). Low vision participants would be expected to show a similar pattern of activation, since they have also had partial vision as their condition deteriorates.

Cortical networks involved in haptic information processing

In the task of traversing a drawing trajectory with a finger or stylus, there is a possible link to the perception of traveling along a trajectory through a visual environment defined by an optical flow field, in that both involve the experience of following a defined trajectory in a conceptual space. Several studies have looked at fMRI blood-oxygen-level dependent (BOLD) activation for navigational optic flow fields in the sighted (Shelton & Gabrieli, 2002; Indovina et al., 2013; Boccia et al., 2015; Ramanoel et al. 2019; Roseblum et al., 2023). Although these studies use different terminology and mapping conventions, with some variation there

seems to be a consensus that flow field navigation activates a network involving the angular gyrus, retrosplenial region, posterior hippocampus, and parahippocampal place area (PPA). (These are in addition to the expected activation of the motion pathway from V1 to hMT+ by the local motion stimulation across the visual field). This network (see Fig. 1, right panel) thus appears to be encoding some combination of the allocentric sense of traveling along a trajectory and of the egocentric sense of self-motion, or vection, which are in common between visual flow-field navigation and the tracing of a raised-line tactile trajectory in the present study.

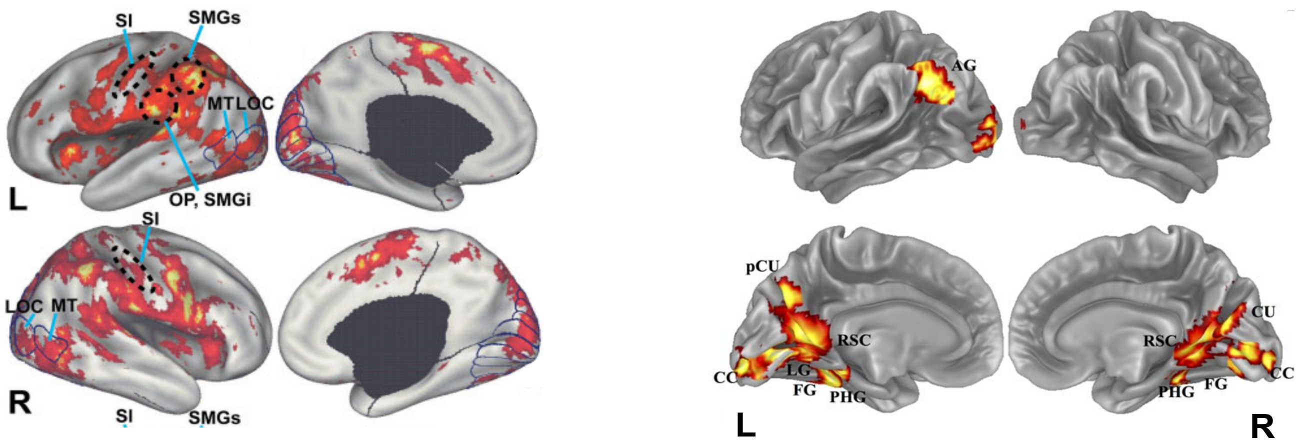

Figure 1. *Left panels: Post-central sulcus and occipital pole activation during vibrotactile discrimination (from Burton et al., 2004. Right panels: V1 and medial retrosplenial activation during mental imaging of familiar environments (from Boccia et al., 2014).*

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Thus, the goal of the present study was to assess the type and overall role of the visual-motion area connectivity in the cases of non-visual haptic exploration and encoding in spatial memory of navigational maps, and of their recall and drawing-from-memory without vision, as learned by the powerful C-K Memory-Guided Drawing method. This assessment involves determining not only which regions of cortex *feed into* or *receive output from* the motion-processing occipital hMT+ cortex, but the *training-induced changes* in the *causal* relationships between these regions and the executive, sensory, motor and bodily representation regions of the brain during the drawing task.

