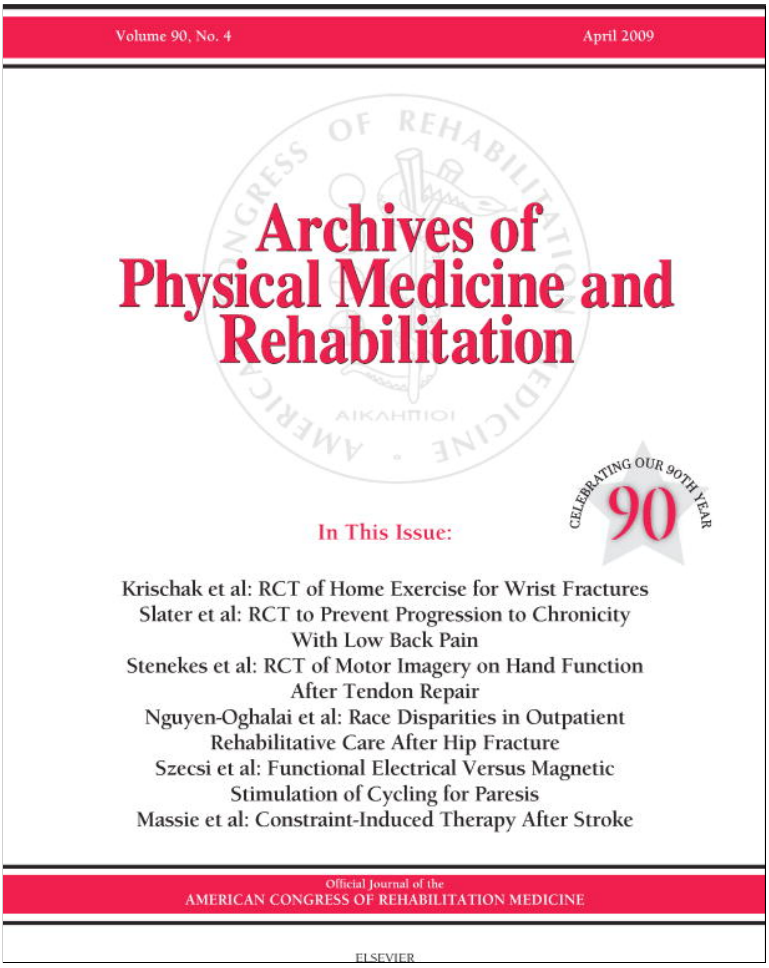
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90
In This Issue:
Krischak et al: RCT of Home Exercise for Wrist Fractures
Slater et al: RCT to Prevent Progression to Chronicity With Low Back Pain
Stenekes et al: RCT of Motor Imagery on Hand Function After Tendon Repair
Nguyen-Oghalai et al: Race Disparities in Outpatient Rehabilitative Care After Hip Fracture
Szecsi et al: Functional Electrical Versus Magnetic Stimulation of Cycling for Paresis
Massie et al: Constraint-Induced Therapy After Stroke
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ORIGINAL ARTICLE

Mirror-Induced Visual Illusion of Hand Movements: A Functional Magnetic Resonance Imaging Study

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ABSTRACT. Matthys K, Smits M, Van der Geest JN, Van der Lugt A, Seurinck R, Stam HJ, Selles RW. Mirror-induced visual illusion of hand movements: a functional magnetic resonance imaging study. Arch Phys Med Rehabil 2009;90: 675-81.

Objective: To identify neural networks associated with the use of a mirror to superimpose movement of 1 hand on top of a nonmoving contralateral hand (often referred to as *mirror therapy* or *mirror-induced visual illusion*).

Design: A functional magnetic resonance imaging (fMRI) study of mirror-induced visual illusion of hand movements using a blocked design in a 1.5T magnetic resonance imaging scanner. Neural activation was compared in a no-mirror experiment and a mirror experiment. Both experiments consisted of blocks of finger tapping of the right hand versus rest. In the mirror experiment, movement of the left hand was simulated by mirror reflection of right hand movement.

Setting: University medical center.

Participants: Eighteen healthy subjects.

Interventions: Not applicable.

Main Outcome Measures: Differences in fMRI activation between the 2 experiments.

Results: In the mirror experiment, we found supplementary activation compared with the no-mirror experiment in 2 visual areas: the right superior temporal gyrus (STG) and the right superior occipital gyrus.

