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DISSERTATION

Cortical Activity Evoked by Mirroring of Hand Movement in Healthy Subjects and Stroke Patients

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Abbreviations

ADL	activities of daily living
ANOVA	analysis of variance
BA	Brodmann area
CRPS	complex regional pain syndrome
CT	Computed Tomography
CI	confidence interval
D test	Kolmogorov-Smirnov test after Lilliefors Significance Correction
EMG	Electromyography
EPI	echo-planar imaging
fMRI	functional magnetic resonance imaging
FWHM	full width half maximum
FDR	false discovery rate
IQR	interquartile range
LH	left hand
LCD	liquid crystal display
MT	mirror therapy
MOT	movement observation therapy
MNS	mirror neuron system
MRI	Magnetic Resonance Imaging
MEPs	motor evoked potentials
MIR	mirrored
MNI	Montreal Neurological Institute
NOR	normal
PC	precuneus
RH	right hand
SPM	statistical parametric mapping software package
TAP	Test of Attentional Performance
TR	repetition time
TE	echo time
VT	video therapy

1 Introduction

Stroke is one of the leading causes for death and permanent disability.[1] According to data from the 2010 Behavioral Risk Factor Surveillance System (Centers for Disease Control and Prevention),[2] 2.6% of men and 2.6% of women (⩾18 years of age) had a history of stroke; 2.4% of non-Hispanic whites, 4.0% of non-Hispanic blacks, 1.4% of Asian / Pacific Islanders, 2.5% of Hispanics (of any race), 5.8% of American Indian / Alaska Natives, and 4.1% of other races or multiracial people had a history of stroke.

There are approximately 795,000 individuals who survive stroke every year in the United States, nearly 70% of whom present physical and / or psychological residual limitations.[2] Among different disabilities after stroke, impairment of upper limb function is one of the most common and difficult issues to treat. However, only 5% to 20% of upper limb paralysis demonstrated completely functional recovery,[3, 4] and in 38% of hemiplegic stroke patients, the paretic upper extremities could be only partly improved.[5] Even though the initial severity of upper extremity paresis has been considered as one of the most important predictors for long-term functional recovery following stroke by far, the therapeutic outcome of upper limb recovery may be influenced by different therapeutic interventions.[4, 6, 7]

On the basis of brain plasticity, the traditional rehabilitation techniques to improve upper limb function in hemiplegic stroke patients mainly focus on therapeutic interventions aiming at stimulating the use of the paretic upper limb in supervised training tasks, including the active movement relearning strategies and passive processes of lesion adaptation. Various rehabilitation approaches, such as repetitive active arm training,[8] repetitive passive sensorimotor stimulation therapy,[9] constraint-induced movement therapy,[10-12] electrical muscle stimulation training,[13] electromechanical and robot-assisted arm training,[14] were applied to facilitate the recovery of upper extremity dysfunction.

The basic principle of aforementioned rehabilitation therapies is the repetitive practice of active / passive movements by a paretic upper limb. However, some of these active training strategies, namely repetitive active arm training, constraint-induced movement therapy, and robot-assisted arm training, require some degree of independent movement of the affected upper extremity. Therefore these approaches based on active movement of paretic upper limb are inapplicable for stroke patients with severe upper limb paresis. Therefore, the conventional strategies in improving upper extremity function severely affected by stroke showed only limited outcomes.[15] As an alternative to conventional rehabilitation therapeutic strategies, primarily built upon actual movement of the affected upper extremity, the visual stimulation strategies, such as mirror therapy (MT) and movement observation therapy (MOT, also called video therapy, VT), recently have shown promising therapeutic effects on facilitating recovery of upper limb dysfunction in hemiplegic stroke patients.[16-19]

1.1 MT

1.1.1 Application of MT in pathological conditions

MT has been proposed as a beneficial therapeutic strategy in different clinical fields. It was originally demonstrated by Ramachandran and co-workers to relieve phantom limb pain in arm amputees.[20] Since then, the positive effects of MT were demonstrated in patients with other pain related syndrome such as fibromyalgia[21] and complex regional pain syndromes (CRPS),[22-26] in which the reduction of pain and improvement of functional disability were showed by mirroring movements following imagination.[23] MT has also been recommended as one of the advantageous rehabilitation interventions to improve the upper extremity functional recovery in hemiparetic stroke patients,[16, 17, 27-30] even in stroke patients with severe upper extremity dysfunction.[16]

During MT, a mirror is oriented parallel to the midline in such a way that movements of the non-affected limb appear as movements of the affected one. Through this strategy, movements of the non-paretic limb evoke the visual illusion of movements of the paretic limb, which was called mirror illusion, whereas movements of the non-affected limb appear in the mirror were described as movement mirroring. The possible advantages of MT are the relatively easy administration using simple equipment and the possibility of self-administered home therapy even for patients with severe motor dysfunction.

Various protocols were applied during MT in different studies. For example, the affected limb was encouraged to move on its own,[16, 17, 30] movements of the affected limb were supervised and controlled by the therapist,[29] or the unaffected limb was requested to perform movements, and simultaneously the patient was asked to watch the movement of the unaffected limb in the mirror which he perceived as the affected limb due to the visual illusion.[26, 31] The glass mirror was generally placed in the subject's midsagittal plane to block the view of the affected limb positioned behind the mirror. In recent studies, mirror-like video or computer graphic setups were proposed to create a similar illusion. Reflection of the moving limb by a video or computer graphic image gave also the impression as if the non-moving limb would move.[32-36]

1.1.2 Neural mechanisms of MT

In spite of these promising results, the underlying mechanisms of MT are not yet expounded explicitly. The mirror neuron system (MNS) was speculated to be one of the underlying neural mechanisms of MT.[17, 37] Mirror neurons discharge not only when actually performing an action, but also while observing a similar action made by others and even during mental practice of motor tasks.[38-41] It was described that mirror neurons, located in the ventral and inferior premotor cortex active during observation and imitation of movements, are responsible for these effects.[42, 43] In addition, increased self-awareness and spatial attention via activation of the superior temporal gyrus, precuneus and the posterior cingulate cortex have also been proposed as one of the potential working mechanisms of MT.[34, 44, 45] Until now, there is still a lack of direct evidence for the mirror-related recruitment of MNS during MT.[46] Dohle and his colleagues found no activations in MNS during movement mirroring, but the precuneus and primary visual areas could be activated contralateral to the perceived limb.[33, 34] Furthermore, Matthys and co-workers reported activation changes in the right superior occipital gyrus during movement mirroring, but no changes were indicated in MNS activation pattern, either.[45] Thus, there is no final agreement yet on the link of MT with MNS in healthy subjects.

Effects of the mirror illusion of movement on brain activity in stroke patients are even less understood. Activations in ipsilateral primary motor cortex (M1) and outer parts of the cerebellum were elicited during movement mirroring.[47] However, the same results could not be shown during unimanual mirroring movements , and activities in precuneus and posterior cingulated cortex appeared only during bimanual mirroring movements.[44] It has to be considered, however, that both studies mentioned above used real mirrors which provided the image of two simultaneously moving hands in the mirror condition. Consequently there is also no consistent conclusion regarding the cerebral activation patterns in stroke patients during mirroring movement. To our knowledge, no study comparing the cerebral activation pattern of normal subjects and stroke patients was reported.

In conclusion, there are no congruent findings of cerebral activation induced by the mirror illusion either in healthy subjects or in stroke patients. This is surprising, considering the beneficial effects found in clinical studies of stroke patients with severe arm paresis. A possible explanation could be that the majority of the studies mentioned above reported group data, and not inter-individual differences between individual healthy subjects and stroke participants. It might be that the inter-individual differences between individual stroke patients and healthy subjects degraded the false-negative from a group analysis and could thus explain the difference of cerebral activation between healthy subjects and stroke patients. Therefore, we performed the following functional magnetic resonance imaging (fMRI) study in order to compare the neural activation pattern during a mirror-like visual illusion of hand movements between healthy and stroke participants on the basis of individual subjects.

1.2 MOT

1.2.1 Clinical application of MOT

With increasing experimental evidence of the existence of MNS in humans, MOT based on visual stimulation was suggested as a new therapeutic strategy to improve motor dysfunction and activities of daily life in patients. While performing MOT, patients are required to watch carefully movements executed by another person (video sequences), which is called movement observation, and to imitate the observed action using the affected limb afterwards, (movement imitation). Positive effects of MOT on motor dysfunction could be shown in patients with moderate and chronic hemiplegia after stroke,[18, 19, 48, 49] Parkinson's Disease,[50] and children with cerebral palsy.[51]

1.2.2 Neural mechanisms of MOT

Compared with MT, pure observation especially of meaningful actions could evoke activation of MNS located in bilateral fronto-parietal circuits.[52, 53] These bimodal neurons were first discovered in primates.[43, 54] It was also confirmed that MNS could be activated in humans during observation of executed actions.[55-58] Imaging studies demonstrated shared motor representations for movement execution and movement observation, but the degree of lateralization in humans for these processes is less clear.[59]

The effects of visual feedback and the actual motor performance on cerebral activation can be separated by visual inversion, i.e. movement mirroring. By this approach, the precuneus and “lower” visual areas were shown to be activated strictly contralateral to the perceived limb,[33, 34] which demonstrated a clear lateralisation during self-initiated movements. However, there is no study to show differences regarding degree of lateralised cerebral activation in humans between movement mirroring and movement observation, which would explain the difference of working mechanisms between MT and MOT.

Furthermore, the semantic analogy frequently leads to the attribution of MT to the function of the MNS, which implies shared working mechanisms of MT and MOT, but this could never be demonstrated explicitly, as explained in the section on mechanisms of MT. A precise understanding of these processes of MT and MOT is of high clinical relevance. In order to answer these questions, we designed the imaging study in human subjects to directly compare movement mirroring and movement observation in an otherwise identical design.