METHODS

Severe Low Vision Participants

The participants were right-handed individuals with form vision of <20/500 acuity in at least one eye, who already relied on either a cane or a guide dog for navigation. All participants gave informed consent for the experimental protocol, as approved by the Smith-Kettlewell Institutional Review Board. Participants were recruited from the local community through flyers, online recruitment ads, word-of-mouth, and the SF Light House for the Blind, and were compensated for their time. All participants were blindfolded through all aspects of the experiment to eliminate any possible visual input.

Navigational Training

As stimuli for the memory-drawing training we used a custom-designed battery of complex tactile raised-line maps of up to 20 segments (Fig. 2A). Through Likova's Cognitive-Kinesthetic Training methodology (Likova, 2012; 2013), the participants were trained how effectively to explore the maps in order to create as accurately as possible *mental* image of an explored tactile map in their memory (see Fig. 2B). Furthermore, they learn how to make these *memories stable*, how to use them for *making navigational decisions*, and how to then use the mental maps for informing motor control for the *successful execution* of respective navigational plans. The Cognitive-Kinesthetic Training is highly effective and efficient – taking only five 2-hr sessions on 5 sequential days. Before and after training we run whole-head functional Magnetic Resonance Imaging (fMRI).

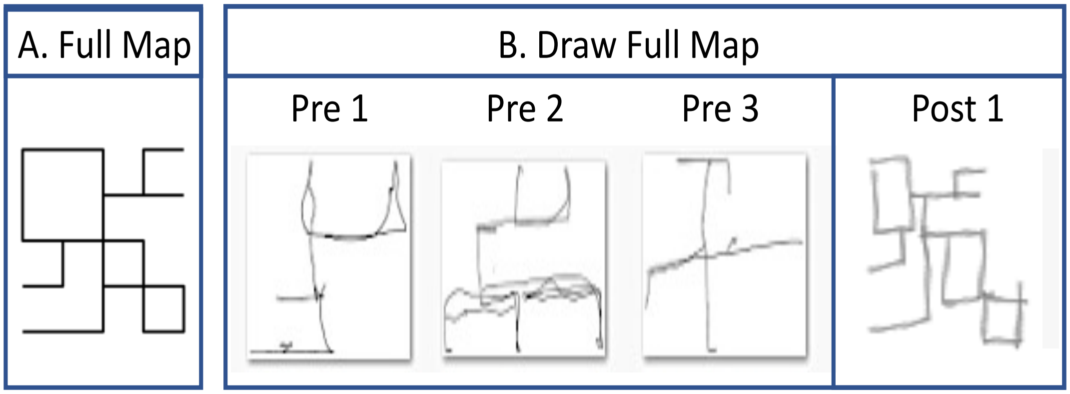

Figure 2. *Examples of navigation learning for drawing-from-haptic-memory a full tactile map through C-K drawing training. A. Sample tactile navigational map. B. The first three attempts (Pre 1-3) by a participant to draw the full map (20 s) after 20s periods of tactile exploration, together with the full map drawn in 20 s after completion of the C-K training (Post 1).*

FMRI experimental design.

The Severe Low Vision subjects underwent five sessions of the Cognitive-Kinesthetic Memory-Drawing Training for spatial navigation. Pre- and post-training, whole-brain scans (Siemens 3T Prisma). The training effect was investigated in a two-task fMRI block paradigm, with interleaved baseline (rest) conditions.

First, in the *Study & Memorize* task, the subject had to tactually explore for 30 sec a raised-line map on the drawing tablet in order to develop a full memory representation of the image in preparation for the *MemoryDraw* task. Then the model image was removed, and the subject rested motionless for 20 s with no image in mind (*RestInterval*), followed by the 30 sec *MemoryDraw* task, during which the subject used a stylus to *draw-from-haptic-memory* the just explored and memorized maps, using the opposite hand; this sequence was repeated three times in each scan for each of the maps. In *MemoryDraw*, a stylus was used to draw the map. The present paper focuses on the training effects in the *MemoryDraw* condition.

FMRI acquisition.

The studies were conducted with a specially-designed drawing lectern that (i) is MRI-compatible, (ii) allows for presenting multiple tactile images in the scanner, (iii) captures and records the drawing trajectory with high precision while the subject is drawing in the scanner, and (iv) is height/distance adjustable.