Conclusions: In this study, we found 2 areas uniquely associated with the mirror-induced visual illusion of hand movements: the right STG and the right superior occipital gyrus. The STG is a higher-order visual region involved in the analysis of biological stimuli and is activated by observation of biological motion. The right superior occipital gyrus is located in the secondary visual cortex within the dorsal visual stream. In the literature, the STG has been linked with the mirror neuron system. However, we did not find activation within the frontoparietal mirror neuron system to support further a link with the mirror neuron system. Future studies are needed to explore the mechanism of mirror induced visual illusions in patient populations in more detail.

Key Words: Brain mapping; Motor activity; Neurology; Neurosciences; Rehabilitation; Visual perception.

THE VIRTUAL REALITY BOX for the treatment of phantom limb pain was first introduced by Ramachandran and Rogers-Ramachandran.[1] When a mirror is placed in a sagittal plane between the intact arm and the phantom limb, the mirror reflection of the intact arm is superimposed on the phantom limb, creating the illusion the amputated extremity is still present. This mirror reflection caused the sensation in patients with phantom limb pain that they could move and relax the often cramped phantom limb and experienced pain relief.[2] Since then, the successful use of mirror reflections has been reported in patients with other pain syndromes, such as complex regional pain syndrome[3-6] and phantom sensations in brachial plexus avulsion,[7] as well as for upper extremity rehabilitation after stroke[8-11] or peripheral nerve injury.[12] The idea of using mirror reflection of the uninjured hand superimposed on the injured hand was later referred to as *mirror therapy*,[4] *mirror visual feedback*, and *mirror-induced visual illusions*.[13] In this article, we consistently use the terms *mirror therapy* and *mirror-induced visual illusions*.

At present, little is known about the influence of the mirror reflections that are used during mirror therapy on brain activation. A study using transcranial magnetic stimulation during hand movements showed a significantly increased excitability of the M1 contralateral to the nonmoving hand behind the mirror compared with a control condition in healthy subjects.[13] In 3 patients with brachial plexus avulsion, Giraux and Sirigu[7] used a virtual reality system—very similar to the concept of mirror therapy—displaying prerecorded movements of a hand to create the illusion of normative hand movement. After an 8-week training program, an increased activation in M1 corresponding with the affected limb was found using fMRI.

Insight in brain activation during mirror-induced visual illusion of hand movements may provide better understanding of the working mechanism of mirror therapy. Several underlying

List of Abbreviations

EPI	echo-planar imaging
fMRI	functional magnetic resonance imaging
M1	primary motor cortex
MNS	mirror neuron system
MRI	magnetic resonance imaging
PMC	premotor cortex
PPC	posterior parietal cortex
SMA	supplementary motor area
SPM	statistical parametric mapping
STG	superior temporal gyrus
STS	superior temporal sulcus
TMS	transcranial magnetic stimulation
V2	secondary visual cortex

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mechanisms for mirror therapy have been proposed. For motor rehabilitation, it has been hypothesized that the alternative input obtained from the mirror reflection might facilitate recruitment of the PMC to assist recovery after stroke through an intimate connection between visual input and premotor areas.[8] Others describe mirror therapy as a form of motor imagery in which the mirror creates visual feedback of successful performance of the imagined action with the impaired limb.[10] Motor imagery itself, the mental performance of a movement without overt execution of this movement, has proven to be beneficial in the rehabilitation of hemiparesis,[14,15] and the visual feedback of the imagined movement using a mirror reflection of hand movement may further facilitate this. Finally, some authors suggested that the MNS may be the underlying neural mechanism of mirror therapy.[11,12] The MNS is a frontoparietal motor network of mirror neurons. Mirror neurons are bimodal visuomotor neurons discharging both when performing a particular action and when observing a similar action performed by another person. The MNS is proven to be activated during several action representations—for example, action observation, mental preparation of movement, and motor execution.[16] Electrophysiologic research on action observation showed a corticospinal facilitation of the M1 based on frontoparietal MNS activation. It has been shown that this facilitation of M1 is effector-specific, lateralized, and significantly greater in a first-person perspective compared with a third-person perspective.[17-19] Therefore, it could be hypothesized that increased M1 excitability during mirror-induced visual illusions is caused by mirror neuron activation because the mirror reflection of the moving hand may provide the ideal image presentation for action observation.