1.3 Aim of this study

The main goal of this study was to investigate the effects of movement mirroring on cerebral activity compared with those of movement observation, and further to explore the related regions and patterns of cerebral activations evoked by movement mirroring in both healthy and stroke participants.

In order to achieve this goal, the data would be evaluated through (1) comparing the differences of cerebral activation between movement mirroring and movement observation in healthy subjects, (2) locating the brain activities elicited by movement mirroring according to the anatomy toolbox in healthy individuals and stroke patients, (3) comparing the neural activation patterns between healthy subjects and stroke patients during movement mirroring on the basis of individual subjects in both healthy and stroke participants.

2 Methods

2.1 Ethics

The study was approved by the Ethics Committee of the Charité – Universitätsmedizin Berlin and all participants gave informed consent prior to the experiment.

2.2 Participants

2.2.1 Healthy subjects

Eighteen healthy volunteers participated in this study. Three individuals were excluded from the final analysis because of excessive artifacts, leaving fifteen healthy subjects for final analysis (six females and nine males; range 22 - 56 years old; mean age 33.7 years). All participants were free of neurological or psychiatric diseases. All of them were screened for use of eyeglasses and correction glasses in the googles (VisuaStim Digital, Resonance Technology, Inc) were used if needed so that they had normal or corrected-to-normal visual acuity. And each healthy participant was right-handed as verified by the German version of the Edinburgh Handedness Inventory.[60]

2.2.2 Patients

Stroke patients with severe arm paresis were recruited among the inpatient population of the rehabilitation department at the MEDIAN Klinik Berlin - Kladow from August 2010 to August 2011. During the recruitment period, five patients (four males, one female; range 50 - 72 years old; mean age 61 years) fulfilled the criteria and participated in the study.

2.2.2.1 Inclusion criteria

Patients had to suffer from a first ever unilateral ischemic stroke confirmed by Computed Tomography (CT) and / or Magnetic Resonance Imaging (MRI) scan resulting in severe arm paresis with an active wrist extension ability of less than 20 degrees and an active metacarpophalangeal joint extension ability of less than 10 degrees. All of them had to be able to follow the instructions and be capable of bearing the fMRI testing of 30 minutes duration. Each patient was inspected for use of eyeglasses and corrective glasses in the googles were used if necessary in order to make sure all of them had normal or corrected-to-normal vision.

2.2.2.2 Exclusion criteria

Patients were excluded if they had experienced previous strokes, presented orthopaedic, rheumatic or other diseases corrupting their ability to move the non-affected upper limb, wear implanted electronic devices, e.g. cardiac pacemaker, or present intracranial metal particles, e.g. aneurysm clips.

2.2.2.3 Clinical assessments

Upper extremity motor subscale of the Fugl-Meyer assessment was used to measure motor function, consisting of finger, hand, and arm function measurements,[61] leaving out the reflex and coordination items due to its poor psychometric properties.[62, 63] Ability in activities of daily living (ADL) was assessed by the 100 points Barthel Index[64] recorded by an experienced nurse who knew the patient from daily ward routine. Motor evoked potentials (MEPs) at the affected side were elicited using a flat coil and a stimulator (MAGSTIM 200, Novametrix Medical Systems, USA) and recorded at the fist dorsal interosseus muscle via surface Electromyography (EMG) recording machine (Medtronic Keypoint V5.06, Medtronic A/S, Skovlunde, Denmark). For assessment of hemiinattention, the Test of Attentional Performance (TAP Version 2.2, Psytest, Herzogenrath, Germany) was applied.[65]

2.4 Experimental design

2.4.1 Setup of the experiment

The experimental paradigm was based on a previous study.[33] The basic task was the performance of an index finger-thumb opposition movement with either the right hand

(RH) or left hand (LH) held above waist level. The hand was filmed from outside the scanner by a video camera (Leutron Vision, Leutron Vision AG) and projected on-line on liquid crystal display (LCD) goggles worn by the subjects. Subjects could not observe their hand directly, but viewed movements of the hand via the goggles. By means of a software package (Leutron Vision software, Version 1.91, Leutron Vision AG), the image of the hand could be inverted horizontally, thus creating the image of a normal (NOR) or mirrored (MIR) moving hand. For example, in condition of RH MIR, subjects moved their right hand which appeared to them as a left hand movement (Figure 1). In addition to this replication of the previous study, a second condition was introduced requiring movement observation without actual movement performance. For both protocols, the length of one sequence of finger movements as well as the corresponding rest conditions with static images was set to 20 seconds (10 scans).

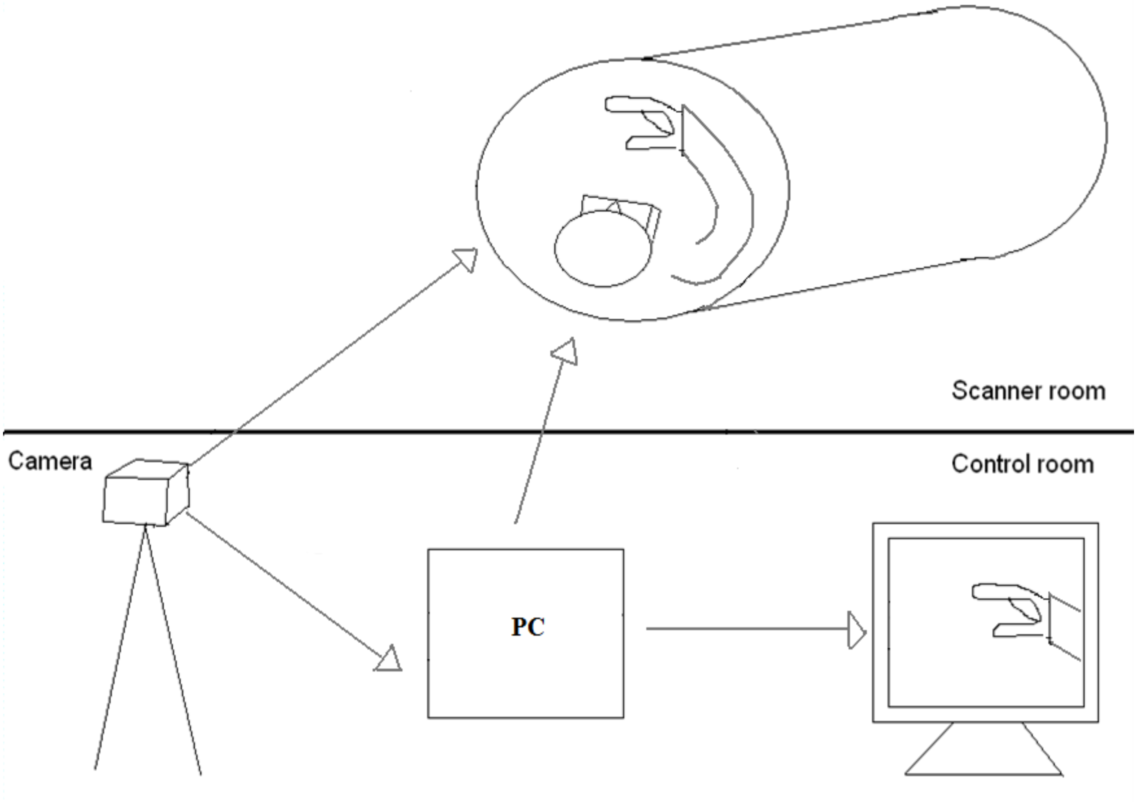

Figure 1. Experimental design. The subject’s hand is filmed from outside the scanner by a video camera. The image is processed by the personal computer software and projected on-line on LCD goggles worn by the subject. PC, personal computer. LCD, liquid crystal display.

2.4.2 Protocol for healthy subjects

Using this setup, the following protocols were performed in normal subjects (Table 1). At the beginning, all healthy participants were presented a video clip showing a sequence of index finger-thumb opposition movements which had to be imitated afterwards. During actual fMRI scanning, healthy participants received verbal instructions through MR-compatible headphones with a “start” signal for performing these movements and a “stop” signal for resting.

Table 1. Experimental conditions

Motor Activity	Visual Perception	
	LH	RH
LH	LH NOR	LH MIR
RH	RH MIR	RH NOR
OBS	LH OBS	RH OBS

RH, right hand; LH, left hand; MIR, mirror condition; NOR, normal condition; OBS: movement observation.

For movement mirroring, subjects had to either hold the hand asked static or perform an index finger-thumb opposition movement. In 50 per cent of the trials, the visual feedback was inverted, leading to the image of a normal or mirrored hand. This resulted in a total number of four conditions (NOR static, NOR moved, MIR static, MIR moved) for either hand. For each hand, seven sequences of 20 seconds (10 scans) length of each of the four conditions were arranged in a pseudo-randomized protocol.

For movement observation, seven video clips of 20 seconds’ length displaying index finger-thumb opposition movements of somebody else’s hand in an identical position (OBS) were demonstrated which had to be performed for 20 seconds afterwards, followed by a 20 seconds’ pause condition while subjects watched the image of a static hand. In all protocols, one scan (2 seconds) was interleaved between each sequence for verbal command and reaction to it which was not included in the analysis. Both protocols were performed for RH and LH separately, leading to four protocol blocks. Order of execution and observation protocols and order of hands were pseudo-randomized across all subjects. These protocols were followed by an imagery task and a resting state scan which were not included in the present analysis.

In order to test our hypothesis, only those six conditions with the visual image of an active hand movement were analyzed, forming a 2 x 3 factorial design (Table 1). In condition LH (RH) NOR, subjects moved their left (right) hand which appeared identical. During condition LH (RH) MIR, subjects were asked to move their left (right) hand which appeared as a right (left) hand. During condition LH (RH) OBS, subjects watched the movements of somebody else's left (right) hand in order to imitate them afterwards. Each condition consisted of seven segments of 20 seconds (10 scans), totalling 140 seconds (70 scans) each.