MR data were collected on a 3T Siemens Prisma scanner equipped with a 64-channel head+neck coil. BOLD responses were obtained using an EPI acquisition (TR = 2 s, TE = 30 ms, flip angle = 45, voxel size = 2.5 x 2.5 x 2.5 mm) consisting of 54 axial slices extending across the whole brain. To facilitate segmentation and registration, a whole-brain high-resolution T1-weighted anatomical scan was also obtained for each participant (voxel size = 0.8 x 0.8 x 0.8 mm). White matter segmentation in this T1 scan was conducted using FreeSurfer and gray matter was generated with the mrGray function in the mrVISTA software package.

FMRI time-course analyses.

The data were averaged from the individual participant brains into the Montreal Neurological Institute (MNI) average of 305 individuals (http://nist.mni.mcgill.ca/?p=957). And analyzed with the Stanford VISTA Lab software. The effective neural activation amplitudes for each task across the repeats of multi-task sequences in the 2 hr scan were estimated by the following procedure. A General Linear Model (GLM) consisting of boxcar neural task activations and an auditory stimulus regressor was convolved with a default canonical hemodynamic response function (HRF) from software package SPM and fitted to the blood-oxygen-level-dependent (BOLD) responses, together with a 4th order polynomial to remove baseline trends. BOLD amplitudes were defined as “task-positive” or “task-negative” according to the sign of the GLM beta fit. Individual voxel significances were assessed relative to the residual noise over the TR samples after removing the full GLM fits.

Granger Causality Analysis Procedures.

For the whole-cortex GC analysis of the connectivity of hMT+ in each hemisphere, causal influences to hMT+ from each cortical voxel, and from hMT+ to each cortical voxel, were computed through the brain. For each voxel-ROI pair, autoregressive models were fitted using ordinary least squares regression, incorporating prior time points from both the voxel and ROI time series. The analysis outputs standardized regression coefficients (z-scores) for the cross-lagged terms, which indicate the strength and direction of significant causal influence.

RESULTS

Whole-brain activation during haptic navigational memory-drawing

The C-K navigational training had a strong impact on the whole-brain activation. Before training, the *MemoryDraw* task showed strong activation in the regions of the Pre- & Post-Central Sulci, the left Insula and the Supplementary Motor Areas. These are motor control and kinesthetic feedback regions that are expected to be involved in an advanced motor coordination task. There was also a weak activation in the anterior calcarine sulcus. After the training, this pattern of motor control and kinesthetic activation greatly strengthened to full bilateral involvement, with the addition of the right Dorsolateral PreFrontal Gyrus (DLPFC), Anterior Calcarine Sulcus, and PreCuneus. The medial activation also expanded to the full medial occipital lobes and the retrosplenial and parahipppocampal regions. Thus, in addition to enhancing the motor control and kinesthetic feedback functions, the training recruited areas for both conscious executive control functions and spatial representation regions that are involved in spatial memory recall.

