Brain activation during manipulation of the myoelectric prosthetic hand: a functional magnetic resonance imaging study

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Neuroimaging data, particularly functional magnetic resonance imaging (fMRI) findings, have not been reported in users of the myoelectric or electromyographic (EMG) prosthetic hand. We developed a virtual EMG prosthetic hand system to eliminate mutual signal noise interference between fMRI imaging and the EMG prosthesis. We used fMRI to localize activation in the human brain during manipulation of the virtual EMG prosthetic hand. Fourteen right-handed normal subjects were instructed to perform repetitive grasping with the right hand with eyes closed (CEG); repetitive grasping with the right hand with eyes open to obtain visual feedback of their own hand movement (OEG); and repetitive grasping with the virtual EMG prosthetic hand with the eyes open to obtain visual feedback of the prosthetic hand movement (VRG). The specific site activated during manipulation of the EMG prosthetic hand was the right ventral premotor cortex. Both paradigms with visual feedback also (OEG and VRG) demonstrated activation in the right posterior parietal cortex. The center of activation of the right posterior parietal cortex shifted laterally for visual feedback with the virtual EMG prosthetic hand compared to a subject's own hand. The results suggest that the EMG prosthetic hand might be recognized in the brain as a high-performance alternative to a real hand, being controlled through a "mirror system" in the brain.
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Introduction

Prosthetic hands include the decorative, power-assisted, and myoelectric or electromyographic (EMG) prostheses. The EMG prosthetic hand is a man–machine system manipulated as one likes by computer-intelligence circuits, and is felt as a part of the user's body (Flor et al., 1995). In contrast, other prosthetic hands can be moved only in a manner of a stick, and are felt as an alien object. The decorative prosthesis is used only for the sake of appearance, and does not move at all. The power-assisted prosthesis works by a spring. The enhanced utility of the EMG prosthetic hand in forearm amputees was found to be associated with reduced phantom limb pain (Lotze et al., 1999a). This suggested that ongoing stimulation, muscular training of the stump, and visual feedback from the EMG prosthetic hand might have a beneficial effect not only on phantom limb pain, but also on cortical reorganization (Ramachandran et al., 1995). The EMG prosthetic hand should not be regarded as a simple alternative.

No findings by neuroimaging with positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) have been reported in users of the EMG prosthetic hand. In particular, fMRI has not been used in research concerning the EMG prosthetic hand because of signal noise mutually disrupting fMRI images and electromyography of the prosthesis. We developed a virtual EMG prosthetic hand system to eliminate this interference. Using the EMG prosthetic hand, which could move virtually as a user directed it in the fMRI examination room, we sought to define the neural network activated when subjects manipulated the EMG prosthetic hand.

Subjects and methods

Subjects

Fourteen right-handed male subjects with no neurologic or psychiatric history participated in the imaging study (age range, 21–26 years). All gave informed consent according to procedures approved by the Ethics Committee of the Hiroshima Prefectural Rehabilitation Center.

Experimental system

Fig. 1 illustrates the EMG measuring system that we developed for use near the fMRI scanner (MAGNETOM SYMPHONY: Siemens, Erlangen, Germany). This MRI instrument has a static

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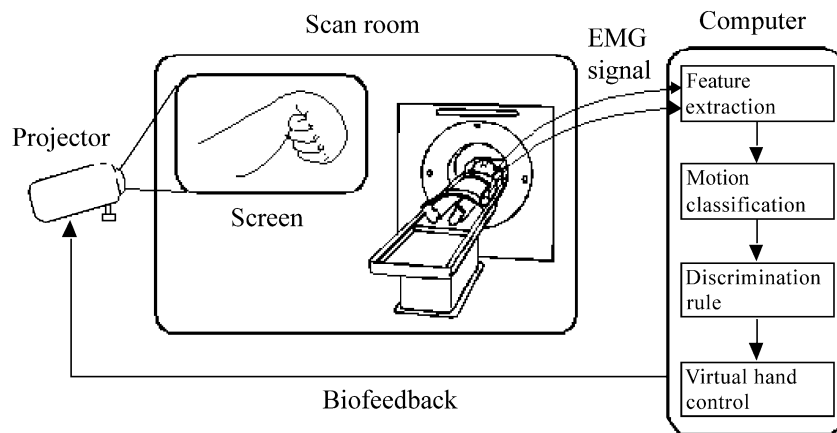**Available online on ScienceDirect (www.sciencedirect.com).**

