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Cortical control of gait in healthy humans: an fMRI study

ChiHong Wang · YauYau Wai · BoCheng Kuo · Yei-Yu Yeh · JiunJie Wang

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Abstract This study examined the cortical control of gait in healthy humans using functional magnetic resonance imaging (fMRI). Two block-designed fMRI sessions were conducted during motor imagery of a locomotor-related task. Subjects watched a video clip that showed an actor standing and walking in an egocentric perspective. In a control session, additional fMRI images were collected when participants observed a video clip of the clutch movement of a right hand. In keeping with previous studies using SPECT and NIRS, we detected activation in many motor-related areas including supplementary motor area, bilateral precentral gyrus, left dorsal premotor cortex, and cingulate motor area. Smaller additional activations were observed in the bilateral precuneus, left thalamus, and part of right putamen. Based on these findings, we propose a novel paradigm to study the cortical control of gait in healthy humans using fMRI. Specifically, the task used in this study—involving both mirror neurons and mental imagery—provides a new feasible model to be used in functional neuroimaging studies in this area of research.

Keywords fMRI · Walking · Standing · Motor imagery · Mirror neurons

YauYau Wai and ChiHong Wang contributed equally to this work.

C. Wang
Department of Neurology, Cardinal Tien Hospital Yung-Ho Branch, Taipei, Taiwan

Y. Wai · J. Wang (✉)
Department of Medical Imaging & Radiological Sciences, ChangGung University, TaoYuan, Taiwan
e-mail: jwang@mail.cgu.edu.tw

Y. Wai
Department of Diagnostic Radiology and Intervention, ChangGung Memorial Hospital, LinKou, Taiwan

Y. Wai · J. Wang
Molecular Imaging Centre, ChangGung Memorial Hospital, LinKou, Taiwan

B. Kuo · Y.-Y. Yeh
Department of Psychology, National Taiwan University, Taipei, Taiwan

Introduction

Walking is a complicated motor act requiring the interplay of information between the brain and spinal cord, with the final motor output shaped by sensory feedback from peripheral receptors (Patla 2004; Rossignol et al. 2006). Most of the knowledge about the neural mechanism of walking has been derived from studies of the nervous system of animals (Grillner 1975; Mori et al. 2001). Sherrington (1910) suggested that walking could be produced entirely by a series of reflexes, but further studies provided evidence for neural networks in the spinal cord, referred to as "central pattern generators" (CPGs), that are capable of governing locomotion (Grillner and Wallen 1985). Supraspinal, sensory, and neuromodulatory influences interact with CPGs to shape the final motor output. Supraspinal inputs play a major role not only in initiating locomotion but also in adapting the locomotor pattern to environmental and motivational conditions (Armstrong 1988; Drew et al. 1996).

The regulation of human bipedal walking differs from that of quadrupedal animals (Nielsen 2003). Although human beings have specialized CPGs for locomotion similar to those observed in experimental animals (Dietz 2003; MacKay-Lyons 2002), human walking is significantly influenced by the supraspinal centers. The functional

roles of cerebral cortex for human walking are still under investigation. The importance of cortical control on human walking has been emphasized by a specific group of clinical conditions termed higher-level gait disorders (Nutt et al. 1993). Higher-level gait disorders are defined as walking difficulties that are out of proportion to those that would be expected on the basis of the bedside neurological examination and that are best explained by disorders of integration of cerebral activity. Patients with higher-level gait disorders have difficulty with gait ignition or initiation when walking through a narrow passage or during turning. These conditions could be due lesions in either cortical (Iansek et al. 2001; Tyrrell 1994) or subcortical areas (Thompson and Marsden 1987). Classification systems for gait disorders have been developed, but the exact pathogenesis of higher-level gait disorders is still unclear (Nutt and Horak 2004). In this context, a better knowledge of the role of the cerebral cortex in the regulation of human walking may hold promise for a better functional classification of these conditions as well as for developing novel therapeutic strategies.

BOLD-based fMRI has been used for analysis of gait in human beings. This technique allows non-invasive imaging of the cortical involvement in gait control, offering whole-brain coverage at a satisfactory spatial resolution. Unfortunately, the apparent incapability to walk inside an fMRI scanner represents a limitation for this kind of study.