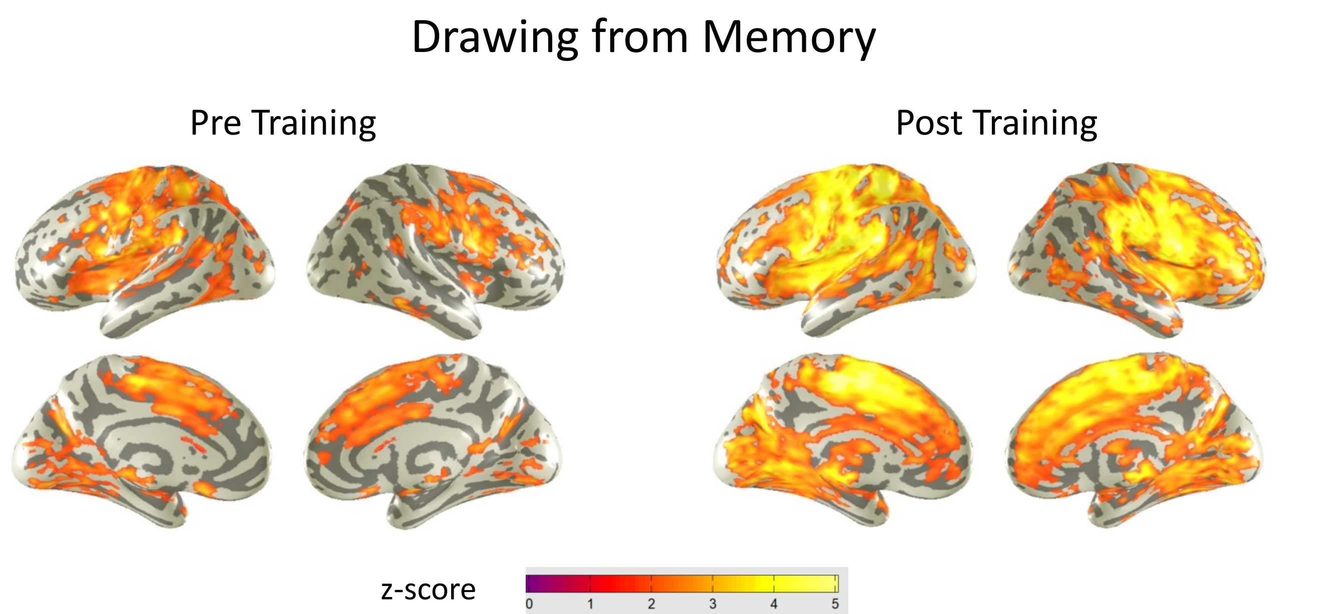

Figure 3. *Whole-brain activation during the MemoryDraw task before (left) and after (right) training. Activation threshold was z = 1.8 (p < 0.035).*

Activation of the motion area during haptic navigational memory-drawing

The stimulation structure consisted of three pairs of alternating epochs of haptic exploration and memorization of raised-line tactile maps with the left hand, and stylus-based haptic memory-guided drawing of the explored map with the right hand, interposed with rest periods (see Methods). During the non-visual memory-guided drawing of the navigational maps after the training, average BOLD activation of the severe low vision participants (Fig. 3) showed the unexpected result of a strong *hemispheric lateralization* in the occipitotemporal visual motion-related area, as defined from the Freesurfer atlas (Fig. 4, upper panels). The left hemisphere had only weak activation during the haptic exploration tasks, but a pronounced response during the memory-guided drawing tasks. In the right hemisphere, on the other hand, its responses were about equal during the two tasks (Fig. 4, lower panels). The focus of the present paper is the whole-cortex analysis of the *inputs to* and *outputs from* the respective motion areas during the present *haptic-memory-drawing* paradigm in a group of *blindfolded* participants with *severe low vision* (but able to process motion, at least in the peripheral visual field).

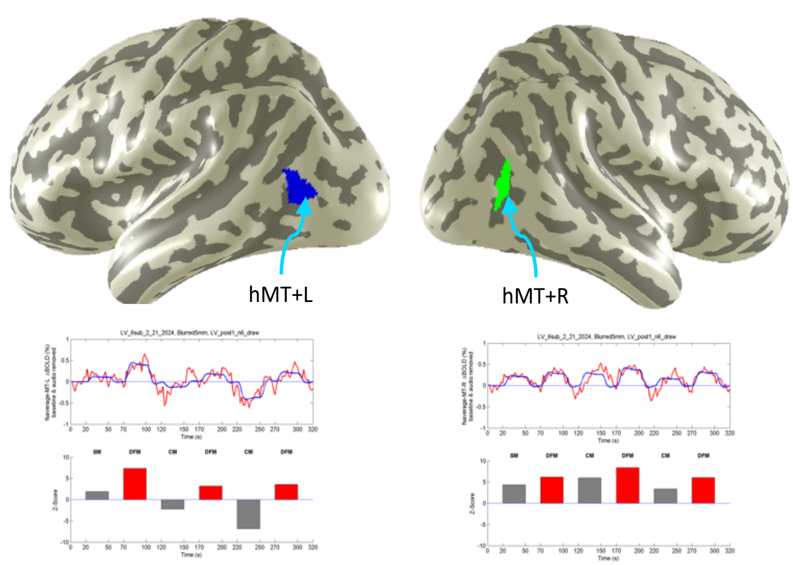

Figure 4. *Average repeats of the activation of the left (blue) and right (green) hMT+ ROIs for the Study&Memorize (gray bars) and MemoryDraw (red bars) experimental tasks for the group of severe low vision participants after training in memory-guided drawing. The pattern of results roughly replicates the asymmetry found for the same pair of training tasks in totally blind individuals, indicating that the asymmetry is not a result of the loss of form vision.*