Fig. 1. The virtual electromyographic (EMG) prosthetic hand system developed by the authors. The system is accessible in the functional magnetic resonance imaging (fMRI) scanning room, but does not degrade fMRI image data in any way. A subject attaches surface electrodes to his forearm and operates the virtual EMG prosthetic hand visualized with three-dimensional (3D) computer graphics using the visual biofeedback projected on a screen in the scanning room. The intended hand motion of the subject was determined from processed EMG signals by a discrimination rule linking EMG patterns to the appropriate hand motions.

magnetic field strength of 1.5 T, a gradient magnetic field strength of 34 mT/m, and a superconductive magnet. A subject attaches surface electrodes to his right forearm and operates the virtual EMG prosthetic hand with three-dimensional (3D) computer graphics, using visual feedback projected onto a screen in the scanning room instead of directly manipulating and observing a prosthetic hand made of magnetic materials.

The EMG signals are measured from two pairs of surface electrodes and amplified 500 times by an EMG amplifier (MEM-4204, Nihon Kohden, Tokyo) outside of the scan room, after passage through a high-pass filter (cutoff frequency, 10 Hz) and a low-pass filter (cutoff frequency, 500 Hz). The preprocessed EMG signals then are recorded by a personal computer with linkage via an analog/digital converter (sampling frequency, 1.0 kHz; quantization, 12 bits). Acquisition timing of fMRI images is controlled by an external trigger signal transmitted from the computer to the MRI system through the electric–optical converter to synchronize initiation of EMG signal measurement and fMRI imaging without introducing external noise into the scanning room.

Since the developed system has powerfully adaptation ability for the individual differences of human operators, a volunteer can operate the virtual EMG prosthesis hand naturally soon after taking a brief training in advance. In addition, the virtual EMG prosthesis hand can respond within 5 ms after measuring EMG signals from the muscles, so that a volunteer does not feel time delay in manipulating it.

Behavioral tasks

In the experiments, the EMG signals were measured form extensor carpi ulnaris and flexor carpi ulnaris of the right forearm by putting two pares of EMG electrodes that linked to the virtual EMG prosthetic hand system described above. Three paradigms were given for each subject to carry out, as outlined below.

First paradigm (CEG): repetitive hand grasping by the right hand at a rate of 0.5 Hz, with the eyes closed.

Second paradigm (OEG): repetitive hand grasping by the right hand at a rate of 0.5 Hz, with the eyes open to obtain visual feedback of movement of one's own hand through a mirror.

Third paradigm (VRG): repetitive EMG prosthetic hand grasping at a rate of 0.5 Hz, with eyes open to obtain visual feedback of movement of the EMG prosthetic hand.

The hand movements were exactly similar in terms of power and complexity among three sessions. The paradigms were organized into an ABAB pattern, in which A involved resting with eyes closed, and B involved performing CEG, OEG, or VRG, each lasting through acquisition of 10 volumes. All subjects performed the paradigms in the order CEG, OEG, and then VRG at intervals of at least 15 min, to prevent confounding aftereffects from earlier paradigms. The system was exactly the same for all paradigms, and the paradigms did not differ in experimental noise introduced in acquiring imaging data.

EMG data processing

Changes in the gradient magnetic field during fMRI measurements cause strong noise signals that have much larger amplitude than EMG signals, essentially precluding assessment of EMG signals for manipulating the virtual prosthetic hand. Therefore, the system does not measure EMG signals during changing of the gradient magnetic field in fMRI measurement, while it holds values of the EMG signals measured just before changing the gradient magnetic field.