In the present study, we propose a novel paradigm to study the cortical control of gait in healthy humans using fMRI. The experimental setting required the observation of video clips of human walking and the mental imitation of the visualized process.

Methods and materials

Study participants

The experiments were conducted at the Chang Gung Memorial Hospital using a 1.5-T MRI scanner (Intera, Philips, Best, Holland). Twelve right-handed gender-balanced subjects aged between 18 and 25 years were investigated. Subjects viewed the stimuli via a mirror system. Contact lenses were used to correct visual acuity during the scans. The participants had their head movements restrained by a plastic fixation pad. Informed consents were obtained from all subjects. The study was approved by the institutional review board of the Chang Gung Memorial Hospital and complied with the ethical standards established in the Declaration of Helsinki. The experiments were undertaken with the understanding and written consent of each subject.

fMRI scanning

MP-RAGE sequences yielding T1-weighted images were used as reference. Imaging parameters were TR/TE/flip angle = 9 ms/4.2 ms/90°. One hundred and eighty sagittal slices were acquired to cover the whole brain. Reconstructed images had spatial resolution of 0.86 mm × 0.86 mm × 1.0 mm. The BOLD sequence used a single-shot T2*-weighted GE-EPI sequence. Twenty-four slices were acquired with a slice thickness of 5 mm to cover the whole brain. Other imaging parameters were as follows: TR/TE/flip angle = 3,000 ms/50 ms/90°, matrix size = 64 × 64, FOV = 192 mm, in-plane resolution = 3 mm × 3 mm.

Paradigm design

Two block-designed fMRI sessions were conducted. Each session comprised six pseudorandomized blocks including three different conditions. Experiments were repeated a single time using different pseudorandomized blocks. Before the experiment, the paradigm was presented to the subjects for approximately 30 min when outside the scanner.

The first session consisted of three different stimuli, namely WALK, STAND, and REST. The stimulus WALK consisted of a video clip that showed an actor firstly standing and then walking in an egocentric perspective. The camera was placed directly in line with the actor's eyes. During the STAND stimulus, the video clip showed an actor while standing upright without any movement, in the same perspective as in the WALK condition. The REST stimulus consisted of a fixed cross.

The second session served as a control experiment. It consisted of three different stimuli, namely HAND IMAGE, HAND MOVE, and REST. During the HAND IMAGE stimulus, study partipants passively viewed a video clip showing the clutch movement of a right hand. During the HAND MOVE stimulus, subjects were required to view the same clip clutching their hands as in the display. The REST stimulus consisted of a fixed cross (Fig. 1).

Throughout the experiments, subjects were asked to identify themselves as the actor and to mentally imitate the movements viewed in the clips. Each stimulus lasted 18 s, with a 6-s interval for preparation. A blank display was shown for 4.5 s during the preparation interval, followed by a 1.5-s instruction sentence.

fMRI data analysis

The fMRI data were analyzed using the SPM2 software (The Wellcome Trust Centre for Neuroimaging, London, UK) running under MATLAB 7.0 (MathWorks, Inc.,