GC connectivity of the visual motion complex hMT+ during the haptic memory-drawing task

A whole brain Granger Causal (GC) connectivity analysis ***to*** and ***from*** area hMT+ in the right and left hemispheres was performed, using a lag or a lead of one fMRI TR of 2 s in the autoregressive Granger-Causal equations at a threshold of 85% of the z-score distributions in each direction of influence (Fig. 5). The lag analysis determines which brain voxels have a causal effect on the hMT+ ROI, while the lead analysis determines which brain voxels are influenced by the signal deriving from hMT+. The results show a remarkable plasticity in the patterns of whole-brain directional influences **to** and **from** hMT+ during this entirely non-visual memory-drawing task, as depicted in Fig. 5.

In severe low vision, the causal influences to hMT+ (green coloration) before training derive largely from the posterior frontal cortex and the marginal gyrus in both hemispheres, with additional input from the post-central sulcus that is identifiable as the kinesthetic sensory area and the insula that houses the proprioceptive body representation. With training, this pattern of influences remains essentially unchanged.

On the other hand, the cortical regions influenced by the hMT+ activation (red coloration) are radically reorganized by the training regimen. Before training, only right hMT+ sends out significant influences, and does so mainly locally to neighboring lateral occipital cortex, and also to ipsilateral precuneus and mid-cingulate regions. The training greatly enhances the influence of hMT+ bilaterally to a powerful causal connectivity throughout the occipital lobe of the right hemisphere, including primary visual cortex and the posterior intraparietal regions encoding 3D depth structure. These influences extend to the retrosplenial navigation center in the right hemisphere. The training also incites each hMT+ to send novel bilateral influences to frontal cortical regions of the executive control centers in the dorsolateral prefrontal cortex (DLPFC) and to some premotor regions.