Denoised EMG signals then were rectified and filtered out through a second-order Butterworth filter (cutoff frequency, 1.5 Hz); a zero-order hold was applied while noise signals were removed. The hand motion during fMRI measurements was determined from the pattern of the EMG signals when the total sum of the filtered EMG signals is larger than the thresh hold determined with one measured at rest $EMG_i(n)$ ($i = 1,2$) (Fig. 2).
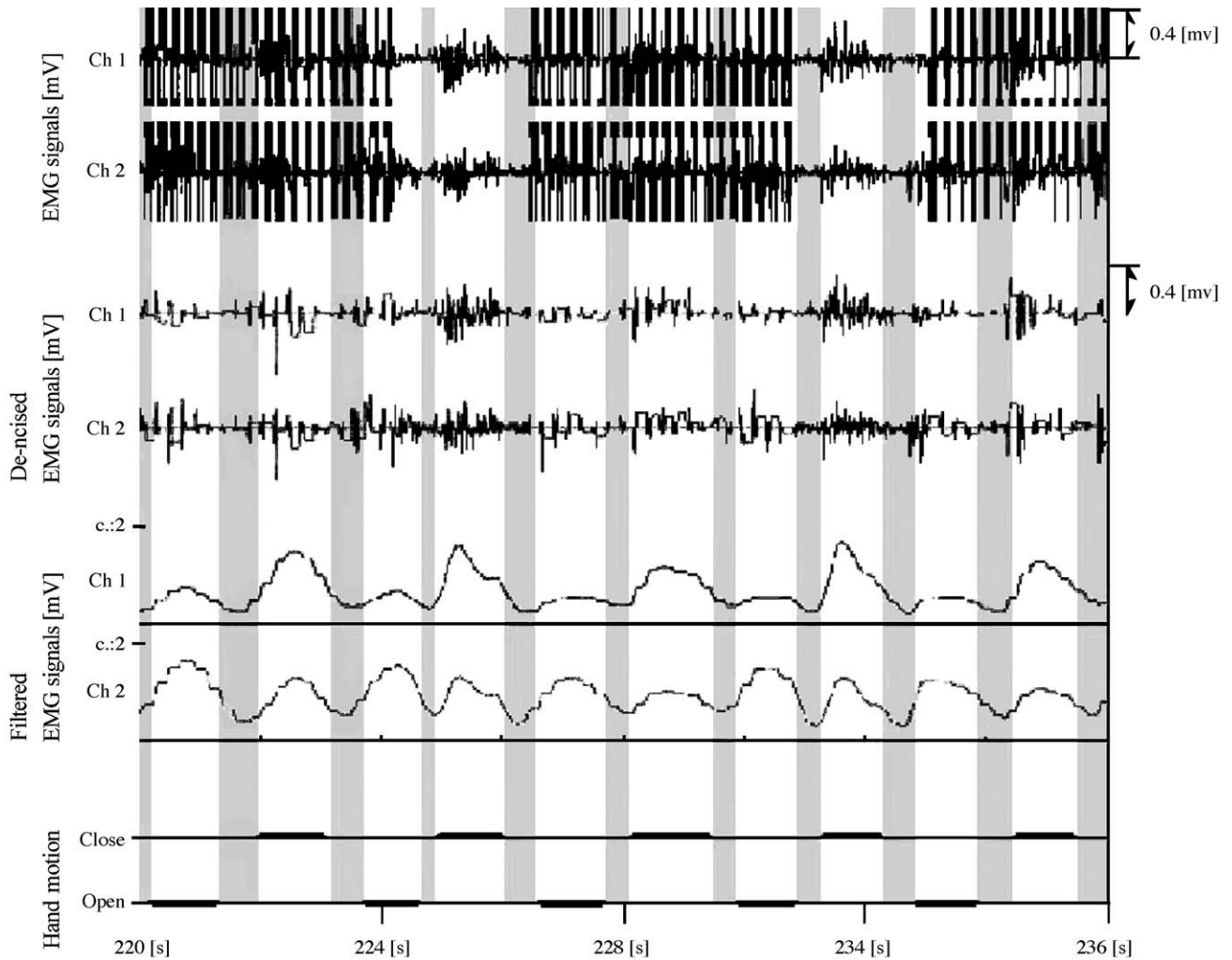
Fig. 2. An example of the measured electromyographic (EMG) signals during task performance by subject 1. Time history of the raw EMG signals, the denoised EMG signals, the filtered EMG signals, and the discrimination results are shown in the order from the top. The shaded zone represents the pending term of the discrimination of hand motions because muscle activation level is smaller than a threshold determined with the level at rest. Time histories of the EMG signals change periodically with respect to the hand-grasping motion. These patterns were confirmed with other subjects.