2.4.3 Protocol for stroke patients

The scan sequence of stroke patients consisted of 14 movement blocks and 14 rest blocks (10 scans / block, 2s / scan), arranged in a pseudo-randomized order. During the movement (MOV) blocks, patients were asked to perform the index finger-thumb opposition sequence as presented in the video. During the rest blocks, the hand had to be held still. In 50 per cent of the trials, the visual feedback was inverted, leading to the image of a normal or mirrored hand, resulting in the 7 repetitions of each condition within the protocol. The addition of two seconds (1 scan) for each verbal command and 20 seconds (10 scans) to achieve a steady state at the beginning of the experiment resulted in a total scanning time of 634 seconds (317 scans). Patients performed the above mentioned movement with their non-affected hands only. For both healthy subjects and patients, a structural image (FLAIR, T1) was acquired after the functional images.

2.5 Data collection

2.5.1 Count of finger movements

The numbers of index finger-thumb opposition movements actually perceived or performed by healthy participants during each condition were video-taped and counted afterwards. For correlation with imaging data, the median value of seven movements was used for each individual subject.

2.5.2 Mirror illusion questionnaire

A questionnaire from our lab consisting of a total number of sixteen questions was delivered to the healthy subjects after the entire experimental protocol. In the following analysis, the questions related to the mirror illusion ("How strong was the mirror illusion while watching the moving right / left hand?") were included in the study. The scale of the question ranged from 0 to 6 (0 representing denial of mirror illusion, 6 representing a very strongly perceived mirror illusion).

2.5.3 Image acquisition

Images were acquired on a 3T MRI Scanner (Siemens MAGNETOM Trio, a Tim system, syngo MR B15) at the Charité – Universitätsmedizin Berlin, Campus Benjamin Franklin, using a 12-channel head matrix coil (Magnetom Tim Trio, Siemens, Erlangen, Germany). For functional imaging, a BOLD-weighted fast gradient echo-planar imaging (EPI) sequence was used (TR / TE = 2000 ms / 25 ms, flip angle: 90°, voxel resolution: 3 x 3 x 3 mm, no gap). For anatomical reference, images obtained after the functional images, a high-resolution 3-dimensional gradient echo inversion T1-weighted image was acquired (MPRAGE, TR / TE = 2000 ms / 2.52 ms, flip angle: 9°, voxel resolution: 1 x 1 x 1 mm, no gap). The functional imaging volume covered the whole brain, excluding the cerebellum.

2.6 Data analyses

2.6.1 Functional image data processing

2.6.1.1 Preprocessing

The functional images were analyzed using the statistical parametric mapping software package (SPM-8, Wellcome Department of Cognitive Neurology, University College London, London) implemented in Matlab 7.5 (The Mathworks, Natick, Massachusetts, USA). For achievement of a steady state, the first 10 scans of each condition were discarded. All images were realigned to remove head movement artefacts, and then coregistered with the corresponding anatomical (T1-weighted) images. For normal subjects, the segmentation-based normalization was used to normalize the images to the standard space. The normalized images were spatially smoothed with a Gaussian filter (full width half maximum， FWHM = 8 mm) to produce final images. Patient images were not normalized due to the lesions.

2.6.1.2 Comparison of movement mirroring and observation in healthy subjects

T-contrasts were calculated between those conditions only differing by the visual feedback, i.e. between MIR and NOR with either hand (RH MIR MOV vs. RH NOR MOV and vice versa, LH MIR MOV vs. LH NOR MOV and vice versa), and between movement observation of both hands (RH OBS vs. LH OBS and vice versa). P values < 0.01 (false discovery rate, FDR) with a minimum cluster size of 20 voxels were considered as statistically significant. The SPM anatomy toolbox was used to label the observed activations.[66, 67] As direct comparison between movement execution and movement observation was confounded by motor activity, an additional effect of interest analysis at both precunei was performed, based on a 3 x 2 analysis of variance (ANOVA) with the factors “motor activity” and “visual feedback” as stated in Table 1.

2.6.1.3 Comparison of image data in individual healthy subjects and stroke patients

T-contrasts were employed to compare activation differences between MIR and NOR with either hand (RH MIR MOV vs. RH NOR MOV and vice versa, LH MIR MOV vs. LH NOR MOV and vice versa) in each individual healthy subject and stroke patient. The significance threshold was set at $P < 0.001$ (uncorrected). As previous study highlighted the prominent role of the precuneus of either hemisphere for representation of visual body configuration,[33] the peak T value at the precuneus, as defined by anatomical criteria,[68] was calculated for both normal subjects and patients and served as measure of strength of activation.

2.6.2 Statistical analysis

Statistical analysis was performed with the SPSS software for windows version 18 (SPSS Inc, Chicago, USA). As Kolmogorov-Smirnov test after Lilliefors Significance Correction (D test) revealed non-normal distribution for index finger-thumb opposition movements, T values at the precuneus and results of the questionnaire, non-parametrical tests were applied throughout the analysis. The Friedman test was applied to test for significant differences between the conditions of finger movement. For T values at the precuneus for the comparisons MIR MOV > NOR MOV and NOR MOV > MIR MOV in normal subjects, 95% confidence interval (95%CI) were calculated for RH and LH separately, using a value of 0.0 for non-significant differences between both conditions. The Spearman correlation test was applied to evaluate relationships between T value at the precuneus and finger movement speed / mirror illusion questionnaire / age of subjects, and the Wilcoxon signed-rank test was applied to test for significant differences. For each test, significance threshold was set at $P < 0.05$.

3 Results

3.1 Demographic data and characteristics of patients

The clinical characteristics of stroke patients are shown in Table 2 and locations of their lesions are depicted in Figure 2.

Table 2. Demographic data and characteristics of patients

Variable	Value				
Patient number	P 1	P 2	P 3	P 4	P 5
Age (years)	53	67	50	67	72
Sex	Male	Male	Female	Male	Male
Handedness	Right	Right	Right	Right	Right
Hemisphere of lesion	Left	Left	Right	Left	Right
Location of lesion	FTPC	Pons	Insula, WM	BG, WM	CNC
Days since stroke as scanning	34	93	21	48	29
Barthel Index (max. 100)	35	55	50	30	40
Motor evoked potentials	—	—	↓	—	—
Fugl-Meyer Score (opposite to the lesion)					
Total (max. 52)	0	13	7	0	0
Finger (max.12)	0	3	2	0	0
Test of Attentional Performance					
Omissions number (max. 24)					
Affected side	19	6	2	5	7
Unaffected side	0	2	0	5	6
Reaction time (ms)					
Affected side	1325	1334	973	1069	1084
Unaffected side	423	1112	743	772	890
Percentile					
Affected side	< 1	< 1	< 1	< 1	< 1
Unaffected side	31	< 1	< 1	5	< 1
T value at precuneus					
MIR > NOR	5.01	7.59	8.74	n.s.	4.28
NOR > MIR	5.31	n.s.	8.42	n.s.	n.s.

FTPC, fronto-temporo-parietal cortex; WM, white matter; BG, basal ganglia; CNC, caput nuclei caudate; —, absent; ↓, low in amplitude; MIR, mirror condition; NOR, normal condition; n.s., no significance.

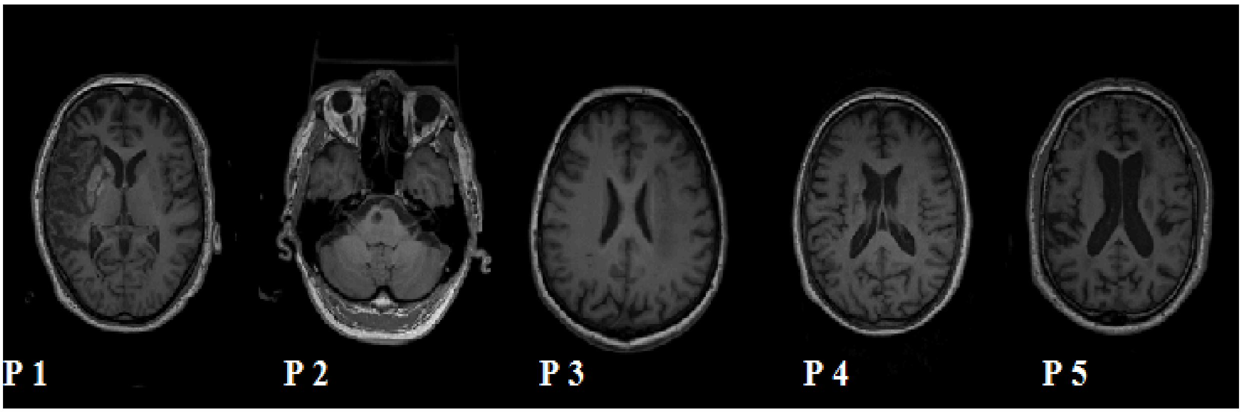

Figure 2. Lesions of patients at the level of maximum infarct volume for each patient as visible in the T1 scans. P1, fronto-temporo-parietal cortex; P2, pons ; P3, insula, white matter; P4, basal ganglia, white matter; P5, caput nuclei caudate.

3.2 Count of finger movements

The numbers of index finger-thumb opposition movements under the different experimental conditions (LH NOR, LH MIR, RH NOR, RH MIR, LH OBS, RH OBS) are shown in Table 3. Data are expressed as median (interquartile range, IQR). For movement performance (i.e. numbers of index finger-thumb opposition movements), The Friedman test revealed no significant difference between any two conditions (P = 0.41). The Wilcoxon signed-rank test revealed no significant difference between the MIR and the NOR conditions for either hand (LH: P = 0.87; RH: P = 0.75).

Table 3. Mean of finger-thumb opposition sequences in different experimental conditions

Motor Activity	Visual Perception	
	LH	RH
LH	LH NOR: 27.0 (25.0-33.0)	LH MIR: 27.0 (25.0-32.0)
RH	RH MIR: 28.0 (25.0-32.0)	RH NOR: 28.0 (24.5-30.0)
OBS	LH OBS: 26.0 (25.0-32.0)	RH OBS: 26.0 (25.0-32.0)

Data are expressed as Median (interquartile range, IQR). RH, right hand; LH, left hand; MIR, mirror condition; NOR, normal condition; OBS: movement observation.