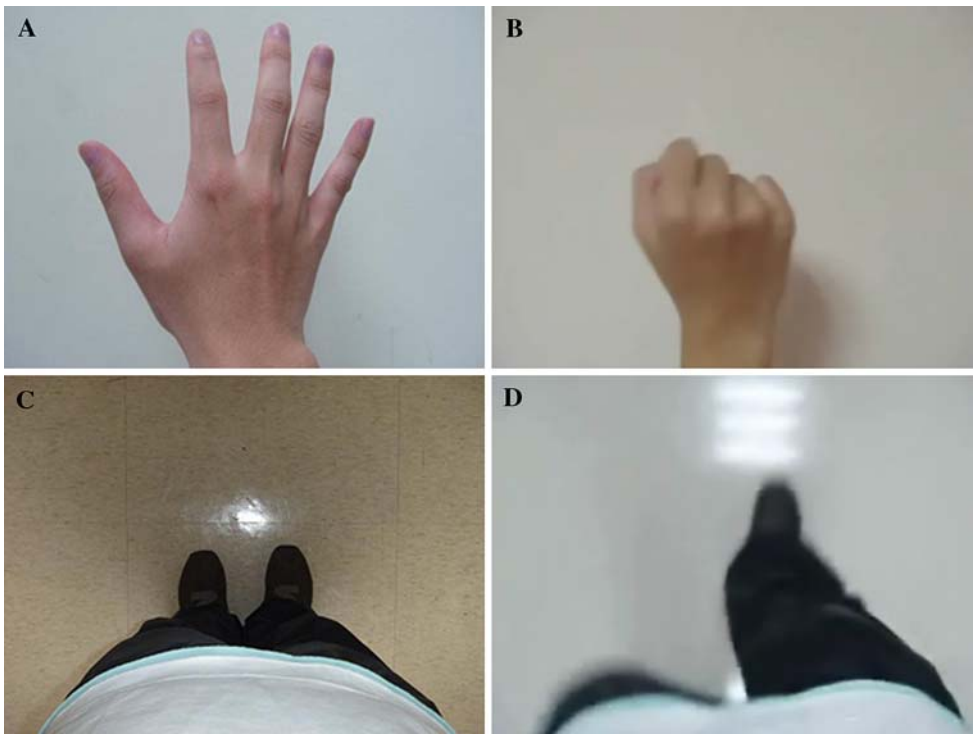

Fig. 1 Video stills of different experimental stimuli. **a** Video still of the right hand used in the HAND IMAGE stimulus. **b** Video still of the HAND MOVE stimulus showing the clutching of a right hand. **c** Video still of a person standing in an egocentric view used in the STAND stimulus. **d** Video still of a person walking in an egocentric view used in the WALK stimulus

Natick, MA, USA). The first two scans of EPI series were excluded to minimize T1 relaxation artifacts. Functional data were corrected for motion via sinc interpolation. The realigned images were then normalized into the standard SPM/MNI template and thus transformed into a standard stereotaxic space and resampled with a resolution of 2 mm × 2 mm × 2 mm. A Gaussian filter of 10-mm full width at half maximum (FWHM) was then applied to smooth the data spatially, to accommodate for anatomical variability across subjects, as well as to satisfy the assumptions of Gaussian field theory (Worsley et al. 1996). The data were then high-pass filtered with a cut-off period of 144 s to remove low frequency drifts in the BOLD signals. The hemodynamic response function was used to identify the activated voxels.

The subject-level statistical analyses were performed using the general linear model (GLM) for blocked designs. Linear contrasts of interest were constructed to obtain subject-specific estimates of cueing-related activity for the following main effects: (1) the WALK stimulus minus the REST condition, (2) the STAND stimulus minus the REST condition, and (3) the WALK stimulus minus the STAND condition. In the control session, the following contrasts were generated: (1) the HAND IMAGE stimulus minus the REST condition, and (2) the HAND MOVE stimulus minus the HAND IMAGE condition. To make broader inferences about the general population from which the subjects were drawn, these estimates for contrasts were entered into a standard SPM second-level analysis with subject treated as a random effect, using one-sample t test (Penny and Holmes 2007). The expected mean differences for t tests were set to zero, with a threshold of $p < 0.001$ (uncorrected) with 11 degrees of freedom. The activated locations were transformed into Talairach space (Talairach and Tournoux 1988). Anatomical labels (lobes, gyri) and Brodmann area (BA) of the local maxima of the activated clusters were determined using a 3D electronic brain atlas (Lancaster et al. 2000).

Results

Areas of activation for all contrasts are depicted in tables and figures (Tables 1, 2, 3, 4, 5). Figure 2 depicts the effect of the HAND IMAGE stimulus minus the REST conditions in the study participants. During the control experiments, activations in visual-related areas (V1, V2, fusiform gyrus, lingual gyrus, and V5/MT) were observed. Activations of motor areas were observed in the left supplementary motor area (SMA) and the left dorsal premotor cortex. Smaller additional activations were also observed in areas related to the cortical processes of imitation (Iacoboni et al. 1999) such as bilateral inferior frontal gyrus, inferior parietal lobule and superior temporal gyrus. Activations were also seen in the bilateral middle frontal gyrus, the right cerebellum, and the left putamen.