To evaluate brain activation during mirror-induced visual illusion of hand movements as used during mirror therapy, we used fMRI to identify the neural networks associated with the visual perception of a moving hand in healthy subjects superimposed on the nonmoving hand.

METHODS

Subjects

Ten male and 8 healthy female volunteers with an average age of 28.5 years (range, 22–48y) were recruited from staff and students of the Erasmus Medical Center and were included in the study. All subjects were right-handed, had good visual acuity, and had no known neurologic history. Subjects were not informed about the purpose of the experiment. The procedures were approved by the institutional review board, and written informed consent was obtained from all subjects.

Experimental Procedure

In this study, subjects participated in 2 experiments, a no-mirror experiment and a mirror experiment (figs 1A and B). Each experiment (no-mirror and mirror) was performed twice

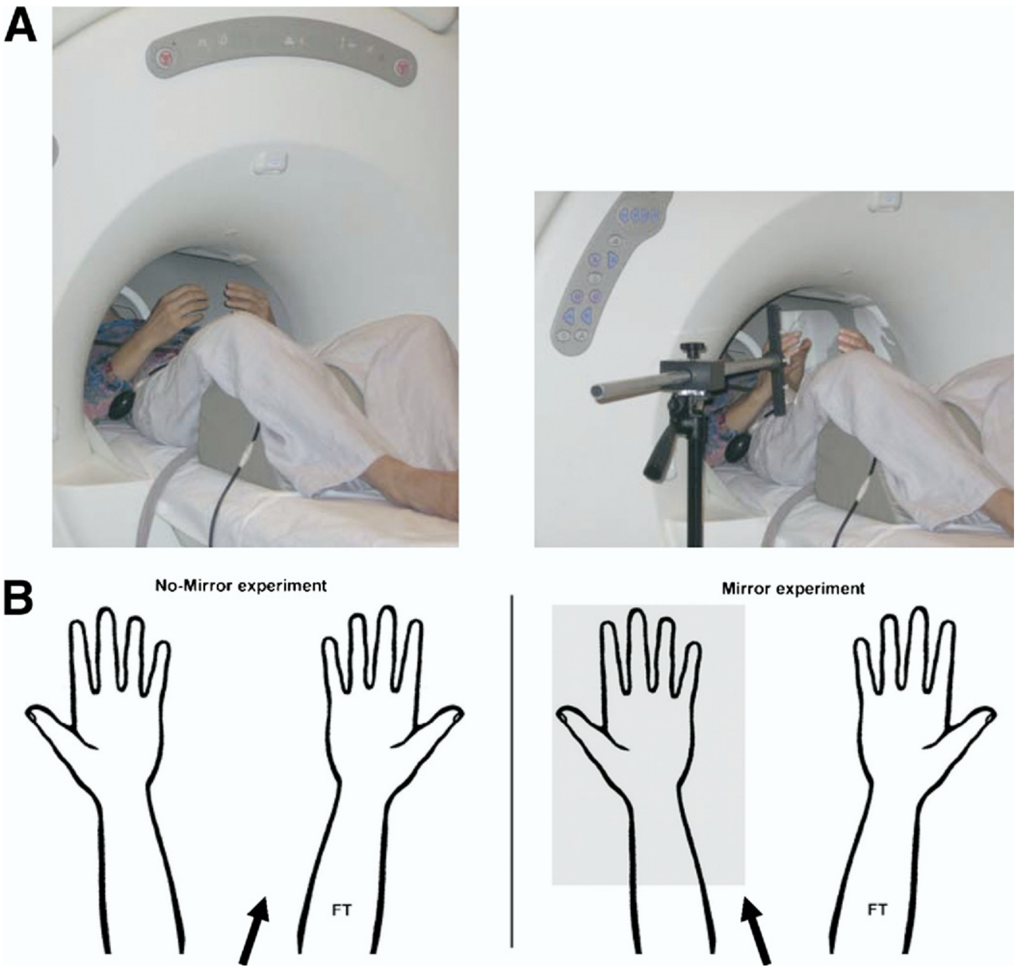

Fig 1. Illustration of the 2 measurement conditions: the no-mirror experiment (left) and the mirror experiment (right). (A) In the fMRI scanner, subjects were able to look toward the outside of the scanner in the direction of their feet to see both hands by using a little mirror that was attached to the top of the head coil and was present in all experiments. In the mirror condition, a mirror was placed between both hands in such a way that the finger tapping of the right was hand was projected on the left nonmoving hand. (B) Schematic representation of the 2 measurement conditions. FT indicates which hand is performing the finger tapping, and the arrow is used to indicate where subjects were asked to look. In the mirror experiment, a mirror was positioned in such a way that the reflection of the moving right hand was projected on the position of the nonmoving left hand.