3.3 Imaging data

3.3.1 Group analyses of image data in healthy subjects

Comparing movement execution against rest showed the bilateral motor activation network predominantly in the hemisphere contralateral to the moving hand. The motor cerebral activations during the hand movements are shown in Table 4. Movement mirroring (e.g. MIR MOV > NOR MOV) induced additional lateralized cerebral activations in primary and higher-order visual areas (including the precuneus) strictly contralateral to the perceived limb (Table 5, Figure 3). This pattern was stronger for movement mirroring of the right hand, including lingual gyrus (V1), cuneus (V2), middle occipital gyrus (V5), fusiform gyrus, precuneus (V6). The reverse comparison (i.e. NOR MOV > MIR MOV) showed a relative increase in the precuneus of the left hemisphere for movements of the right hand only (Table 5). In contrast, comparison of brain activity during movement observation of a right or left hand (RH OBS > LH OBS and vice versa) revealed no significant difference (Table 5).

This lack of difference was confirmed by an effects-of-interest analysis at the precunei in both hemispheres, additionally demonstrating that significant lateralization was only present during movement execution, but not during movement observation (Figures 3 - 5). Activation patterns of mirroring movement of right hand (RH MIR > NOR; RH NOR > MIR) are shown in Figure 3. Activation differences during RH movements plotted on a standard 3-D brain, viewed from behind, which demonstrate significant lateralization displays during movement execution. The activation strengths of both precunei are shown in Figures 4 and 5. Effects of interest (mean standardized effect sizes and 90 % CI) at both precunei in all six conditions (LH NOR, LH MIR, RH NOR, RH MIR, LH OBS, RH OBS) also demonstrate that prominent activation type of lateralization is only present during movement execution, but not during movement observation.

Table 4. Main effect of movement (moved > static)

Activation during movements																Responding brain areas	
Right hand								Left hand									
LHS				RHS				LHS				RHS					
X	Y	Z	T	X	Y	Z	T	X	Y	Z	T	X	Y	Z	T	AS	FA
-34	-14	54	8.67	56	-12	40	4.65	-40	-10	54	8.73	44	-12	54	5.88	PCG	M1
-32	-20	62	8.90	40	-8	56	5.87					34	-6	60	4.20	PCG	PMC
-4	-10	60	6.28	30	-6	56	4.19	-12	-6	68	7.13					MFG/ SFG	PMC
-42	-68	6	5.34	54	-66	4	5.19									FG	
								-58	6	30	6.92	60	6	30	6.44	DLPFC	
												58	14	4	5.06	IFG	Broca's area
-48	-74	4	5.05									52	-70	4	6.60	MOG	V3,V4,V5
								-30	-54	60	4.95	28	-58	58	3.92	SPL	SSAC

P < 0.001 (uncorrected) with a minimum cluster size of 20 voxels was considered statistically significant. Cluster size is not reported due to confluent activations. Centre of activation foci in MNI (Montreal Neurological Institute) coordinates. LHS, left hemisphere; RHS, right hemisphere; T, T-value; AS, anatomical structure; FA, functional area; PCG, precentral gyrus; MFG, medial frontal gyrus; SFG, superior frontal gyrus; FG, fusiform gyrus; DLPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; MOG, middle occipital gyrus; SPL, superior parietal lobule; M1, primary motor cortex; PMC, premotor cortex; SSAC, somatosensory association cortex.

Table 5. Activation foci of movement mirroring

Contrast	Centre of activation focus in MNI coordinates				T-value	AS	FA
	Hemisphere	X	Y	Z			
RH MIR > NOR	R	18	-78	2	7.98	Lingual gyrus	V1
	R	12	-86	16	8.12	Cuneus	V2
	R	52	-72	6	8.23	Middle occipital gyrus	V5
	R	16	-84	38	7.18	Precuneus	V6
	R	24	-40	-12	6.49	Fusiform gyrus	
RH NOR > MIR	L	-8	-92	28	10.22	Precuneus	V6
LH MIR > NOR	L	-18	-86	34	8.89	Precuneus	V6
LH NOR > MIR	No significant difference						
OBS RH > LH	No significant difference						
OBS LH > RH	No significant difference						

$P < 0.01$ (FDR) with a minimum cluster size of 20 voxels was considered statistically significant. Cluster size is not reported due to the confluent activations. MNI, Montreal Neurological Institute; T-value, the peak of the activation area; AS, anatomical structure; FA, functional area; RH, right hand; LH, left hand; MIR, mirror condition; NOR, normal condition; OBS: movement observation; FDR, false discovery rate.

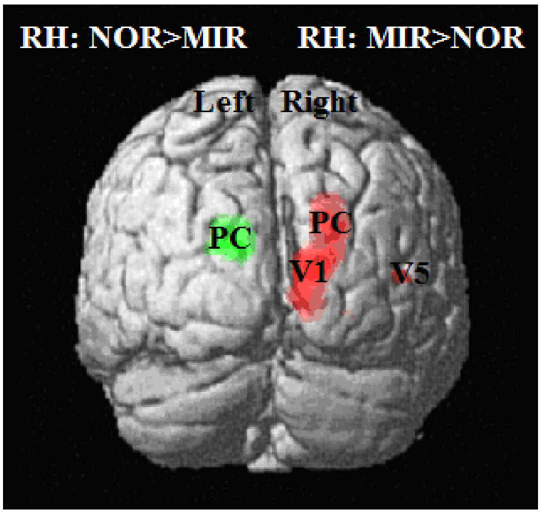

Figure 3. Activation pattern during RH movement mirroring. Differences during RH movements are plotted on a standard 3-D brain, viewed from behind. Red: RH MIR > NOR, green: RH NOR > MIR. RH, right hand; MIR, mirror condition; NOR, normal condition; Left, left hemisphere; Right, right hemisphere; V1, primary visual cortex; V5, associative visual cortex; PC, precuneus.

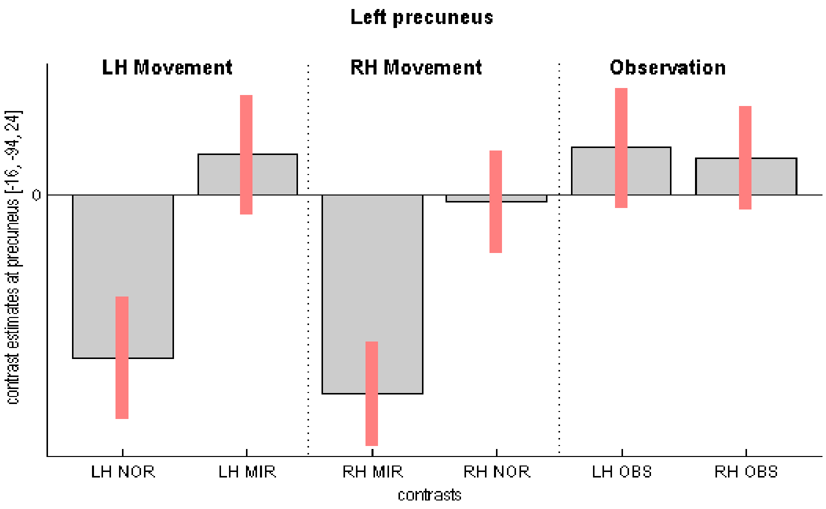

Figure 4. Activation strength of left precuneus. Effects of interests (mean standardized effect sizes and 90 % confidence intervals) at left precuneus in all six conditions. Note that location (left: [-16, -94, -24]) are slightly different from Table 5, resulting from the different approach (ANOVA). RH, right hand; LH, left hand; MIR, mirror condition; NOR, normal condition; PC: precuneus.

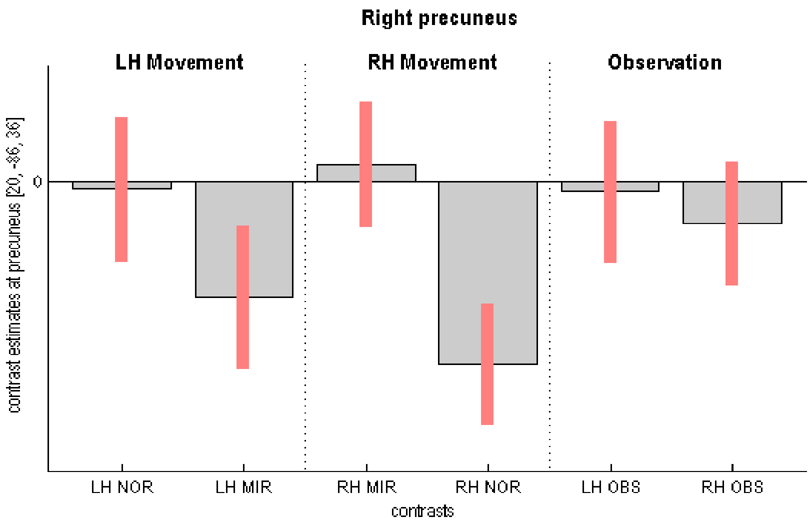

Figure 5. Activation strength of right precuneus. Effects of interests (mean standardized effect sizes and 90 % confidence intervals) at right precuneus in all six conditions. Note that location (right: [20, -86, 36]) are slightly different from Table 5, resulting from the different approach (ANOVA). RH, right hand; LH, left hand; MIR, mirror condition; NOR, normal condition; PC: precuneus.

3.3.2 Brain activations during movement mirroring in individual healthy subjects

As expounded in the group imaging analysis of healthy subjects, movement mirroring produced additional activation in primary (V1) and higher-order visual areas (including the precuneus) strictly contralateral to the perceived limb. This group result could be replicated on an individual-subject basis for the majority of healthy subjects, but not the entire group of subjects (Figures 6 - 8). Figure 6 shows the primary visual areas and the precuneus in the right hemisphere were evoked during movement mirroring of the right hand in an individual healthy participant (RH MIR MOV > RH NOR MOV).