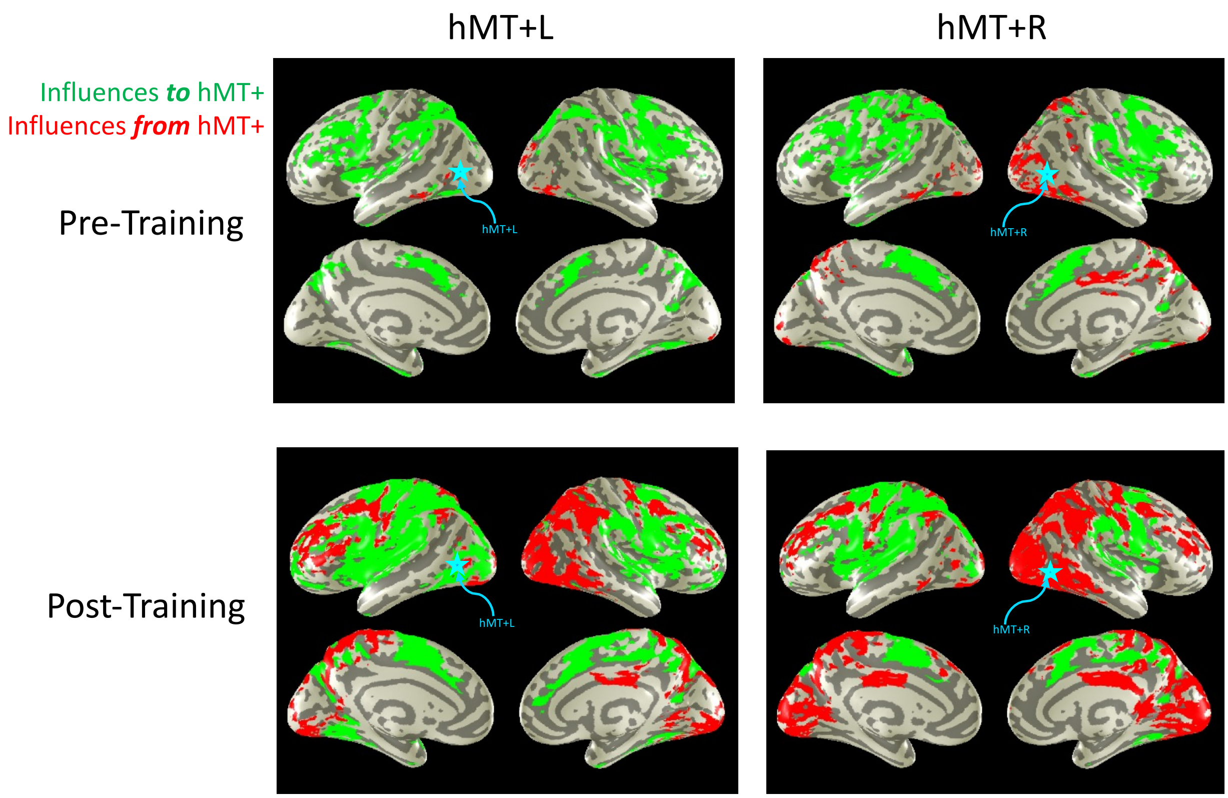

Figure 5. *Post-training Granger-causal whole-brain connectivity maps of **input to** (green coloration) and **output from** (red coloration) motion area hMT+ in each hemisphere (cyan stars) for a representative participant.*

In summary, before training the hMT+ regions are heavily influenced by the brain activation circuitry required to access the memory of the trajectory to be drawn and perform the controlled haptic drawing movements to complete the trajectory. This involvement is controlled predominantly by pre- and post-central cortex before training, suggesting multisensory input to process the stylus motion.

Output from hMT+, on the other hand, is quite weak before training, expanding to areas involved in visualization and visual representation, on which individuals with low vision must increasingly rely to substitute for their loss of detail vision. The extra posterior medial hemisphere targets of right hMT+, which are a part of the "intrinsic" system, may suggest that it is more involved in the internal awareness (the sense of the self as navigating through the map), rather than of the task control demands that are associated with the "extrinsic" system of the awareness of the external environment (Vanhaudenhuyse et al., 2011).

DISCUSSION

The hMT+ connectivity results make it evident that the drawing process in the task of full-reconstruction of the navigational-map guided solely by memory requires an extensive synchronization throughout the brain, which is successfully developed through the five-day two-hour complex interactive procedure of the Likova C-K training (e.g., Likova (2012, 2013, 2014, 2016, 2017, 2018; Likova et al., 2019, 2021). Remarkably, following this training, individuals with severe low vision were able to learn how to effectively develop accurate and robust internal representations, and how to externalize them through the precise spatiomotor control of drawing the complete images of tactilely-explored maps with as many as 20 segments in as little as 30 s.

The present study focused on the role of the (nominally visual) motion-processing complex hMT+, which should be of key significance in this group of severe low vision participants, showed strong BOLD activation in the map-drawing task, with differential patterns of activation in the two hemispheres (Fig. 4). While the right hemisphere hMT+ was strongly involved in both the tactile exploration/memory encoding and the memory-drawing of the maps, its left hemisphere counterpart was almost exclusively involved in the task of the drawing per se. There is thus a profound functional asymmetry in the way that hMT+ operates, along with an extensive network of motor control, kinesthetic feedback and spatial representation regions of the cerebral cortex.

The motion area involvement on the haptic memory-guided drawing task shows that it does not only process visual information, but movement representations from any sensory input. In the present study, the cortical inputs to hMT+ before training suggest a predominance of multisensory input to process the motion of the drawing stylus. Output from the motion area before training, on the other hand, was minimal, shifting after training to a large swath of areas involved in mental-visualization and mental representation (on which individuals with low vision must increasingly rely to substitute for their loss of detail vision), together with input to the prefrontal control mechanisms after training.