Since muscle force is almost proportional to the integrated EMG (IEMG, Dowben, 1980), we first analyzed muscle activations in each behavioral task by

$$J_{\text{IEMG}} = \sum_{i=1}^{2} \overline{\text{IEMG}_i}, \tag{1}$$

where $\overline{\text{IEMG}_i}$ represents a mean value of IEMG signal during hand grasping movements for the ith channel. The IEMG, however, did not include any muscle information in the period of acquiring fMRI image data. Therefore, we also evaluated with the following performance index J_{EMG} using the sampled EMG signals as

$$J_{\text{EMG}} = \sum_{n=0}^{N} \sum_{i=1}^{2} (\text{EMG}_i(n) - \text{EMG}_i^{\text{Rest}}) \Delta t, \tag{2}$$

where N indicates the number of sampled data in the experimental trial; Δt is a sampling time; and $\text{EMG}_i^{\text{Rest}}$ indicates a mean value of $\text{EMG}_i(n)$ measured in relaxing.

Image data acquisition

A 1.5-T SYMPHONY system (Siemens) was used to acquire 20 T*2-weighted transverse echo-planar (EPI) images (FOV = 192 × 192 mm; matrix size = 64 × 64; in-plane resolution = 3 × 3 mm²; flip angle = 90; T_E = 60 ms) with blood oxygenation level-dependent (BOLD) contrast. EPIs represented 6.0-mm-thick axial slices obtained every 6.0 mm, acquired continuously by an interleaf method during a 3-min session. An automatic shimming procedure was performed before each session. For each subject, 51 functional volumes were collected within a single scanning session, with an effective repetition time (T_R) of 4.4 s/vol. The first volumes obtained were discarded to allow for T1 equilibration effects. Image processing was carried out using SPM99 (Wellcome Department of Imaging Neuroscience, London, UK; see http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB 5.3 (Mathworks, Sherborn, MA). Images were realigned to the first volume by rigid body transformation, sync-interpolated over time to correct for phase advance during acquisition, and normalized into standard stereotactic space using the Montreal Neuro-

logical Institute template (MNI). Normalized images of $3 \times 3 \times 6$ mm^3 were spatially smoothed by a Gaussian kernel of FWHM 8–8–16 mm (Ashburner and Friston, 1997; Friston et al., 1995). Treating the volumes as a time series, the data were high-pass filtered to 1/120 Hz.

Image data analysis

We analyzed the data in three ways. First, we analyzed the main effects. These results are presented only where relevant. Second, we used conjunction analyses to study effects in common among the tasks. Finally, we estimated interactions between contexts to find activations that were greater for OEG than CEG, as well as greater for VRG than CEG. We also estimated interactions between contexts to find activations that were greater for VRG than OEG.

Data were analyzed using SPM99 employing a random-effects model implemented in a two-level procedure. At the first level, in a subject-specific analysis, we specified a general linear model to each context (CEG, OEG, VRG). For each comparison of interest, for each subject, a contrast of parameter estimates was calculated in a voxel-wise manner to produce a "contrast image." At the second level, the contrast images from all subjects were entered in a one-sample t test to assess population mean effects. In this way, the variance estimates at the second level incorporated were weighted appropriately between subject variance effects. To test for interactions between contexts for each event of interest, different second-level analyses were performed, including a contrast image for each event of interest for each subject. To examine responses commonly evoked by each paradigm (CEG, OEG, VRG), we carried out a conjunction analysis in all paradigms (CEG + OEG + VRG). The conjunction analysis addressed whether activations were jointly significant in a series of paradigm pairs, thus permitting us to identify paradigm-invariant regional responses.