Among the group of 15 normal subjects, eleven subjects showed significant lateralized cerebral activations during movement mirroring of their right hand (RH MIR MOV > RH NOR MOV), four of them did not present significant brain activations. Thirteen presented a significant difference in brain activity when mirroring movements of their left hand (LH MIR MOV > LH NOR MOV), two subjects did not. Only one of the subjects displayed no significant cerebral activation during movement mirroring of either hand.

Among fifteen healthy participants, the reverse comparison (NOR MOV > MIR MOV) showed significant brain activation induced by normal movements of the right hand (RH NOR MOV > RH MIR MOV) in twelve subjects and by normal movements of the left hand (LH NOR MOV > LH MIR MOV) in ten subjects. Three of all healthy subjects showed no significant brain activation for movements of the right hand, and five of them presented no remarkable activation for movements of the left hand. Only one of the participants displayed no significant cerebral activation during movements of either hand.

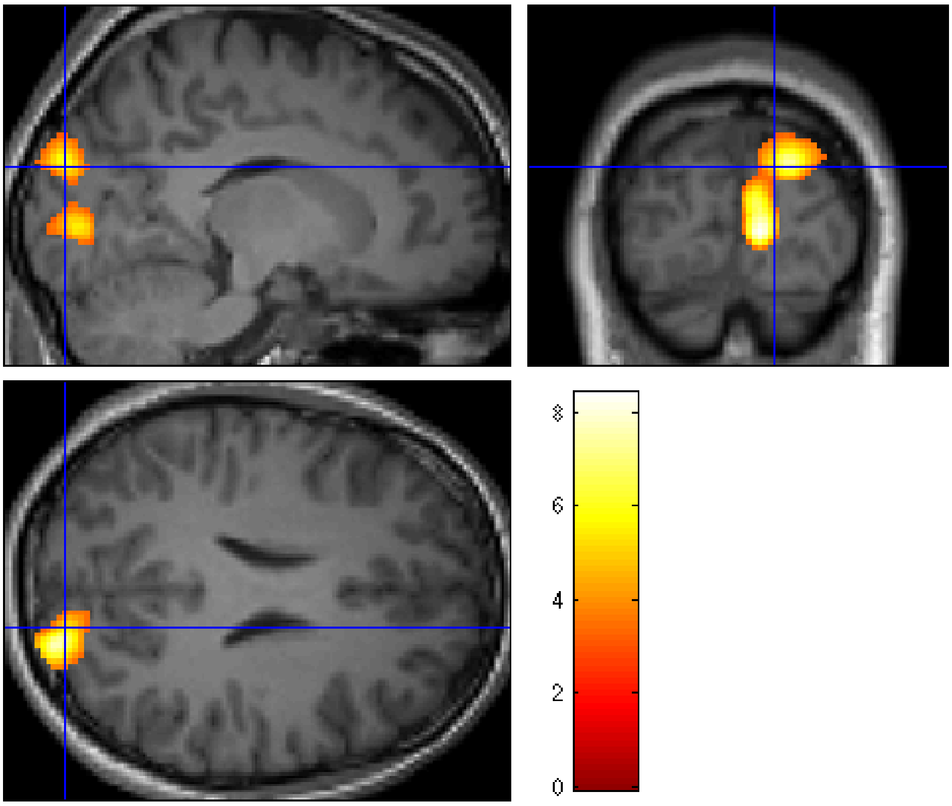

Figure 6. Cerebral activation of an individual healthy subject during mirroring movement of right hand (RH MIR MOV > RH NOR MOV). The threshold was set at $p < 0.001$ (uncorrected) with a minimum cluster size of 20 voxels. The location of cross represents precuneus. The color bar, augmenting from 0 to 8, represents the intensity of activation.

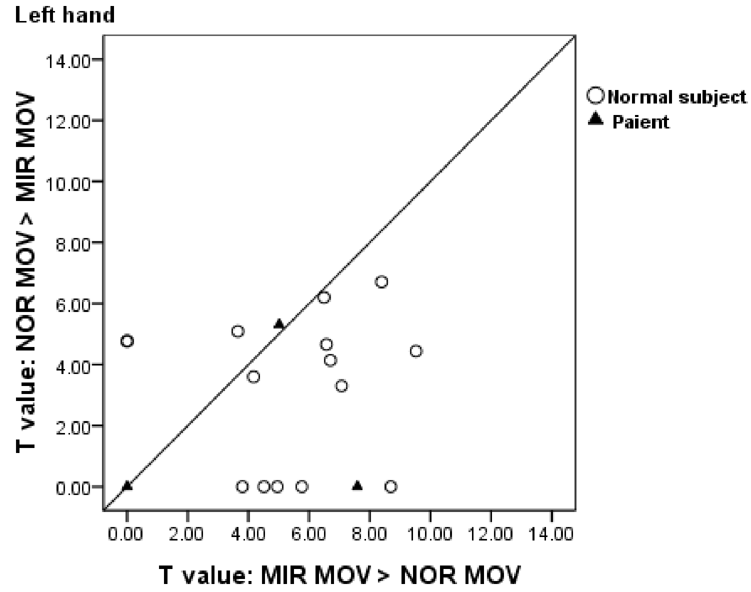

Figure 7. T values at the precuneus in the contralateral hemisphere evoked by the comparisons MIR MOV > NOR MOV and NOR MOV > MIR MOV during movements of left hand. MIR, mirror condition; NOR, normal condition; MOV, movement.

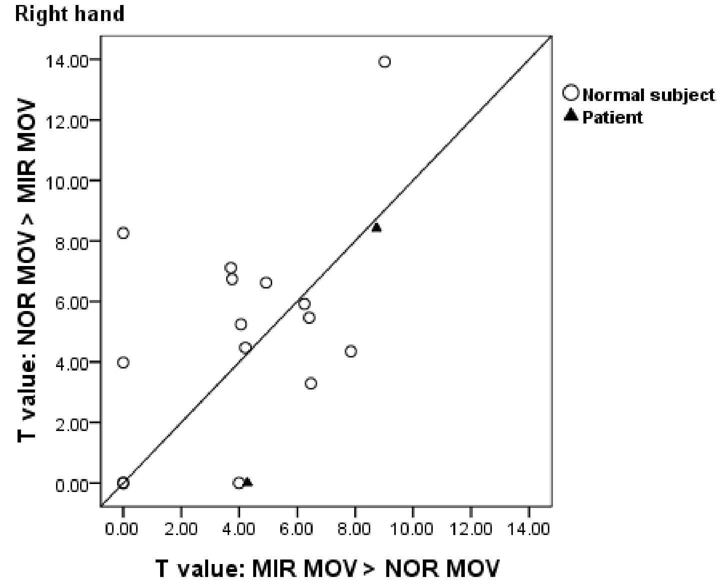

Figure 8. T values at the precuneus in the contralateral hemisphere evoked by the comparisons MIR MOV > NOR MOV and NOR MOV > MIR MOV during movements of right hand. MIR, mirror condition; NOR, normal condition; MOV, movement.

3.3.2.1 T values at the precuneus during movement mirroring

95% CI of T values (peak value of activation) at the precuneus during movement mirroring in healthy participants (i.e. MIR MOV > NOR MOV) were 0.00 – 9.02 for RH and 0.00 – 9.52 for LH, respectively.

There was no correlation of T values at the precuneus between either hand during mirroring movement (Spearman correlation: r = 0.17, P = 0.54). Wilcoxon signed-rank test showed no difference of T values at the precuneus between either hand (P = 0.12). The T values at the precuneus correlated neither with the number of index finger-thumb opposition movements (RH: r = 0.13, P = 0.64; LH: r = - 0.21, P = 0.46) nor with the intensity of the subjective experience of the mirror illusion as evaluated by the questionnaire (RH: r = 0.11, P = 0.70; LH: r = - 0.36, P = 0.19).

3.3.2.2 T values at the precuneus during normal movement

95%CI of T values at the precuneus were 0.00 – 13.92 for RH and 0.00 – 6.71 for LH movements, respectively during normal movement. There was no correlation between the strength of the activation at the precuneus in the comparison (MIR MOV > NOR MOV) and (NOR MOV > MIR MOV) for either hand during normal movement (RH: r = 0.23, P = 0.40; LH: r = -0.07, P = 0.81). However, a significant difference with higher T values in MIR condition (i.e. MIR > NOR) could be observed for the left hand only shown in Figure 9 (P = 0.04), but not for the right hand (P = 0.51).

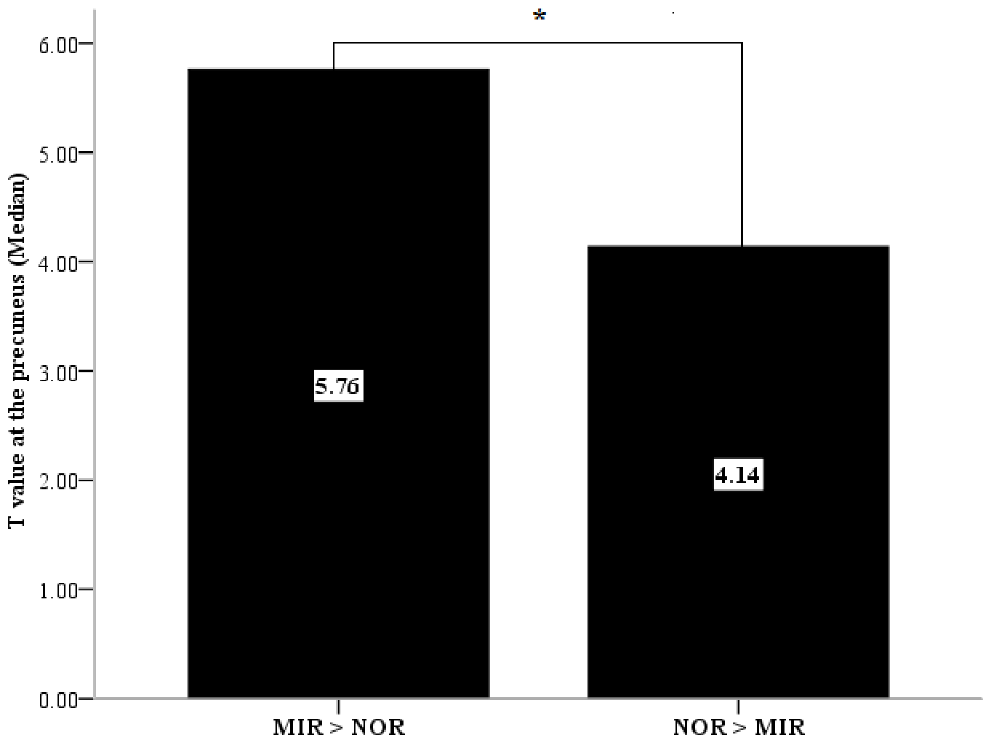

Figure 9. The difference of T values at the precuneus between mirror condition (MIR > NOR) and normal condition (NOR > MIR) for the movement of left hand. MIR, mirror condition; NOR, normal condition. The median of T value: 5.76 for MIR, 4.14 for NOR. * P = 0.04.