Figure 3 shows the contrast between the HAND MOVE stimulus and the HAND IMAGE stimulus during the

Table 1 Brain areas activated in fMRI during the HAND IMAGE—REST stimulus

Localization (Brodmann area)	*X*	*Y*	*Z*	*T*
Left side				
SMA (6)	−12	−7	59	5.04
Superior temporal gyrus (42/22)	−69	−23	12	4.93
Inferior parietal lobule (40)	−65	−26	33	5.58
MT/V5 (37/19)	−38	−64	0	8.48
Middle occipital gyrus (18)	−20	−89	14	4.51
Inferior frontal gyrus (46)	−48	32	9	6.36
Middle frontal gyrus (46)	−32	24	15	7.67
Putamen	−20	8	0	4.53
Right side				
Inferior parietal lobule (40)	65	−24	21	6.44
Lingual gyrus (17)	16	−85	1	4.07
MT/V5 (37/19)	46	−57	−7	6.7
Inferior frontal gyrus (45)	49	25	2	4.62
Middle frontal gyrus (46)	38	30	24	9.29
Cerebellum (posterior lobe)	40	−58	−24	6.71

X, *Y*, *Z* indicate the Talairach coordinate system. *T*: *t* test, degree of freedom = 11, $p < 0.001$ (uncorrected)

Table 2 Brain areas activated in fMRI during the HAND MOVE—HAND IMAGE stimulus

Localization (Brodmann area)	*X*	*Y*	*Z*	*T*
Left side				
SMA (6)	−6	−15	47	4.68
Cingulate motor area (24)	−2	−2	41	6
Postcentral gyrus (1)	−53	−17	45	9.86
Superior temporal gyrus (22/42)	−48	−19	14	8.24
Cerebellum (anterior lobe)	−34	−56	−24	13.14
Cerebellum (posterior lobe)	−16	−63	−15	10.96
Midbrain	−14	−20	−7	8.6
Thalamus	−18	−19	5	5.26
Right side				
Postcentral gyrus (3)	40	−19	49	11.99
Superior temporal gyrus (22/42)	40	−23	7	8.56
Inferior parietal lobule (40)	51	−32	24	7.07
Parahippocampal gyrus (19)	32	−54	−1	4.7
Cerebellum (anterior lobe)	34	−42	−30	8.62
Cerebellum (posterior lobe)	18	−67	−17	11.69
Thalamus	24	−25	3	5.05

X, *Y*, *Z* indicate the Talairach coordinate system

T: *t* test, degree of freedom = 11, $p < 0.001$ (uncorrected)

Table 3 Brain areas activated in fMRI during the STAND—REST stimulus

Localization (Brodmann area)	*X*	*Y*	*Z*	*T*
Left side				
Dorsal premotor area (6)	−28	1	52	6.28
Superior temporal gyrus (22)	−50	−46	12	5.64
Superior parietal lobule (7)	−20	−57	62	5.89
MT/V5 (19)	−42	−81	11	4.64
Inferior frontal gyrus (45)	−57	28	15	6.49
Middle frontal gyrus (8)	−51	16	40	5.67
Cerebellum (anterior lobe)	−38	−42	−23	6.38
Right side				
Dorsal premotor area (6)	22	−1	52	4.81
Superior parietal lobule (7)	14	−51	62	4.65
Lingual gyrus (18)	26	−72	−10	5.67
MT/V5 (19)	38	−75	11	5.06
Middle occipital gyrus (18)	14	−96	16	5.3
Inferior frontal gyrus (45)	59	11	22	5.23
Cerebellum (posterior lobe)	34	−53	−16	5.3

X, *Y*, *Z* indicate the Talairach coordinate system

T: *t* test, degree of freedom = 11, $p < 0.001$ (uncorrected)

control experiment. Activated pixels were located in areas related to the motor execution process such as bilateral primary sensorimotor cortices, SMA, and cingulate motor areas. Smaller additional activations were also observed in cerebellum, midbrain, bilateral thalamus and right parahippocampus.

Figure 4 depicts the effect observed during the STAND stimulus compared with the REST condition. Besides the visual areas, activated areas included bilateral dorsal premotor area, bilateral superior temporal gyrus, bilateral superior parietal lobule, left precuneus, left middle frontal gyrus, and right inferior frontal gyrus.