On the basis of previous studies of the mirror system, we had a prior hypothesis for differential activity in the ventral premotor cortex and the posterior parietal cortex. The threshold of $Z > 3.09$ ($P = 0.001$, uncorrected, $T > 4.02$) was accepted for the group analysis concerning the mirror system (Grezes et al., 2003). We report activations of 10 or more contiguous voxels surviving the

threshold of $Z > 3.09$ ($P = 0.001$, uncorrected). Anatomical identification was carried out by superimposing the maxima of activation foci both on the MNI template and on the normalized structural images of each subject and labeled using the atlas of Talairach and Tournoux (1988).

Results

EMG data

We evaluated muscle activations from measured EMG signals with respect to hand movements in each of the behavioral tasks (Table 1). No significant differences were evident in characteristics of muscle activation and the hand movement patterns among CEG, OEG, and VRG with a threshold of $P < 0.05$ corrected for multiple comparisons.

Conjunction analysis

We performed conjunction analyses to describe the neural network common to all context (CEG, OEG, VRG), which meant the circuits of gripping (Table 2). Significant activations occurred in the left primary motor cortex, left supplementary motor area, and both cerebellar hemisphere. Activations were also detected in the premotor cortex and inferior parietal cortex with the left dominancy.

OEG vs. CEG

To identify brain regions more active in the context of OEG than in the context of CEG, we analyzed interactions between contexts. The interaction OEG–CEG (showing activity specific for visual feedback of the subject's right-hand grip) was associated with activation of the right posterior parietal cortex (30 −56 46, $Z = 4.49$), as well as right and left visual cortices (Fig. 3a).

VRG vs. CEG

To identify brain regions more active in the context of VRG than in the context of CEG, we again analyzed interactions

Table 1
Muscle activation with respect to hand movements in three behavioral tasks

	Subject	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CEG	J_{IEMG}	0.249	0.104	0.079	0.177	0.149	0.136	0.184	0.120	0.196	0.499	0.130	0.214	0.252	0.070
	J_{EMG}	19.20	9.10	8.74	16.25	11.57	11.77	17.37	11.07	16.88	48.81	14.28	23.04	25.98	10.53
	No. of hand, close	28	22	37	38	29	35	29	19	33	28	33	30	35	36
	No. of hand, open	28	22	36	38	29	35	30	18	33	29	35	31	33	36
OEG	J_{IEMG}	0.228	0.095	0.086	0.164	0.142	0.148	0.175	0.115	0.196	0.503	0.145	0.232	0.167	0.091
	J_{EMG}	24.30	6.92	8.56	14.98	13.37	13.55	18.23	10.87	21.00	60.45	13.64	22.99	20.37	9.35
	No. of hand, close	32	23	42	35	30	41	31	20	33	26	40	37	37	40
	No. of hand, open	32	24	42	34	29	40	32	20	33	27	40	37	37	40
VRG	J_{IEMG}	0.351	0.093	0.076	0.180	0.191	0.135	0.147	0.147	0.209	0.498	0.138	0.229	0.188	0.092
	J_{EMG}	28.64	10.08	6.53	18.95	20.43	14.13	16.57	16.00	22.14	59.41	13.52	23.06	19.25	9.74
	No. of hand, close	33	22	36	31	30	36	31	25	28	27	42	38	37	39
	No. of hand, open	31	24	35	31	29	36	31	24	30	29	42	39	37	38

Significant differences in muscle activities between the three groups were not evident with the threshold set at $P < 0.05$, corrected for multiple comparisons. CEG = repetitive grasping by the right hand at a rate of 0.5 Hz, with the eyes closed. OEG = repetitive grasping by the right hand at the rate of 0.5 Hz, with the eyes open to obtain visual feedback of movement of one's own hand. VRG = repetitive EMG prosthetic hand grasping at a rate of 0.5 Hz, with eyes open to obtain visual feedback of movement of the EMG prosthetic hand.