3.3.2.3 Relationship between T values and age

There was a significant negative correlation between age of healthy subjects and T values at the precuneus during movement mirroring of the right hand, presented in Figure 10 (r = - 0.55, P = 0.03). No significant correlation was shown between age and cerebral activations during movement mirroring of the left hand (r = 0.68, P = 0.81). There was no correlation between age and T value at the precuneus during the reverse comparison (i.e. NOR MOV > MIR MOV) of either hand (RH: r = 0.22, P = 0.94; LH: r = - 0.12, P = 0.67).

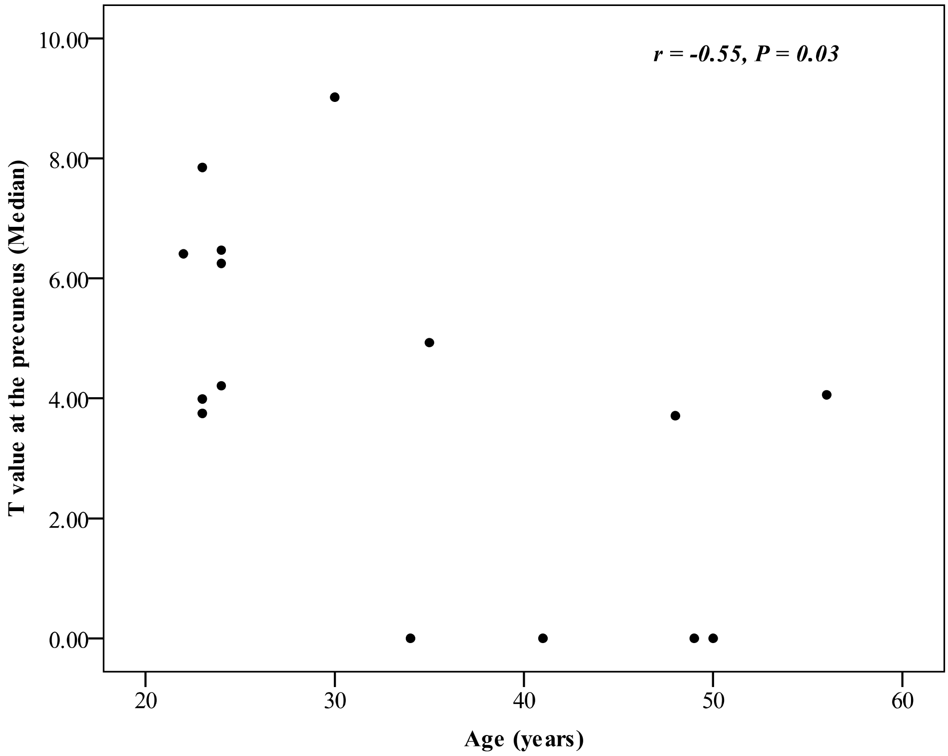

Figure 10. The correlation between age and T values at the precuneus during movement mirroring of right hand.

3.3.3 Neural activations during movement mirroring in individual stroke patients

The cerebral activation pattern during movement mirroring (MIR MOV > NOR MOV) of the non-affected hand in stroke patients was comparable to that of normal subjects (Table 2, Figure 11). As stated in both group imaging analysis and individual-subject analysis of healthy subjects, mirroring of movement in stroke patients produced additional cerebral activation in primary and higher-order visual areas (including the precuneus) strictly contralateral to the perceived limb. Only one out of five patients showed no significant activation difference during mirroring movement. The strengths of activations at the precuneus of all patients were in the range of the 95% CI of normal subjects.

In the reverse comparison (NOR MOV > MIR MOV), only one patient showed a significant difference of activation, which was in the range of the 95% CI of the normal subjects.

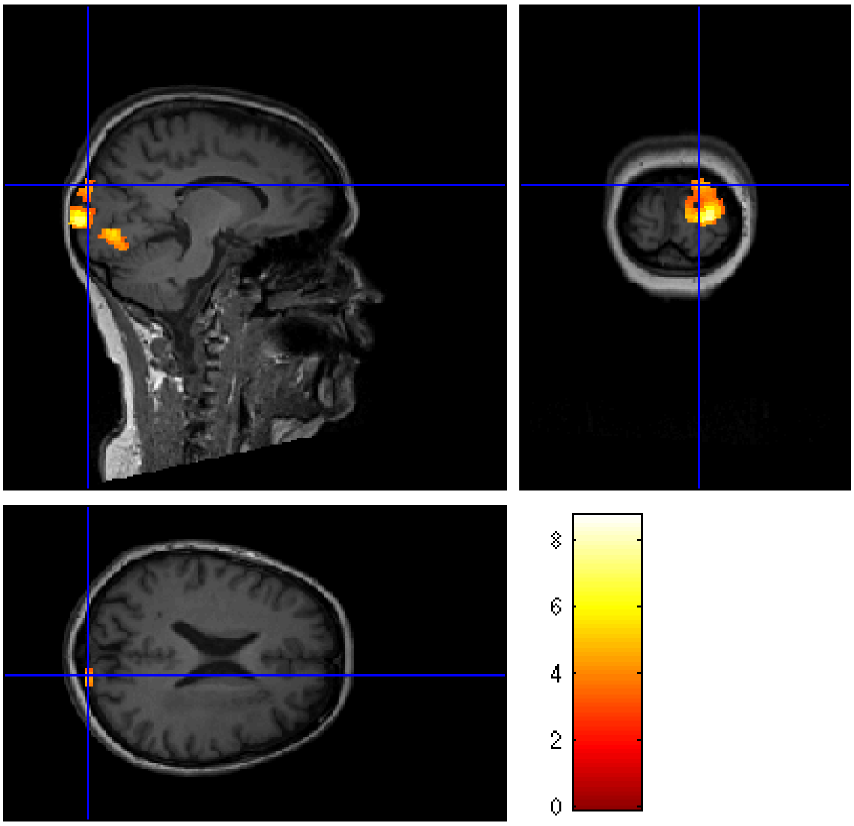

Figure 11. Activation induced by the movement mirroring in one stroke patient (P3) (RH MIR MOV > RH NOR MOV). The threshold was set at $p < 0.001$ (uncorrected) with a minimum cluster size of 20 voxels. The location of cross represents precuneus. The color bar, augmenting from 0 to 8, represents the intensity of activation.

4 Discussion

4.1 Movement mirroring and movement observation in healthy subjects

4.1.1 Cerebral activations elicited by movement mirroring

Additional activation of the contralateral hemisphere by movement mirroring has been found employing both a real mirror[45] and a video chain.[33] In principle, our findings match those of the previous study with a related setup.[33] However, in that study, both static and moving trials were analyzed together. In contrast, in the present study, only movement trials were analyzed in order to allow comparison with the movement observation task. Now, lateralised activations were no longer found to be symmetrical for both hands, but more pronounced for mirroring movements of the right hand. Besides, the reverse comparison (i.e. NOR MOV vs. MIR MOV) for the right hand showed additional activation as well, which was not noted in the previous study with a smaller number of healthy subjects. For all comparisons, the strongest effect was found in the precuneus of either hemisphere, which was previously reported to process upper limb configuration.[34, 37]

Previously, MNS was proposed as one of the underlying neural mechanisms of MT.[17] However in our study, no additional activation in the MNS was elicited during movement mirroring. We assume that the parieto-occipital cortex, namely the precuneus, is crucial for the processing of visually perceived limb configuration of one body side, thus mediating the effects of MT.

4.1.2 Brain activations evoked by movement observation

To the best knowledge of the authors, movement observation of a right or left hand with central fixation has never been compared directly. In our study, there was no significant difference while comparing brain activity during movement observation of a right or left hand (RH OBS > LH OBS and vice versa). One study reported a significant difference at the pars opercularis as part of the mirror neuron system, but hand laterality and visual hemifield was changed simultaneously.[39] However, based on our data, it cannot be excluded that the MNS is activated during all movement observation conditions in a uniform fashion. Cabinio and co-workers compared the degree of lateralization in right-handers and left-handers and showed left lateralised activation pattern in the former and a bilateral activation in the latter.[59] Apparently, this pattern is modulated with a changing sense of agency.[69] Importantly, these binding processes seem to be strictly lateralized.[70]

4.1.3 Comparison of neural activations in movement mirroring and observation

Our study clearly demonstrates that only mirroring of own active movement performance, but not passive movement observation, elicits lateralised cerebral activations in the parieto-occipital cortex strictly opposite to the visually perceived hand. The asymmetry of the reverse comparison (i.e. NOR MOV vs. MIR MOV) and the lack of difference during the action observation tasks exclude the possibility that the observed activation pattern during movement mirroring can be attributed to a form of pure visual hemifield stimulation.