Figure 5 shows the difference between the WALK and the REST stimuli. Activated voxels were located in the visual areas (e.g. V1, MT/V5) and in motor-related areas such as left dorsal premotor cortex, SMA, cingulate motor area, and especially in bilateral precentral gyrus. Significance responses were also evident in bilateral inferior parietal lobules and superior temporal gyrus, bilateral cerebellum, and bilateral inferior and middle frontal gyrus. Smaller additional activations were also observed in bilateral precuneus, left thalamus, and part of right putamen.

Figure 6 shows the difference between the WALK and the STAND stimuli. When the threshold was set to an uncorrected p value < 0.001, activation patterns were observed a mainly in visual-related areas including bilateral cuneus, lingual gyrus and MT/V5. When the threshold was elevated to an uncorrected p value < 0.05, smaller additional activations were observed in SMA, bilateral superior temporal gyrus, and the bilateral inferior parietal lobule.

Table 4 Brain areas activated in fMRI during the WALK—REST stimulus

Localization (Brodmann area)	*X*	*Y*	*Z*	*T*
Left side				
SMA (6)	0	−11	59	5.26
Cingulate motor area (24)	−6	4	38	5.54
Dorsal premotor area (6)	−30	−2	44	7.03
Precentral gyrus (6)	−16	−18	58	5.43
Superior temporal gyrus (22)	−51	−29	9	5.89
Inferior parietal lobules (40)	−57	−41	28	16.7
Superior parietal lobules (7)	−32	−52	47	8.19
Precuneus (7)	−22	−48	48	7.79
Middle occipital gyrus (18)	−18	−89	12	10.01
MT/V5 (19/37)	−44	−70	2	12.76
Inferior frontal gyrus (45)	−53	14	−1	5.05
Middle frontal gyrus (46)	−59	19	27	8.32
Posterior cingulate gyrus (31)	−16	−24	34	6.89
Cerebellum (anterior lobe)	−16	−36	−18	6.9
Right side				
Precentral gyrus (6)	8	−22	60	5.42
Precentral gyrus (6)	46	−8	28	5.1
Superior temporal gyrus (42)	57	−32	16	6.61
Inferior parietal lobules (40)	61	−33	31	4.89
Superior parietal lobules (7)	20	−59	58	5.17
Precuneus (7)	20	−43	32	9.67
Middle occipital gyrus (18)	28	−91	10	12.85
MT/V5 (19/37)	51	−73	13	9.64
Inferior frontal gyrus (47)	36	23	−5	6.16
Middle frontal gyrus (46)	51	25	26	6.23
Cerebellum (anterior lobe)	18	−34	−22	7.86
Cerebellum (posterior lobe)	22	−67	−15	16.49

X, *Y*, *Z* indicate the Talairach coordinate system

T: *t* test, degree of freedom = 11, $p < 0.001$ (uncorrected)

Table 5 Brain areas activated in fMRI during the WALK—STAND stimulus

Localization (Brodmann area)	*X*	*Y*	*Z*	*T*
Left side				
SMA (6)*	−10	1	55	2.68
Inferior parietal lobule (13)	−53	−38	24	4.76
Cuneus (18)	−4	−97	7	8.94
MT/V5 (19)	−48	−72	5	7.96
Cerebellum (anterior lobe)	−14	−38	−15	4.79
Thalamus	−24	−27	5	5.47
Right side				
Cuneus (18)	12	−88	17	5.04
MT/V5 (37/19)	48	−70	0	8.17
Cerebellum (posterior lobe)	10	−74	−13	6.81

X, *Y*, *Z* indicate the Talairach coordinate system

T: *t* test, degree of freedom = 11, $p < 0.001$ (uncorrected)

* $p < 0.05$ (uncorrected)

