Mirror Observation of Finger Action Enhances Activity in Anterior Intraparietal Sulcus: A Functional Magnetic Resonance Imaging Study

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ABSTRACT. Mirror therapy can be used to promote recovery from paralysis in patients with post-stroke hemiplegia. There are a lot of reports that mirror-image observation of the unilateral moving hand enhanced the excitability of the primary motor area (M1) ipsilateral to the moving hand in healthy subjects, but the neural mechanisms underlying its therapeutic effects are currently unclear. To investigate this issue, we used functional magnetic resonance imaging to measure activity in brain regions related to visual information processing during mirror image movement observation. Thirteen healthy subjects performed a finger-thumb opposition task with the left and right hands separately, with or without access to mirror observation. In the mirror condition, one hand was reflected in a mirror placed above the abdomen in the MRI scanner. In the masked mirror condition, subjects performed the same task but with the mirror obscured. In both conditions, the other hand was held at rest behind the mirror. A between-task comparison (mirror versus masked mirror) revealed significant activation in the ipsilateral hemisphere in the anterior intraparietal sulcus (aIP) while performing all tasks, regardless of which hand was used. The right aIP was significantly activated while moving the right hand. In contrast, in the left aIP, a small number of voxels showed a tendency toward activation during both left and right hand movement. The enhancement of ipsilateral aIP activity by the mirror image observation of finger action suggests that bimodal aIP neurons can be activated by visual information. We propose that activation in the M1 ipsilateral to the moving hand can be induced by information passing through the ventral premotor area from the aIP.

Key words: Hemiplegia, Rehabilitation, Mirror therapy, Anterior intraparietal sulcus

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It has been reported that therapy using visual information is effective for rehabilitation of patients with post-stroke hemiplegia. Several methods have been developed for providing visual information, such as directly showing the action of the paralyzed limb1) and using virtual reality technology2). Ramachandran et al.3) reported that symptoms in patients with phantom sensations could be improved by observing the intact arm reflected in a mirror placed vertically to the sagittal plane, with the phantom arm placed behind the mirror to prevent it being seen by the patient (mirror therapy). At present, mirror therapy is used as a method to promote motor recovery from hemiplegia, and its effectiveness has been reported in a number of studies4–8). Altschuler et al.4) reported that mirror-image observation of the non-paralyzed hand induced an illusion in which the paralyzed hand behind the mirror was perceived to move as if it were normal. A transcranial magnetic stimulation (TMS) experiment conducted with healthy subjects to examine primary motor cortex (M1) excitability when they directly observed the action of a unilateral hand reported that M1 excitability...
Wheaton et al. involved motion control of various parts of the body. Similar results were obtained in another study using functional magnetic resonance imaging (fMRI). These results suggest the possibility that mirror therapy optimizes neuroplasticity and promotes recovery from paralysis in brain-injured patients.

However, the mechanism by which ipsilateral M1 activation is induced by visual information from a mirror image remains unknown. The parietal lobe, especially anterior intraparietal sulcus (aIP), integrates visual information and somatosensory information, and is closely involved in motion control of various parts of the body. Wheaton et al. examined activated brain regions during video-observation of motions of various body parts (hands, feet, and face) to study the occurrence of selective cortical activity depending on the body part. This suggests that the visual and motor cortical regions have particular neurocircuitry depending on the specific body part, and that visual information has a strong effect on the motor cortical region.

The parietal lobe, especially aIP, seems to play an important role in M1 activation during mirror-image observation. This study used fMRI to investigate the neural mechanisms underlying mirror therapy. Specifically, we measured activity in brain regions related to visual information processing during mirror image processing of unilateral hand motion in healthy subjects.