Finally these results might lead to further speculations on the effect of MT and MOT on inter-hemispheric rivalry. For stroke patients, it is now well established that the unaffected hemisphere could further inhibit the affected hemisphere by transcallosal inhibition mechanism, thus resulting in deteriorating motor performance.[71] One might speculate that only MT, but not MOT could selectively activate the affected hemisphere and beneficially influence this inter-hemispheric balance, which might further explain the positive effect of MT especially in severe hemiparesis.[16]

4.2 Neural activation patterns elicited by movement mirroring in individual subjects

4.2.1 Cerebral activations by the movement mirroring in individual healthy subjects

In extension of previous findings of group studies,[33, 45, 72] the present study demonstrates that lateralized cerebral activation due to movement mirroring could not only be found in a group analysis, but also in individual subjects. This was valid for the majority of normal subjects, but not for all of them. As found in the group analysis with related design,[33, 72] the strength of the additional activation at the precuneus evoked by the mirror illusion (MIR MOV > NOR MOV) is higher than in the reverse comparison (NOR MOV > MIR MOV). In the individual-subject analysis, this could be confirmed to be statistically significant for the left hand only. The activation difference cannot be attributed to differences in movement performance (i.e. number of finger-thumb opposition sequences). This further suggests that the observed activation pattern during movement mirroring cannot be attributed to the simple hemifield stimulation, but results from higher-level processing of the mirror illusion. As indicated by the results of the questionnaire, this objective measure can not be attributed to the subjective rating of the experience of the mirror illusion. For left hand movements, there is a tendency for activation differences to diminish with age.

4.2.2 Brain activations by the movement mirroring in individual stroke subjects

For stroke patients, strength and magnitude of the activation pattern found in the visual areas and precuneus of the hemisphere contralateral to visually perceived hand movement was comparable to those of normal subjects. This was even the case for the patients with left-hemispheric lesions and left-hand movements that were older than the control group, considering that a decrease of activation strength with age was found in normal subjects. This result is different from the results of the group analysis of Michielsen and colleagues, who found a significant effect of the mirror illusion not for unimanual movements, but during bimanual movements only.[44] Our findings indicate that the mirror illusion can also be elicited in patients with severe hemiparesis whose representation of active movements of the contralesional limb are expected to degrade.

This might be the neurophysiologic basis of the clinical improvement seen in this patient group when applying MT.[16] The results of our study suggest that the strength of the activation due to the mirror illusion has no value on its own. Rather, one might assume that this additional activation at all is either present or not. It is tempting to assume that MT is only effective in those patients where this activation can be elicited. Clinical studies with correlation of brain activity before therapy with clinical improvement after therapy are necessary to answer this hypothesis.

4.2.3 The precuneus

As showed in the healthy subjects and stroke patients, the precuneus was activated strictly contralateral to the perceived hand during movement mirroring, which may indicate one of the important cortex locations for the advanced functional process of mirroring movement. With progress of functional neuroimaging technology, the precuneus locating in the posteromedial portion of the parietal lobe has gradually received attention. Based on the traditional anatomical landmarks, the precuneus positions among the marginal branch of the cingulate sulcus, the medial portion of the parieto-occipital fissure and the subparietal sulcus (Figure 12).[73] In the cytoarchitectonic map of Brodmann as an important anatomical reference for functional imaging studies,[74] the corresponding area of the precuneus is mainly located in the Brodmann area 7 (BA 7) (Figure 13).[75] Functional imaging studies in healthy subjects suggested that the precuneus contributed to the implementation of a multifold array of highly integrated tasks, which included visuo-motor coordination (for example, in reaching to grasp an object),[76, 77] representation of visual body configuration,[33] processing upper limb configuration,[34, 37] motor imagery,[78, 79] and self-processing operations.[80] The precuneus is also involved in the activities of mirror-induced visual illusions. Dohle and colleagues certified that the precuneus and primary visual areas were shown to be activated opposite to the seen limb during movement mirroring in healthy participants.[33, 34] The mirror illusion increases brain activities in precuneus and posterior cingulated cortex during bimanual mirroring movements in patients with stroke, but not during unimanual mirroring movements.[44] There is no consistent viewpoint regarding the relationship between the mirror illusion and the precuneus in either healthy individuals or stroke patients.

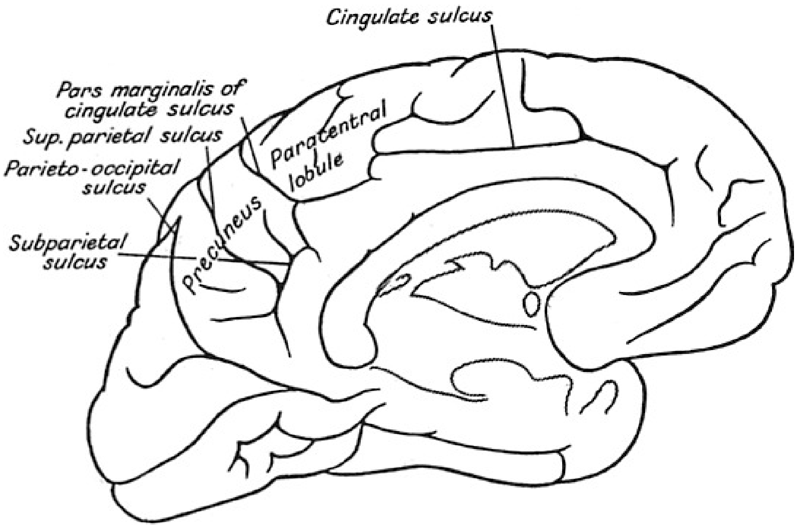

Figure 12. The precuneus and its traditional anatomical boundaries (medial view). The anterior: the cingulate sulcus; the posterior: the medial portion of the parieto-occipital fissure; and inferior: the subparietal sulcus.[73]

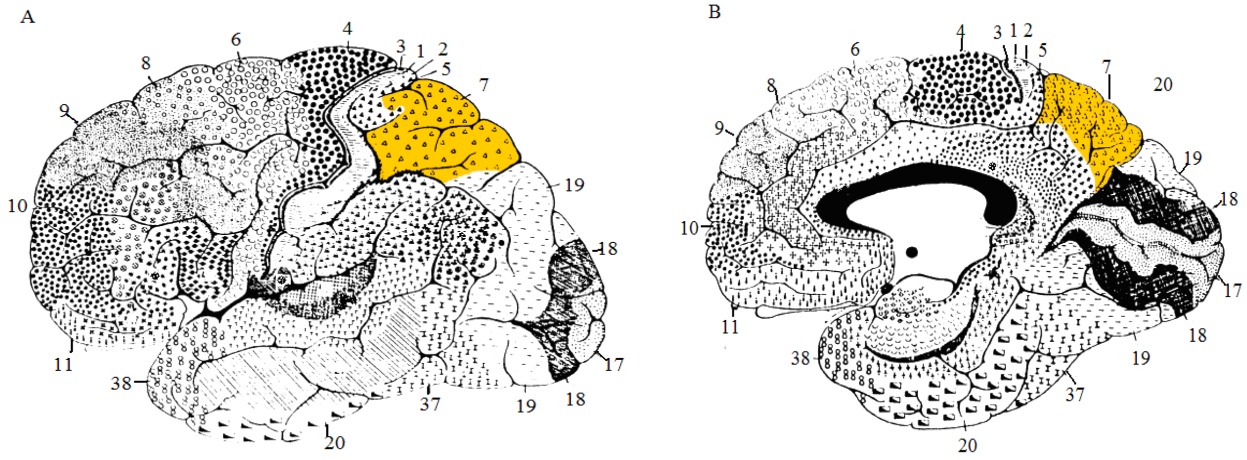

Figure 13. The cytoarchitectonic maps of the BA 7 shown in yellow (A: lateral view; B: medial view). BA 7 Situated posterior to the primary somatosensory cortex (BA 3, 1 and 2), and superior to visual cortices (BA 17, 18and 19).[74] BA: Brodmann area.

4.3 Features of the setup in the study compared with those of previous studies

In our study, observation of one's own moving hand was investigated by employment of a video chain. A further study using positron emission tomography (PET) during mirroring of a computer graphic image of a human arm movement provided similar activations at the precuneus contralateral to the seen arm.[34] Other researchers made use of a real mirror. Using this approach, Shinoura and colleagues found activation differences in the outer part of the cerebellum and the ipsilateral primary motor cortex.[47] This result is similar to that of Diers and colleagues, who investigated the primary motor cortex only [46]. In contrast, Matthys and colleagues found activations located in the superior temporal sulcus and V2 ipsilateral to the moving hand.[45] In a replication of this study in stroke patients, activation differences in the precuneus and posterior cingulate were found, but during bimanual movements only.[27, 44] In summary, there are diverging results from different groups which can in part be attributed to differences in the setup. There is some evidence that increased activity in ipsilateral M1 is induced by the mirror-induced illusion of two synchronously moving hands.[46, 47] To the best knowledge of the authors, studies by our group are the only ones isolated varying the laterality of the visual feedback by means of technical aids. This was intended to ensure that changes in activity can be attributed to only one single factor (the visual image), but are not corroborated by other factors such as spatial transformations.[33, 34] Using this approach, a stable activation pattern could be reproduced using two different fMRI settings in Düsseldorf[33] and Berlin[33, 72].

4.4 Limitations of the study

Some potential limitations in the study have to be acknowledged. First, the age of the normal subjects group (34 years) was not comparable to that of the stroke subjects (66 years). However, correlation of age and activation strength in normal subjects indicated a negative correlation for movements of the right hand only, i.e. older subjects showed less activation due to the mirror illusion. Thus, it is even more remarkable that the lateralized activation was found in older, left-hemispheric lesioned patients as well.

Second, the numbers of index finger-thumb opposition movements of patients were not recorded. However, the data from normal subjects indicated that movement speed was not influenced by the mirror illusion. Finally, the sample size of stroke patients included in the study is rather small. However, given the relatively small number of patients that fulfilled the inclusion and exclusion criteria and that were suitable and willing to participate in a fMRI study. Further studies are needed to reproduce these pilot data in a greater number of patients.