in each subject, and the 4 scanning sessions were pseudorandomized across subjects. During each scanning session, subjects lay in the scanner in a supine position and were able to look outside the scanner in the direction of their feet by using a little mirror that was attached to the top of the head coil and that was present in all experiments. In this setting, subjects were able to see their hands when they were in front of their waist. Throughout the experiments, the upper arms of the subjects rested comfortably on the scanner table, while the elbows were slightly flexed such that both hands were about 20cm apart in front of the waist of the subjects (see fig 1). Auditory instructions were presented using an MRI-compatible headphone system by means of simple words (start, rest) generated by a computer program (Matlab 6.5[a]).

The stimulation paradigm for both experiments consisted of a blocked design of finger tapping with the right hand only versus rest (30s/block; 10 blocks a scanning session). Subjects were instructed at the start of the experiment on how to perform a self-paced constant finger tapping rhythm at approximately 1.5Hz. Subjects were asked not to create a continuous movement pattern, but to perform separate movements of each finger with a short rest period between each movement. We chose not to use a metronome to pace the movement, to ensure that participants would fully concentrate on the visual image during both experiments.

In the mirror experiment, a large mirror was placed between the subjects' hands in such a way that the right hand was superimposed on the position of the left hand, which was behind the mirror and therefore not visible. The large mirror was made of MRI-compatible material (plexiglass) and was shaped in such a way that it fit inside the scanner bore and fully obstructed the view of the hand behind the mirror (see fig 1B).