CONCLUSION

These multidimensional results from cortical activation and causal connectivity analyses illuminate the non-visual roles of the human motion area hMT+, revealing novel patterns of interhemispheric asymmetry. They underscore how memory-guided learning drives functional reorganization of brain architecture. Together, the findings point to a previously unrecognized mechanism of rapid cross-modal reorganization and provide critical insights into neuroplasticity and sensory compensation under conditions of severe visual input deprivation.

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AUTHOR BIOGRAPHIES

Lora Likova, Ph.D., *has a multidisciplinary background that encompasses studies in cognitive neuroscience and computer science, with patents in the field of magnetic physics and many years of experience in brain imaging, brain plasticity, human vision, and neurorehabilitation research. Her work was the first to identify the cortical mechanism of dynamic depth perception using fMRI, a discovery that has been instrumental in opening a new field in binocular motion research. In the field of enhancing memory and learning, Dr. Likova has developed a paradigmatically novel training technique – The Cognitive-Kinesthetic Training, based on drawing from memory, which has shown dramatic behavioral and causal brain reorganization effects in a range of cognitive and spatio-motor domains. It is highly effective in enhancing brain plasticity even in late adulthood, and has shown tremendous potential as a neurorehabilitative intervention across neurological dysfunctions in the blind, low vision and the sighted. Dr. Likova leads an NIH Clinical Trial based her Cognitive-Kinesthetic Training in the blind and visually impaired. She led an International Collaborative Network applying her training to improve STEM education in the sighted. She is the Director of "Brain Plasticity, Learning & Neurorehabilitation Lab" at Smith-Kettlewell Eye Research Institute in San Francisco. Dr. Likova is a long-standing member of the HVEI Organizing Committee.*

Kristyo Mineff, M.Eng. *was an engineer and a former TV host, who served as a Director and Board Member of several engineering companies. Before his untimely death he devoted his time to implementing a wide range of brain imaging methodologies to advanced applications in neuroplasticity and blindness rehabilitation. He was particularly focused on unravelling the principles underlying the function and architecture of complex dynamic systems such as the human brain.*

Zhangziyi Zhou. M.S. *is a research data analyst at the Smith-Kettlewell Eye Research Institute Brain Imaging Center. He has a M.S. in Magnetic Resonance Imaging in Medicine from Cedars-Sinai Medical Center, and a B.S. in Physics from Rutgers University. His expertise is in MR physics and signal processing, and is responsible for analyzing various neuroimaging data types, including functional MRI, EEG, and electroretinograms.*

Michael Liang, M.S.(K), *is a Research Assistant over at Smith-Kettlewell Eye Research Institute working in the Likova and Tyler labs. He has a B.S. degree in Kinesiology concentrated in Exercise Science from California Polytechnic State University, San Luis Obispo. He is knowledgeable in movement science and rehabilitation. In the labs at Smith-Kettlewell Eye Research Institute, he conducts and manages the study testing and training along with AI-inspired data analyses.*

Christopher W. Tyler, Ph.D., D.Sc., *is Head of the Brain Imaging Center of the Smith-Kettlewell Eye Research Institute in San Francisco, specializing in visual, cognitive and rehabilitation research. His research career is in visual neuroscience and computational vision with emphasis on form, symmetry, flicker, motion, color, and stereoscopic depth perception in adults and tests for the diagnosis of eye diseases in infants and of retinal and optic nerve diseases in adults. His particular interest is the cortical mechanisms involved in the stereoscopic processing of 3D images, including his origination of the general algorithm for the random-dot autostereogram method of presenting 3D information in a single image rather than a stereopair. He developed a rapid method of recording brain responses across a wide range of conditions (the "sweep VEP") in only 10 seconds. He has recently been developing advanced non-invasive methods for estimating the neural signal dynamics and evaluating deficits of the ERG and motor control of eye movements in individuals with Traumatic Brain Injury. He has received support for his research through many federal agencies and has international research collaborations as far afield as the UK, France, Australia, Germany, Israel, India and Taiwan. He is a long-standing member of the HVEI Organizing Committee.*