5 Conclusions and perspectives

In conclusion, data in this study clearly demonstrate that only movement mirroring, but not movement observation evokes lateralised cerebral activations in the primary and higher-order visual areas (i.e. the precuneus) strictly opposite to the visually seen hand. The magnitude of this effect in the precuneus contralateral to the perceived hand might be independent of movement speed and subjective experience of the mirror illusion. The lateralized cerebral activations due to movement mirroring can be elicited only in the majority of individual subjects, but not in all of them. Cerebral activation due to the movement mirroring in stroke patients is comparable to that of healthy subjects, even in stroke patients with severe hemiparesis. Further studies in stroke patients are needed in order to investigate whether the activation pattern could be considered as a predictor of success in MT, and how the precuneus contributes to the successful cerebral reorganization or clinical recovery, which may ultimately help with screening those patients who might benefit from application of MT.

6 Summary

Background

Stroke is one of the leading causes for death and permanent disability. The upper limb dysfunction is one of the most difficult complications to treat after stroke. The conventional therapeutic techniques mainly focus on stimulating the use of the paretic upper limb in supervised training tasks, such as repetitive active arm training, constraint-induced movement therapy and robot-assisted arm training. However, the traditional strategies in improving upper extremity dysfunction severely affected by stroke presented limited outcomes. Recently, new strategies built upon visual stimulation, such as mirror therapy (MT) or movement observation therapy (MOT) were recommended for improving upper limb dysfunction after stroke. Although there is increasing evidence for positive therapeutic effects of these therapies, their neural mechanisms are poorly understood, particularly regarding the contribution of the two hemispheres. Furthermore, the effect of movement mirroring on brain activity in stroke patients is even less understood.

Objectives

To investigate the effects of movement mirroring on cerebral activity compared with those of movement observation in healthy subjects, and to explore the regions and patterns of cortex activations evoked by the movement mirroring in individual healthy and stroke participants.

Methods

Fifteen healthy volunteers and five stroke patients with severe paresis of the upper limbs participated in the functional imaging study. Movement mirroring was carried out in healthy subjects and stroke patients. Movement observation was only performed in healthy volunteers. Cerebral activations were recorded with functional magnetic resonance imaging. We compared the image data during movement observation and movement mirroring from either hand in healthy subjects, and compared the cerebral activation pattern of individual stroke patients elicited by movement mirroring with that of healthy participants. Imaging data were processed using a statistical parametric mapping software package. SPSS was employed for further statistical analyses. The

Spearman correlation test was used to evaluate relationships between T value at the precuneus and movement speed / mirror illusion questionnaire / age. The Wilcoxon signed-rank test was applied to test for significant differences. For each test, significance threshold was set at $P < 0.05$.

Results

Movement mirroring induced additional activations in primary and higher-order visual areas (i.e. the precuneus) strictly contralateral to the perceived hand. In contrast, comparison of brain activity while observing somebody else's movement of either hand revealed no significant difference.

On an individual-subject basis, for normal subjects, cerebral activations were evoked by movement mirroring of the right hand in 11 out of 15 subjects and that of the left hand in 13 out of 15 subjects. There was no correlation between T value at the precuneus contralateral to the perceived hand and movement speed / subjective experience of the mirror illusion. Negative correlation of activation strength with age was found for the right hand only. The activation pattern in stroke patients was comparable to that of normal subjects and presented in four out of five patients.

Conclusions

The study demonstrates that it is movement mirroring rather than pure movement observation elicits lateralised cerebral activations. The magnitude of this effect in the precuneus contralateral to the perceived hand might be independent of movement speed and subjective experience of the mirror illusion. On an individual-subject basis, cerebral activation contralateral to the moving hand can be evoked in the majority of healthy subjects and stroke patients with severe hemiparesis, but not in all of them.

Zusammenfassung

Hintergrund

Der Schlaganfall ist eine der führenden Ursachen für Pflegebedürftigkeit und Invalidität. Der paretische Arm nach Schlaganfall stellt dabei für die Rehabilitation eine der größten Herausforderungen dar. Die herkömmlichen therapeutischen Methoden, die auf aktiven Übungen der oberen Extremität beruhen, wie repetitives Armtraining, Constraint-induced movement therapy (CIMT), auch als forced-used training bezeichnet, und roboter-assistiertes Arm-Training setzen jedoch meistens eine motorische Restfunktion voraus und sind daher für den schwer betroffenen Arm weniger geeignet. Neue Strategien, die komplexe visuelle Stimuli benutzen, wie Spiegeltherapie (mirror therapy, MT) oder Therapie durch Bewegungsbeobachtung (movement observation therapy, MOT) wurden zur Verbesserung der Armfunktionen in jüngster Zeit empfohlen. Ihre Wirksamkeit wurde in einigen Studien dargelegt. Obwohl die Effektivität dieser Therapien dadurch nachgewiesen wurde, ist über die neuronalen Mechanismen der Spiegelillusion und der Bewegungsbeobachtung nur wenig bekannt. Das gilt sowohl für Normalpersonen als auch für Schlaganfallpatienten. Insbesondere welche Rolle beide Hemisphären dabei spielen, ist noch weitgehend unbekannt. Welche Wirkung die Bewegungsspiegelung auf die Hirnaktivität bei Schlaganfallpatienten hat, ist in der Literatur noch wenig beschrieben.

Ziele

Es sollte die zerebrale Aktivierung bei einer Bewegungsspiegelung (MT) und einer Bewegungsbeobachtung (MOT) bei gesunden Probanden verglichen werden und die Effekte der Bewegungsspiegelung (MT) mit denen von Schlaganfallpatienten verglichen werden.

Methoden

Fünfzehn gesunde Probanden und fünf Schlaganfall-Patienten mit schweren Lähmungen der oberen Extremität nahmen an der Studie mit funktioneller Bildgebung teil. Aufgaben zur Bewegungsspiegelung (MT) wurden von gesunden Probanden und Schlaganfall-Patienten durchgeführt. Aufgaben zur Bewegungsbeobachtung (MOT)

wurden nur von gesunden Probanden durchgeführt. Die zerebralen Aktivierungen wurden mit Hilfe der funktionellen Magnetresonanztomographie (fMRI) bestimmt. Wir verglichen die Bilddaten während der Bewegungsbeobachtung (MOT) mit denen der Bewegungsspiegelung (MT) von jeder Hand in gesunden Probanden und verglichen ebenso die zerebralen Aktivierungsmuster einzelner Schlaganfall-Patienten bei Bewegungsspiegelung (MT) mit der Aktivierung bei gesunden Probanden. Die bildgebenden Daten wurden unter Verwendung eines statistischen parametrischen Mapping-Software-Pakets ausgewertet und mittels SPSS für weitere statistische Auswertungen verwendet. Der Spearman-Korrelationstest wurde verwendet, um Beziehungen zwischen dem T-Wert im Precuneus-Bereich für Bewegungsgeschwindigkeit, Spiegel-Illusion-Fragebogen, Alter auszuwerten. Der Wilcoxon-Test wurde angewandt, um signifikante Unterschiede zu testen. Für jeden Test wurde die Signifikanzschwelle bei $P < 0{,}05$ festgelegt.

Ergebnisse

Die Bewegungsspiegelung (MT) induziert zusätzliche Aktivierungen in visuellen Arealen primäres und höherer Ordnung (d.h. im Precuneus) strikt kontralateral zur wahrgenommenen Hand. Im Gegensatz dazu zeigte die Aktivierung bei Bewegungsbeobachtung (MOT) –wenn eine andere Person eine Hand bewegte - keinen signifikanten Seitenunterschied.

Bei normalen Probanden wurde bei einer Analyse der Einzelpersonen eine zerebralen Aktivierung durch Bewegungsspiegelung der rechten Hand in 11 von 15 Patienten und der linken Hand in 13 von 15 Probanden beobachtet. Es gab keine Korrelation zwischen T-Wert im Precuneus-Bereich kontralateral zur wahrgenommenen Hand und der Bewegungsgeschwindigkeit bzw. der subjektiven Stärke der Spiegelillusion. Es wurde eine negative Korrelation der Aktivierungsstärke mit zunehmendem Alter, aber nur für die rechte Hand gefunden. Die Aktivierungsmuster bei Schlaganfall-Patienten waren vergleichbar mit jener von gesunden Probanden (in vier von fünf Patienten).

Schlussfolgerungen

Die Studie zeigt, dass es die Bewegungsspiegelung (MT) und nicht die reine Bewegungsbeobachtung (MOT) ist, die eine lateralisierte zerebrale Aktivierung auslöst.

Das Ausmaß dieses Effekts im Precuneus kontralateral zur wahrgenommenen Hand war von der Bewegungsgeschwindigkeit und der subjektiven Stärke der Spiegel-Illusion nicht beeinflusst. Bei einer Analyse der Einzelpersonen (individual-subject analysis) ergibt sich, dass eine zerebrale Aktivierung kontralateral zur bewegten Hand in der Mehrzahl bei gesunden Personen und bei Patienten mit schwerer Parese nach Schlaganfall zu beobachten ist, jedoch nicht bei jeder Einzelperson.

7 References

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8 Curriculum vitae

My career will not be published, for privacy reasons in the electronic version of my work.

9 Expression of thanks

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10 Declaration on oath

I hereby declare that the study described in the dissertation was carried out by me.

Erklärung

Ich, Jing Wang, erkläre, dass ich die vorgelegte Dissertation mit dem Thema: „Cortical Activity Evoked by Mirroring of Hand Movement in Healthy Subjects and Stroke Patients“ selbst verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel benutzt, ohne die (unzulässige) Hilfe Dritter verfasst und auch in Teilen keine Kopien anderer Arbeiten dargestellt habe.

Berlin, den 29.11.2012 Jing Wang