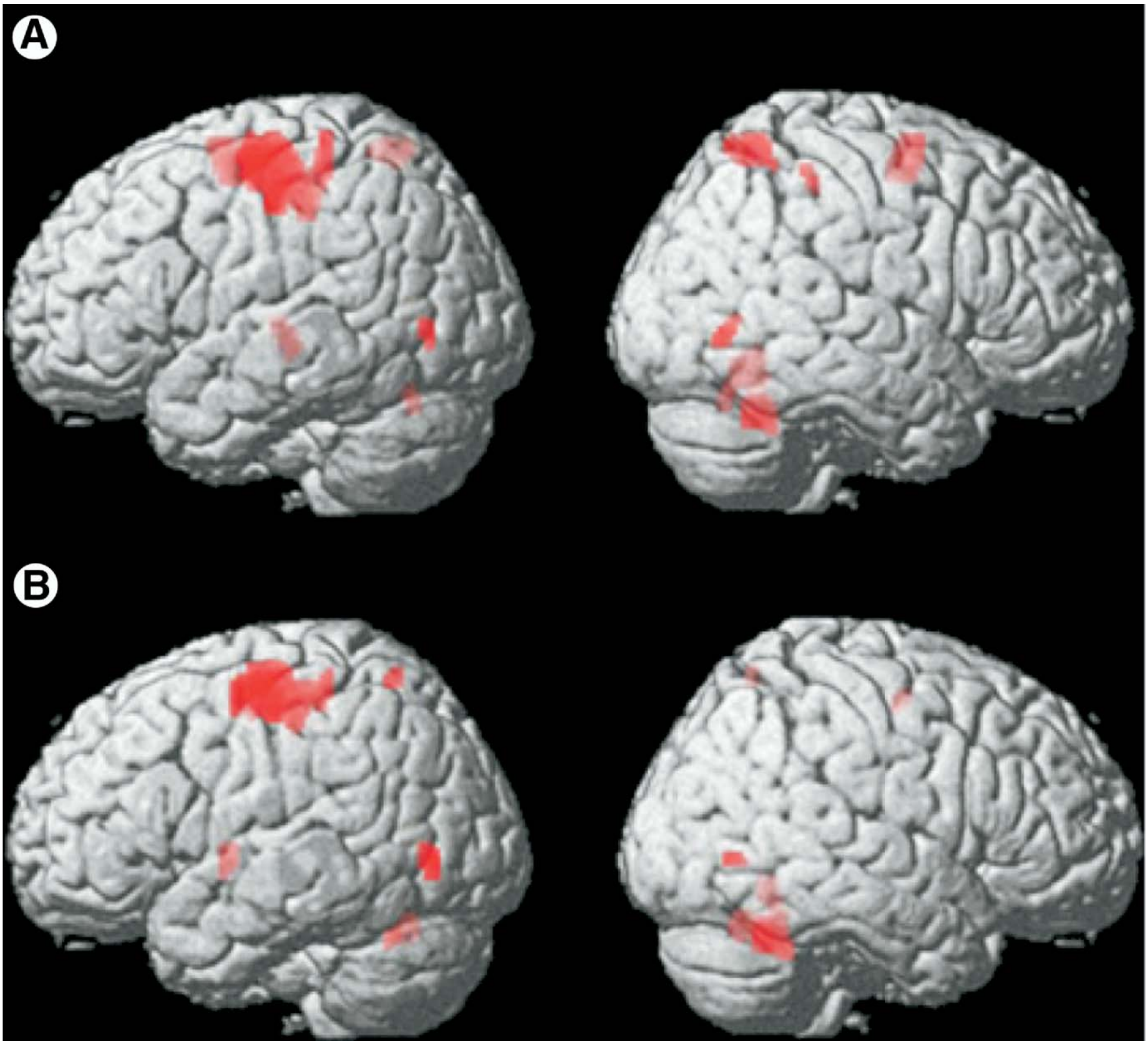

Fig 2. (A) Illustration of the brain activation in the no-mirror condition compared with rest. (B) Illustration of the brain activation in the mirror condition compared with rest.

In this way, we aimed at creating the visual illusion of a moving instead of a nonmoving left hand. While the presence or strength of the illusion could not be objectified, subjects reported that the illusion of seeing the left hand moving was similar to their experience during mirror exercises outside the MRI scanner.

Throughout both experiments, the subjects could always see 2 hands. In the no-mirror experiment, subjects were instructed to focus visually on the right hand both during the finger tapping and during the rest condition (see fig 1A). In the mirror experiment, subjects were instructed to focus visually on the mirror reflection of the right hand (ie, the illusory left hand) during both the finger tapping and the rest condition.

To evaluate a potential confounding effect of the number of finger taps performed in either of the 2 experiments, the number of finger taps for each experiment was counted during the experiments by an observer in a subsample of 9 subjects. The difference in the average number of finger taps between the 2 experiments was compared using a paired *t* test.

Data Acquisition

For each subject, the images were acquired on a 1.5T MRI scanner[b] using a dedicated 8-channel receiver head coil. For the anatomical image, a high-resolution 3-dimensional T1-weighted fast spoiled gradient-echo inversion recovery sequence covering the whole brain was acquired (repetition time/echo time/inversion time 9.9/2.0/400ms; Array Spatial Sensitivity Encoding Technique factor 2; acquisition matrix 320×224; field of view, 24cm; slice thickness, 1.6mm; no gap). For the functional images, a single shot gradient-echo EPI sequence in transverse orientation was used that is sensitive to blood oxygenation level–dependent contrast (repetition time/echo time 3000/40ms; acquisition matrix 96×96; field of view, 26cm; slice thickness, 5mm; gap, 1mm). The imaging volume covered the entire brain including the cerebellum. Acquisition time was 5:15 minutes a scanning session, which included 15 seconds of dummy scans that were discarded from further analysis.

Data Analysis

The imaging data were analyzed using SPM software 2[c] implemented in Matlab 6.5.[a]

On a single-subject level, all functional images were realigned to the first volume of the functional imaging series, and additional correction for motion artifacts was performed using the unwarp toolbox of SPM2.[c] All functional images were then coregistered with the subjects' anatomical (T1-weighted) images. Subsequently, the resulting images were normalized to the standard space defined by the Montreal Neurological Institute template; the anatomical images were normalized to the T1-weighted template, the functional images to the EPI template. The normalized data were spatially smoothed with a Gaussian filter (kernel with full width half maximum of 8mm) to compensate for intersubject gyral variability and to ensure the validity of the inferences.[20,21]

Statistical parametric maps were calculated using the general linear model by modeling the active and the rest condition as a box car function convolved with a standard hemodynamic response function.[22] Realignment parameters were implemented into the design matrix as regressors of no interest. The model was estimated with removal of global effects, and with a high-pass filter with a cut-off of 128s. For each experiment, data from the 2 scanning sessions were pooled, and a t-contrast was calculated for the active (finger tapping) minus the rest condition. This resulted in 2 t-contrast maps a subject: [finger tapping $>$ rest]$_{\text{Mirror}}$ and [finger tapping $>$ rest]$_{\text{No-Mirror}}$.