Materials and Methods

Subjects

Thirteen neurologically healthy right-handed subjects (six male, seven female, mean age 23.5 years, range 20 to 32 years) studying at Ibaraki Prefectural University participated in this study. All subjects completed the Edinburgh inventory to confirm their handedness. All procedures were approved by the Ethics Committee of Ibaraki Prefectural University.

fMRI task

Subjects were instructed to perform a finger-thumb opposition task using one hand in a self-paced manner at approximately 1 Hz. For scanning, subjects were placed on the bed of an MRI machine in the supine position, with their hands placed on their chest approximately 30 cm from their eyes. A plastic mirror (15 × 40 cm) was fixed vertically above the chest (at an angle of approximately 10 degrees to the long axis of the trunk) so as to reflect one of their hands (moving hand). To prevent the moving hand from being seen by the subject, a piece of cardboard (12 × 15 cm) was placed in an intermediate position between the hand and the eyes. The subjects were instructed to place the other hand (non-moving hand) at rest behind the mirror. fMRI imaging was performed under two different conditions: 1) a mirror condition where the subjects observed the moving hand reflected in the mirror, and 2) a masked mirror condition where the subjects were not allowed to observe the moving hand, and the mirror was covered by a piece of white paper. Block-design fMRI imaging was started with dummy recording (in the resting phase) for 9 seconds, then recorded during the movement phase (18 sec) and the resting phase (12 sec) five times each (159 sec in total). The eyes were open in the resting phase. An experimenter notified the subjects of the time to start the movement phase and the resting phase by tapping their knee. The experimenter stood on the side of the non-moving hand of the subjects during the experiment to visually check that their non-moving hand did not move. One session of each task was performed for each hand (four sessions in total). The order of the conditions was pseudo-randomized. All subjects participated in a rehearsal session for approximately 5 minutes before starting the test.

fMRI measurements

fMRI images were acquired using a 1.5 Tesla scanner (TOSHIBA, Japan). The subject’s head was immobilized with a foam pad in the scanner. Functional data were acquired with T2*-weighted gradient-echo planar imaging (EPI) using blood oxygen level-dependent (BOLD) contrast (repetition time [TR] = 3 sec, echo time [TE] = 50 msec, flip angle [FA] = 90 degrees, slice thickness = 4 mm, between slice = 5 mm, field of view [FOV] = 256 × 256 mm, 64 × 64 matrix). Thirty three slices were collected with a voxel dimension of 4 × 4 × 4 mm³. The first three volumes of each run were discarded to reach signal equilibrium. Additionally, the anatomical (T1-weighted) images were coregistered with the subject’s corresponding mean realigned EPI volume and normalized with the same deformation parameters.

fMRI data analysis

Data were analyzed using statistical parametric mapping software (SPM2; Wellcome Department of Cognitive Neurology, London), running under MATLAB 5.3 (Mathworks, Sherbon, MA). For each subject, images were realigned to the first volume to correct for head movement, and normalized into standard stereotaxic space using the Montreal Neurological Institute template (MNI). The transformed data set for each subject was smoothed with a Gaussian filter (full width half maximum = 8 mm) to compensate for normal variation in anatomy across subjects. The time series was high-pass filtered (120 sec) to remove low-frequency artifacts.
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Image analysis

Within-task analysis. Statistical analysis was performed for each subject, and the stereotaxically normalized fMRI time series data from all subjects were pooled for random effects group analysis. Analysis of the four conditions of the task (mirror and masked mirror) used a subtraction design (using a box-car function with a hemodynamic response function, in a general linear model) to reflect statistically significant activation.

Data analysis

All images were examined with a voxel-specific *t*-test {SPM(t)} across all subjects. In contrasts between movement and rest conditions, regionally specific differences that survived an uncorrected threshold of \( p < 0.001 \) (\( Z = 3.33 \), cluster size = 5 pixels) were considered statistically significant. Similarly, in a contrast between mirror versus masked mirror conditions, the threshold was calculated as \( p < 0.01 \) (\( Z = 2.52 \), cluster size = 5 pixels), and the volume of interest (VOI) of each activated region was calculated with definition at the cluster level. The stereotactic coordinates of the voxels that showed significant activation were then matched with the anatomical localization of the local maxima in the MNI (Montreal Neurological Institute) template brain.

Results

Activation in the mirror condition versus rest

Subjects who observed the mirror image of their moving hands showed strong activation in cortical regions, especially in the movement-related area of the hemisphere contralateral to the moving hand (Table 1, Fig. 1). When the right hand was moved, activation was exhibited in the left precentral gyrus (BA4), postcentral gyrus (BA3, 1, 2), premotor area (BA6), supplementary motor area (BA6), inferior frontal gyrus (BA44), and right cerebellum (Fig. 1a). Similarly, when the left hand was moved, activation was observed in the right precentral gyrus (BA4), postcentral gyrus (BA3, 1, 2), bilateral premotor area (BA6), and left cerebellum (Fig. 1b).