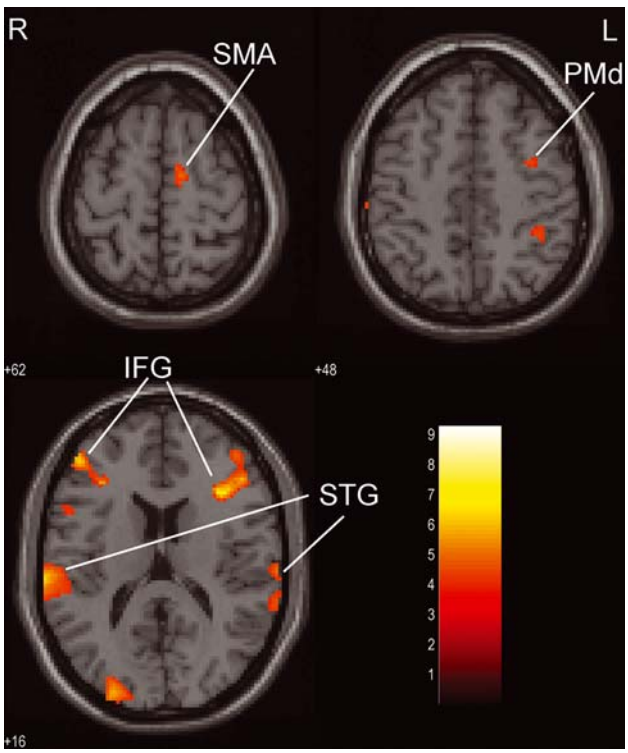

Fig. 2 Cortical activation during the HAND IMAGE and REST stimuli. Activations were seen in the left supplementary motor area and in the left dorsal premotor cortex. Additional activations related to the mirror neuron system were observed in bilateral inferior frontal gyrus, inferior parietal lobule and superior temporal gyrus. *SMA* supplementary motor area, *PMd* dorsal premotor area, *IFG* inferior frontal gyrus, *STG* superior temporal gyrus, *L* left

Discussion

Cortical control of gait according to neuroimaging findings

Findings from functional neuroimaging studies can contribute to a better understanding of the cortical control of human gait (Bakker et al. 2007). Thus far, however, studies of brain activity during actual walking have been only conducted using ^{18}F-fluorodexoyglucose positron emission tomography (FDG-PET) (Mishina et al. 1999), single-photon emission computerized tomography (SPECT) (Fukuyama et al. 1997), or near-infrared spectroscopy (NIRS) (Miyai et al. 2001). In FDG-PET studies, a period of separation of 7 days between data acquisition of walk and rest was used. It should be noted, however, that SPECT and NIRS are limited by their spatial resolution (Wintermark et al. 2005). Additionally, SPECT imaging may be affected by the accumulation of background activity that may limit the number of experimental replications (Holschneider and Maarek 2004). Notably, NIRS

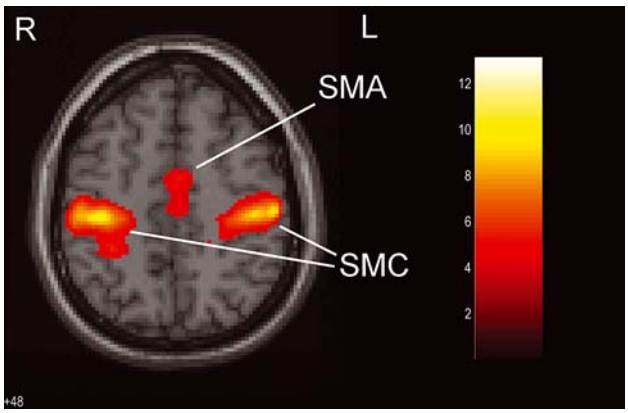

Fig 3 Contrast between the HAND MOVE and HAND IMAGE stimuli. Activated pixels were seen in areas related to motor execution, including the bilateral primary sensorimotor cortices and SMA. *SMA* supplementary motor area, *SMC* primary sensorimotor cortex