The individual statistical maps of the mirror and the no-mirror experiments were then used for a second level random-effects group analysis. For each of the experiments, a 1-sample *t* test across all 18 subjects was performed to assess group effects for each of the experiments separately. The significance threshold was set at $P<.05$ (family-wise error corrected for

Table 1: Cortical Activation Patterns Associated With Finger Tapping Compared With Rest in the No-Mirror and the Mirror Experiment: Foci of Significant Activation and Their MNI Stereotaxic Coordinates

	No-Mirror					Mirror				
			Coordinates					Coordinates		
	Cluster Size	Maximum *z* Score	x	y	z	Cluster Size	Maximum *z* Score	x	y	z
Left premotor cortex, left primary motor cortex		6.24	−38	−18	60		6.2	−38	−18	60
Left somatosensory cortex		5.48	−34	−36	64					
Left somatosensory cortex, left primary motor cortex		5.47	−36	−26	48		5.71	−38	−24	52
Left premotor cortex	787					656	5.88	−30	−14	56
Left supplementary motor area		5.92	2	−4	56					
Right supplementary motor area	200	5.56	2	0	64					
Right cerebellum VI	171	5.53	24	−54	32		5.9	24	−52	−32
Right cerebellum IV-V							5.11	8	−52	−20
Cerebellar vermis 4,5	113	6.31	4	−58	−10	318	5.63	4	−56	−10
Cerebellar vermis 6		5.22	4	−66	−24	49	5.48	6	−66	−24
Right superior parietal lobule	117	5.61	20	−58	60					
Left thalamus	41	5.44	−14	−22	2					
Right middle temporal gyrus	40	5.22	46	−68	−2	18	5.1	48	−68	0
Left middle occipital gyrus	26	5.14	−46	−72	0	77	5.46	−50	−74	−2
Left superior parietal lobule						17	5.4	−22	−60	62
Right somatosensory cortex	16	5.02	38	−38	54					

NOTE: Family-wise error corrected 0.05.
Abbreviation: MNI, Montreal Neurological Institute index.

multiple comparisons) and at a minimum cluster size of 15 voxels. Differences between the 2 experiments, presumably induced by the mirror reflection of the moving hand, were assessed using a paired *t* test, and a t-contrast map was calculated for the mirror minus the no-mirror experiment ([finger tapping > rest]$_{Mirror}$ > [finger tapping > rest]$_{No\text{-}Mirror}$) and vice versa ([finger tapping > rest]$_{Mirror}$ < [finger tapping > rest]$_{No\text{-}Mirror}$). A more liberal threshold at voxel level was used ($P<.0001$; not corrected for multiple comparisons) although with a threshold corrected for multiple comparisons at a cluster level ($P<.05$). Minimum cluster size was set at 15 voxels. For anatomic labeling of the observed activations in SPM2, we used the Anatomy toolbox.[23]

RESULTS

No difference in the average number of finger taps was found between the 2 experiments (39.9 finger taps/block for the no-mirror experiment vs 40.2 finger taps/block for the mirror experiment; $P=.54$). Visual inspection indicated that subjects did not move the hand behind the mirror in the mirror conditions.

Cortical Activation for the No-Mirror and Mirror Experiments Separately

Group analysis t-contrast maps of finger tapping versus rest for each of the experiments are presented in figures 2A and B. The corresponding Montreal Neurological Institute index coordinates, *z* scores, and cluster size are summarized in table 1. We found similar activation patterns for both experiments, which were in accordance with the expected activation for a finger tapping task.

In both experiments, activation was seen in the left precentral and postcentral gyrus (primary motor and somatosensory cortex, respectively), the left precentral gyrus/superior frontal gyrus (premotor cortex), the right middle temporal gyrus, the left middle occipital gyrus, and the cerebellum (right VI, vermis 4/5/6). Activation was also seen in the superior parietal lobule: in the right hemisphere during the no-mirror experiment and in the left hemisphere during the mirror experiment. In the no-mirror experiment, additional activation was seen in the right postcentral gyrus (primary somatosensory cortex), although to a lesser extent than on the left side, the medial superior frontal gyrus bilaterally (SMA), and the left thalamus.