Table 2
Activations found by conjunction analyses between contexts for each event

Anatomic location	Talairach coordinates (MNI template)			
	X	Y	Z	Peak Z score
L. supplementary motor area (SMA)	−2	2	56	5.35
R. cerebellum, anterior lobe	2	−62	−26	5.33
L. cerebellum, posterior lobe	−26	−68	−34	3.69
L. central gyrus	−34	−32	66	5.19
L. postcentral gyrus	−50	−26	18	3.98
L. precentral gyrus (PMd)	−38	−10	60	5.02
L. inferior frontal gyrus (PMv)	−60	8	22	3.44
L. inferior parietal lobe (IPL)	−38	−48	50	5.18

MNI = Montreal Neurological Institute.

between contexts. The interaction VRG–CEG (showing activity specific for visual feedback of virtual EMG prosthetic hand grip) was associated with activation of the right ventral premotor cortex (52 22 32, Z = 4.12) and the right posterior parietal cortex (36 −52 46, Z = 5.09), as well as both visual cortices (Fig. 3b). Notably, the center of activation in the right posterior parietal cortex was shifted laterally from the center for OEG–CEG.

VRG vs. OEG

To determine brain regions more active for subjects' grip with visual feedback for the EMG prosthetic hand than for their own hand, we analyzed the interaction VRG–OEG (showing activity specific for manipulation of the EMG prosthetic hand associated with right hemispheric activation in the ventral premotor cortex) (50 14 34, Z = 5.24; Fig. 3c). No significant voxels were detected in the right posterior parietal cortex.

Comparison of activated sites in the posterior parietal cortex

Activated area in the right posterior parietal cortex was calculated for each subject (Table 3). The shift of activated areas was statistically significant in lateral direction (P < 0.05, paired