Activation in the masked mirror condition versus rest

Even in the condition where subjects could not observe the mirror image of their hand movement, activation was found in the movement-related area of the hemisphere contralateral to the moving hand (Table 1, Fig. 1). When the right hand was moved, activation was exhibited in the left precentral gyrus (BA4), postcentral gyrus (BA3, 1, 2), premotor area (BA6), supplementary motor area (BA6), inferior frontal gyrus (BA44), and right cerebellum (Fig. 1a). Similarly, when the left hand was moved, activation was observed in the right precentral gyrus (BA4), postcentral gyrus (BA3, 1, 2), bilateral premotor area (BA6), and left cerebellum (Fig. 1b).

Activation in the mirror versus masked mirror conditions

Since the activation related to the movement of the subjects’ hands in each condition cancels out, only the regions of activation directly related to the mirror image are shown here (Table 2, Fig. 2). Whether the left or right hand was moved, the ipsilateral anterior intraparietal sulcus (aIP) showed the strongest activation. The aIP activation

<table>
<thead>
<tr>
<th>Moving hand</th>
<th>Anatomical area (Broadmann’s area)</th>
<th>MNI Coordinates of cluster center</th>
<th>Z-max</th>
<th>MNI Coordinates of cluster center</th>
<th>Z-max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right hand</td>
<td>Left pre &amp; post central gyrus (4, 1, 2, 3)</td>
<td>-38 -22 54 5.94</td>
<td></td>
<td>Right hand</td>
<td>-36 -22 52 4.58</td>
</tr>
<tr>
<td></td>
<td>Left premotor cortex (6)</td>
<td>-46 -6 50 5.16</td>
<td></td>
<td></td>
<td>-54 -4 50 4.58</td>
</tr>
<tr>
<td></td>
<td>Left supplementary motor cortex (6)</td>
<td>-2 -2 54 4.48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Left inferior frontal gyrus (44)</td>
<td>-50 4 -4 5.38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Right cerebellum</td>
<td>4 -60 -18 4.88</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left hand</td>
<td>Right pre &amp; post central gyrus (4, 1, 2, 3)</td>
<td>38 -26 54 5.17</td>
<td></td>
<td>Left hand</td>
<td>38 -26 52 4.27</td>
</tr>
<tr>
<td></td>
<td>Right premotor cortex (6)</td>
<td>42 -14 48 5.25</td>
<td></td>
<td></td>
<td>40 -14 46 4.50</td>
</tr>
<tr>
<td></td>
<td>Left premotor cortex (6)</td>
<td>-50 2 54 4.27</td>
<td></td>
<td></td>
<td>-48 6 52 4.06</td>
</tr>
<tr>
<td></td>
<td>Left cerebellum</td>
<td>-6 -56 -18 4.57</td>
<td></td>
<td></td>
<td>-4 -58 -12 4.21</td>
</tr>
</tbody>
</table>

Threshold at \( p < 0.001 \) (\( Z = 3.33 \), cluster size = 5 pixels).

Table 1. Areas of brain activation when subjects observed mirror images of their own hand movements (mirror condition versus rest) and when subjects could not observe the mirror images (masked mirror condition versus rest).
was stronger when the right hand was moved (Fig. 2a) than when the left hand was moved (Fig. 2b). When the right hand was moved, more voxels in the right aIP were activated than in the left, but when the left hand was moved, very few voxels were activated on the right, showing a large difference between the hands. In contrast, only a few voxels were activated in the left aIP with movement of either hand compared with that of the right aIP (Table 2). Activation was also observed in the ipsilateral occipital lobe when either hand was moved.

**Discussion**

In this study, activated regions in the brain were examined during the observation of one-hand motion reflected in a mirror. There was only a slight difference in the location of activated regions between the mirror condition and the masked mirror condition, with the main areas of activation located in the motor areas and parietal lobe in the hemisphere contralateral to the moving hand, regardless of whether it was the left or right. These regions of activation are broadly consistent with the results of previous studies.
using observation of hand motion in a similar manner to this study\(^{17,18}\), and other studies without observation of the moving hand\(^{19–21}\).