Differences in Cortical Activation Between the No-Mirror and the Mirror Experiments

Two areas were activated more in the mirror experiment than in the no-mirror experiment, as shown in figure 3 and table 2. These were located in the right STG and in the right superior occipital gyrus (visual area V2). No brain areas were activated more in the no-mirror experiment compared with the mirror experiment.

DISCUSSION

The aim of the present study was to identify the neural networks associated with mirror-induced visual illusion of hand movements, as an experimental substrate of mirror therapy to facilitate motor rehabilitation. A direct comparison of the 2 experiments in this study revealed that the illusion of left

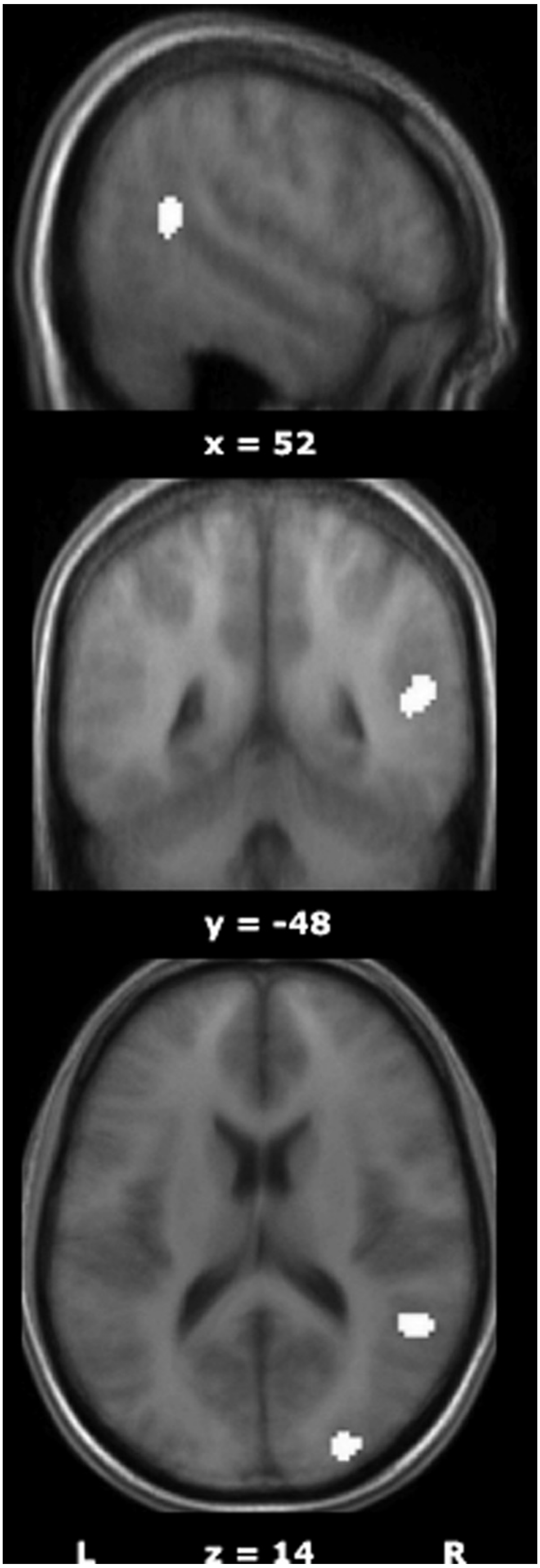

Fig 3. Illustration of brain activation in the mirror condition more than the no-mirror condition after group analysis. Results are presented in sagittal, coronal, and axial views.

Table 2: Group Result of the Mirror is Greater Than No-Mirror Contrast

	Cluster	MNI X	MNI Y	MNI Z	*z* Score	Cluster Size	Region
Mirror > No-Mirror	1	52	−48	14	4.53	100	Right STG
	2	26	−88	12	4.43	71	Right superior occipital gyrus (V2)

NOTE: At a threshold of $P<.0001$ (uncorrected) at voxel level and $P<.05$ (family-wise error corrected) at cluster level and minimum cluster size of 15 voxels.
Abbreviation: MNI, Montreal Neurological Institute index.

handed finger tapping (while in fact the left hand was not moving) induced activation in 2 visual areas: the right STG and the right superior occipital gyrus.