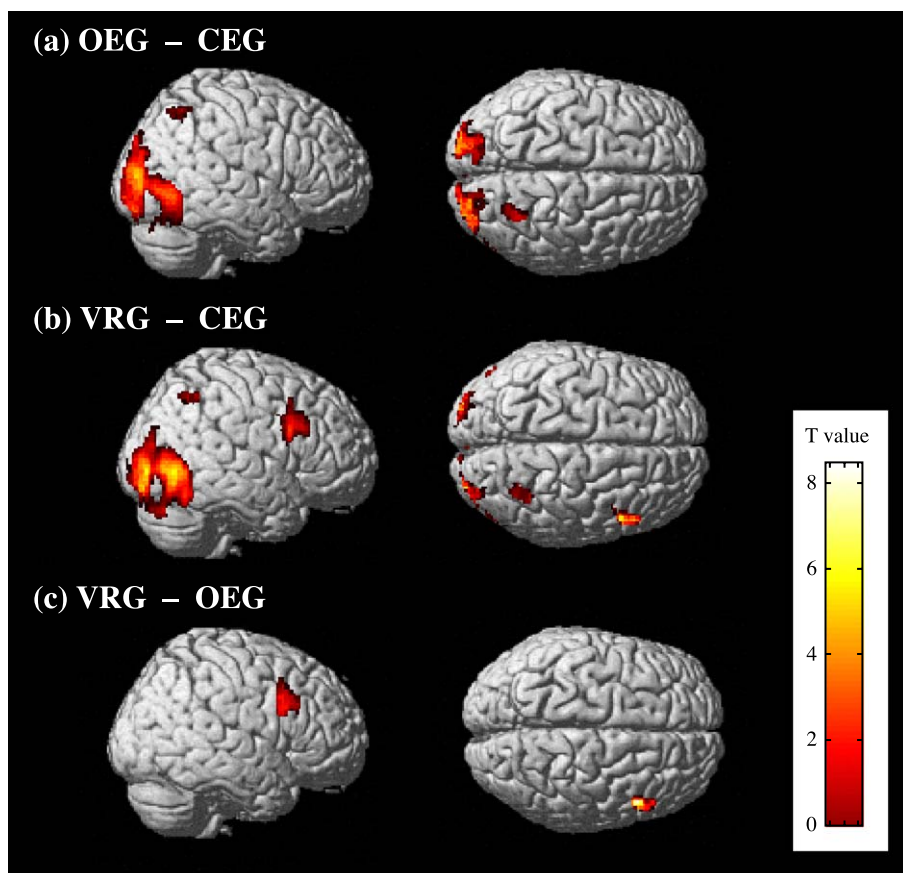

Fig. 3. Activation maps showing significant task-related increases in the blood oxygenation level-dependent (BOLD) contrast signal (P < 0.001, uncorrected for multiple comparisons). Data correspond to a group analysis of 14 subjects. Results are displayed on a reference brain (Montreal Neurological Institute, MNI) with the Talairach coordinates indicated. (a) Open-eye grasp (OEG) vs. closed-eye grasp (CEG) showed activation in the right posterior parietal cortex, as well as visual cortices bilaterally, during visual feedback of the subject's right hand grip. (b) Virtual grasp (VRG) vs. OEG was associated with activation in the right ventral premotor cortex (PMv) and the right posterior parietal region, as well as right and left visual cortices, during visual feedback while performing virtual electromyographic (EMG) prosthetic hand grip. Note that the center of activation of the right posterior parietal cortex is shifted anterolaterally compared to the image in 'a'. (c) VRG vs. OEG showed activation in the right ventral premotor cortex, representing activity that was specific for manipulating the EMG prosthetic hand.

Table 3
Comparison of activated sites in the posterior parietal region

Subject	OEG−CEG			VRG−CEG		
	Talairach coordinates (MNI template)			Talairach coordinates (MNI template)		
	X	Y	Z	X	Y	Z
1	32	−60	48	38	−52	52
2	28	−46	56	36	−54	54
3	28	−46	56	38	−44	56
4	24	−56	44	28	−54	42
5	30	−50	52	34	−52	54
6	38	−46	52	38	−48	50
7	22	−56	36	28	−58	34
8	30	−56	56	30	−54	54
9	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
10	28	−55	56	34	−62	58
11	28	−56	42	n.d.	n.d.	n.d.
12	36	−62	56	36	−60	52
13	28	−56	60	38	−50	60
14	26	−58	64	32	−58	62
Mean	29.1*	−54.1	52.2	34.2*	−53.8	52.3

$*P < 0.05$, paired t test.

t test). The actual distance between the centers of the two foci was 5.1 mm.

Discussion

We investigated brain activation during manipulation of the EMG prosthetic hand, by functional neuroimaging for the first time, using a virtual prosthetic hand to avoid interfering signal noise. This is also the first fMRI study for brain activation by manipulation of the man–machine system. The right ventral premotor cortex played an important role in manipulating the EMG prosthetic hand, while the right posterior parietal cortex might show a neural representation of the EMG prosthetic hand representing a shift of the body schema to show the prosthesis as an extension of the hand.

Activation in the ventral premotor cortex

In the monkey premotor cortex (area F5), some neurons discharge both when the monkey performs specific hand movements such as grasping an object and when the animal observes another individual performing an identical or similar action (Gallese et al., 1996; Rizzolatti et al., 1996a). A hypothesis was proposed that these neurons, called ''mirror neurons'', allow individuals to recognize actions made by others. Growing evidence supports the existence in humans of a mirror system, similar to that described in monkeys.

Activation of the premotor cortex is among the most conspicuous findings in hand movement irrespective of simulation state. Strong activation of the dorsal and ventral premotor cortex was found during imagined hand movements (Decety et al., 2002; Gerardin et al., 2000; Grafton et al., 1996; Stephan et al., 1995). This also is true for perceptually based motor decisions (Parsons et al., 1995) and visual presentation of graspable objects (Chao and Martin, 2000). Observation of hand movements is associated with activation in the same areas, located mainly in the ventral premotor cortex (Decety et al., 1997; Grafton et al., 1996;

Iacoboni et al., 1999; Rizzolatti et al., 1996b), showing a somatotopic organization when actions involving different body parts are observed (Buccino et al., 2001). Lateral premotor cortex activation during covert actions overlaps with movement execution for what concerns dorsal premotor (Gerardin et al., 2000; Rizzolatti et al., 1996b) and involves an equivalent number of activated pixels whether the action is covert or overt one (Lotze et al., 1999b). Activation of the ventral premotor cortex in the inferior frontal gyrus, however, which is highly prominent in covert actions, is less frequently reported during execution (Binkofski et al., 1999).