The main finding of the current study was significant activation in the aIP, with which anterior BA40, BA7 and primary sensory areas (S1) intersect, during the observation of hand motion reflected in a mirror. In addition, it was shown that the aIP tended to be activated more intensely in the ipsilateral hemisphere than in the hemisphere contralateral to the moving hand. In patients with post-stroke hemiplegia, mirror-image observation of the hand can induce a visual illusion in which the paralyzed hand was felt to move as if it were normal\(^4,6\). Zampini et al.\(^6\) reported that illusory movements are not generated in the primary cortices, but are probably linked to higher order, multimodal areas concerned with the integration of primary inputs into a unitary image of the body. These findings suggest that the aIP, as a higher-order processing region of the parietal lobe, may be involved in the expression of illusory movements.

Previous studies have reported that there is a type of bimodal neuron in the anterior intraparietal sulcus (aIP) of the monkey that responds to somatosensory and visual information, and plays an important role in visual-motor integration\(^{12–14}\). Obayashi et al.\(^14\) found that, after visual-motor learning, the intraparietal sulcus (IPS) bimodal (somatosensory and visual) neurons of a monkey still functioned according to the learned motor skill, even if visual information was blocked. They argued that physical movement is coded in IPS bimodal neurons, and that movement is imagined based on positional information from proprioceptors even if visual information is blocked. In a study of the aIP bimodal neuron of humans, Lloyd et al.\(^22\) used fMRI to examine brain areas activated by vibrational stimulation when the right hand was placed on the left hemifield across the midline of the trunk. In the eyes-closed condition, the contrast of tactile stimulation to the right hand when it was across the midline compared with when it was in the right-side hemispace revealed activation solely in the right ventral intraparietal sulcus. When the stimulated site of the right hand was fixated with the eyes open in the same position, aIP activation was completely shifted to the left hemisphere. The authors speculated that such a shift of lateralization occurred because, when visual information was blocked, the hand was represented in an up-to-date manner by information about the hand from the proprioceptor. They also speculated that visual information codes the anatomical position of the hand, regardless of where it lies in external space. In our study, observation of hand movement reflected in a mirror intensely activated the contralateral aIP of the non-moving hand (the hand behind the mirror). This result suggested that activation of the contralateral aIP was induced by subjects recognizing the mirror image of the hand as their anatomical hand, even though proprioceptive information from the hand behind the mirror was blocked. In other words, our findings suggest that bimodal aIP neurons may have been activated by visual information from
the mirror image. It has been suggested that AIP of the monkey is closely connected with the ventral premotor cortex (PMv), and that a kinesthetic copy of joint movement is formed in the parietal lobe during observation of motion then transmitted to the PMv and used for the control of movement. Using TMS, Aziz-Zadeh et al. reported that excitability of the M1 contralateral to the moving hand was increased during the observation of direct unilateral hand motion. This finding suggests that visual information regarding a part of the body has a direct connection with movement, and that visual information about the body is likely integrated in the aIP and transmitted through the PMv to induce M1 activation (i.e. a sensory-motor loop system).

Another characteristic finding regarding aIP activation in the current study is that, while the right aIP showed a higher level of activation during movement of the right hand (mirror image of the left hand), the left aIP exhibited a lower level of activation, but was activated during movement of both hands. This finding suggests that the left aIP is dominant for visual information, because the right aIP responds to only one of the hands, but the left aIP responds to both hands. However, Garry et al. used TMS to examine ipsilateral M1 activation during the observation of a mirror image of the left or right hand, and reported no difference in activation between hands. In addition, it has been previously reported that no asymmetry exists in contralateral M1 activation between the left and right hands during direct observation of the moving hand. It is not possible to fully elucidate the relationship between asymmetry of IP activation and M1 activation based solely on the current results. In addition, no previous study has reported a difference in recovery from paralysis by mirror therapy between the left and right hands. As such, more detailed investigations, including clinical studies, are required in the future.

References