The STG is a higher-order visual region involved in the analysis of biological stimuli and is activated by observation of biological motion.[24] The coordinates of STG activation in our study are very similar to the coordinates of the STS reported in a study on imitation of hand movements. Based on his results, Iacoboni et al[25] suggested a model for imitation with feedforward and feedback mechanisms between STS and the frontoparietal MNS. The right superior occipital gyrus is located in the V2 and lies within the dorsal visual stream. The dorsal visual stream is connected with the PPC, a large associative cortical region, where afferents from different sensory modalities are integrated to provide the basis for perceptual processes.[26] The PPC is considered a part of the motor system and may be crucial for visuomotor transformations—that is, an automatic conversion of visual information into motor commands.[27] Based on this, the superior occipital gyrus activation found in this study as a result of the mirror reflections may indicate that mirror-induced visual illusions may influence the PPC.

Study Limitations

The present study has some potential limitations we would like to address. One limitation may be that, although we have tried to reproduce the visual illusion that is successfully used for mirror therapy in a number of clinical studies, it was impossible to quantify the strength of the illusion induced during the fMRI experiment. However, when asked, subjects reported that the illusion during the fMRI measurements was similar to the mirror exercises outside the MRI scanner. Second, we simulated a setting in an MRI scanner with healthy subjects as an experimental substrate of mirror therapy, which is normally used in a different environment in a patient population (such as patients with stroke, phantom limb pain, or complex regional pain syndrome). In these patients, the mirror reflection creates the illusion of normative movement of a hand that is absent or that is not able to move normally. Our results, therefore, need to be evaluated further in patients to understand better the underlying mechanism of mirror therapy. Third, we used a statistical threshold which, albeit stringent, was not corrected for multiple comparisons because of the limited statistical power of our study. Finally, it should be mentioned that as a consequence of the difference in the gaze direction, there is also a difference in the amount of visual input in both experiments. In the no-mirror experiment, subjects observed 1 moving hand, while in the mirror experiment they observed 2 moving hands. In addition, in the mirror experiment, subjects were asked to focus on the mirror reflection of the right moving hand superimposed on the left hand, while in the no-mirror experiment, subjects observed the right hand.

To our knowledge, our fMRI study is the first to evaluate the effect of mirror-induced visual illusions of hand movements on brain activation patterns. Two recent TMS studies have suggested that mirror reflections increase the corticospinal excitability of M1 corresponding with the hand behind the mirror.[13,28] In the present study, we did not find an increased activation of M1 in the right hemisphere. However, it should be noted that both TMS studies reported a significantly increased M1 excitability only when the mirror condition was compared with a control condition in which the subjects moved the right hand but did not directly observe this hand movement. When the mirror condition was compared with a control condition in which the subjects directly observed the moving right hand, no significant differences were found. The latter situation is more comparable to the control condition in our study in which subjects observed hand movements of the right hand during the no-mirror experiment. The apparent contradiction between our findings and those previously reported with regards to M1 activation, therefore, is most likely a result of differences in experimental setup.

CONCLUSIONS

In literature, several hypotheses on underlying working mechanisms for mirror therapy in motor rehabilitation have been proposed. While Altschuler et al[8] suggested that the mirror reflections may help to recruit the premotor cortex through the intimate connection between visual input and premotor areas, in our study we did not find activation in the premotor areas that are uniquely associated with mirror-induced visual illusions. Other authors suggested that mirror therapy could be a specific form of visual-guided motor imagery.[10] Areas found to be activated during motor imagery are M1, PMC, SMA, anterior cingulate cortex, parietal lobule, and cerebellum.[29] In this study, we did not find activation located in these areas, suggesting that mirror therapy may not be similar to motor imagery. However, it should be noted that we did not instruct the subjects to perform imagery of the hand behind the mirror, but rather to focus on the visual illusion of a moving hand superimposed on a nonmoving hand. It has also been suggested that there is involvement of the mirror neuron system in mirror therapy.[11,12] The mirror neuron system is located in the Broca area, the ventral premotor area, and the posterior parietal lobe with a visual extension area in the STS. Given the lack of activation within the Broca or premotor area, nor within the parietal lobe in this study, interpretation of the STG activation located within the region of STS is difficult, and is not sufficient to prove an involvement of the mirror neuron system. But it does provide a suggestion of a link between mirror therapy and the mirror neuron system. However, our study may direct future studies, especially in patient groups, to indicate the relevance of the mirror neuron system for mirror therapy.

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