In visuomotor control, many PET studies detected brain activation in the premotor and the posterior parietal cortex (Jeannerod, 2001; Jong et al., 2001). These previous data support the possibility of greater activation in the comparisons of OEG−CEG, VRG−CEG, and VRG−OEG. Failure to find activation of the ventral premotor cortex in the context of OEG−CEG can be attributed to insufficient behavioral demand of the task (Grafton et al., 1996). Gripping with visual feedback using the subject's own hand was simple and easy to perform. Such simple, non-goal-directed finger movements induced less activation of the ventral premotor cortex. (Colebatch et al., 1991; Fink et al., 1997; Matelli et al., 1993). The ventral premotor cortex showed a clear dominance within the right hemisphere, in accord with the finding that even when sequences are performed or learned with the right hand, the right premotor cortex appears to play a greater role than its left-sided counterpart in sequence production (Jenkins et al., 1994; Sadato et al., 1996; Seitz and Roland, 1992).

Since no significant differences in muscle activation were evident between CEG, OEG, and VRG, the hand movements were exactly same in terms of power and complexity among three sessions. Visual feedback information was different between the OEG and the VRG, which was subjects' own hands in the OEG and the ''virtual hand'' in the VRG. Therefore, the visual feedback information supposed to affect the output behaviors differentially between OEG and VRG. The VRG may need more intensive learning of visuomotor control. It may be a reason of the right ventral premotor cortex activation in manipulating the EMG prosthetic hand. In other reports analyzing executive tasks of hand, motor performance was not accurately matched.

Activation in the posterior parietal cortex

The posterior parietal cortex may be the site where action representations are stored and/or generated. A portion of the right posterior parietal cortex was found to be strongly activated during an unpracticed finger movement sequential learning task (Jenkins et al., 1994) and a visuospatial conditional learning task (Deiber et al., 1997) that required conversion of visuospatial information into a hand motor domain. In a PET study, the right posterior parietal cortex was activated especially during right-handed stick-use tasks (Inoue et al., 2001). Integration of multimodal sensory information concerning our body parts is necessary for forming the body schema, which changes continuously as we move. Many authors have described neuronal activity that appears to process multimodal sensory information (Andersen et al., 1997). In a recent study in monkeys, Iriki et al. (1996) reported that the visual receptive field of neurons in the anterior bank of the intraparietal sulcus (IPS) changed when the monkeys were using a rake, covering not only the area around the hand but also the area along the rake. Their results demonstrate neural representation of

the body schema for both the hand and the rake used as an extension of the hand. These results suggest that when we use a rake, processes that integrate multiple sensory modalities—particularly visual and somatosensory information—will change to project our recognition of movement of our body part to movement at the end of a rake.

Our study also demonstrated that the focus of activation in the right posterior parietal cortex shifted laterally when subjects manipulated EMG prosthetic hands. Such changes would be needed for perceptual assimilation of the EMG prosthetic hand and correspond to changes in the body schema for the hand.

These differentially modulated foci were 5.1 mm distant from one another, and some activated regions overlapped each other, precluding clear separation given the 8-mm spatial resolution of our images. A statistical limitation therefore was present when one considers the 3- to 5-mm spatial dispersion of the BOLD response (Maloneck and Grinvald, 1996). Then, we compared activated sites for each subject, and found that shift of activated areas was statistically significant in lateral direction ($P < 0.05$, paired t test). Our study showed that a man–machine system like the EMG prosthetic hand can alter the body schema.

Conclusions

In conclusion, our study demonstrated that the right ventral premotor cortex played an important role in manipulating the EMG prosthetic hand, and the right posterior parietal cortex mediated neural representation of the prosthesis in the body schema as an extension of the hand. The EMG prosthetic hand, which might be recognized in the brain as a high-performance alternative to the real hand, may be controlled by a "mirror system" in the brain.

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