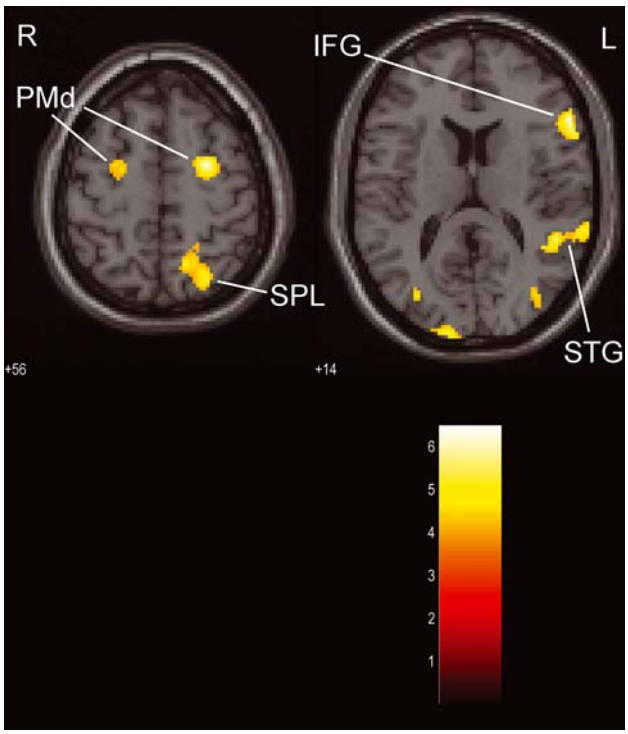

Fig. 4 Effect of the STAND minus the REST stimulus. Activations were seen in the bilateral dorsal premotor area, bilateral superior temporal gyrus, bilateral superior parietal lobule and right inferior frontal gyrus. *PMd* dorsal premotor area, *IFG* inferior frontal gyrus, *STG* superior temporal gyrus, *SPL* superior parietal lobule

has limited depth penetration that does not permit whole brain coverage (Hanakawa 2006).

Modified paradigms for BOLD-based fMRI

Many efforts have been made to study the cortical control of gait using BOLD-based fMRI. Sahyoun et al. (2004)

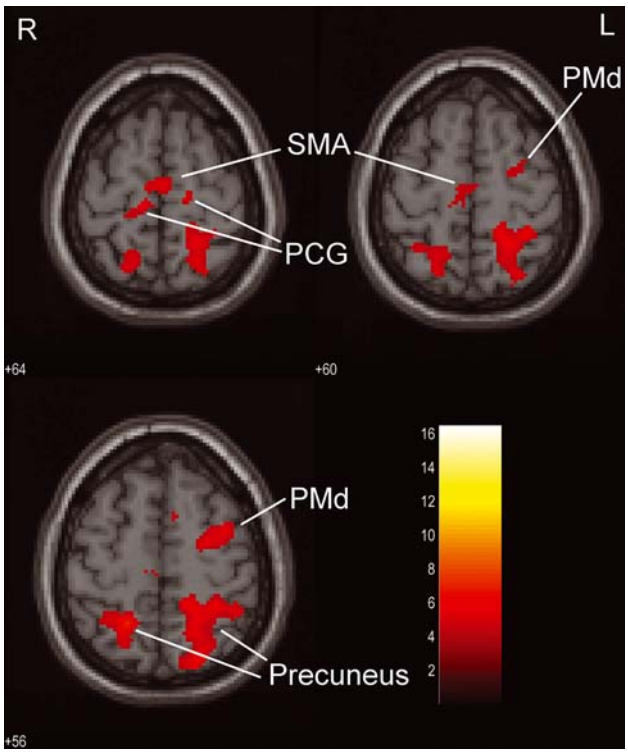

Fig. 5 Contrast between the WALK and the REST stimuli. Activations of motor related areas were seen in the left dorsal premotor cortex, SMA and especially in the bilateral precentral gyrus. *SMA* supplementary motor area, *PCG* precentral gyrus, *PMd* dorsal premotor area, *L* left

studied brain responses to visually cued active and passive movements of the right foot. Dobkin et al. (2004) used the ankle dorsiflexion as the experimental task. It should be noted, however, that muscles involved in walking are not limited to the right foot but are widely distributed in the proximal lower-limb as well as in the trunk. Hence, these studies cannot entirely investigate the complex muscle activity activated during walking.

It has been shown that activation maps during movement execution are similar to those observed during the imagery of the same task (Deiber et al. 1998; Gerardin et al. 2000). Accordingly, imagined locomotion in functional magnetic resonance imaging has been proposed as a novel paradigm to study brain activation during walking (Jahn et al. 2004). By using NIRS, Miyai et al. (2001) have previously shown that similar brain regions are activated during actual and imagined walking. Although scattered activation over the premotor areas were consistently found on an individual basis, strong interindividual differences were evident (Jahn et al. 2004). The basic mental process of the imagination can vary widely across different subjects.

Mirror neurons are a particular class of visuomotor neurons that discharge when an individual performs a particular action but also when he/she observes the same

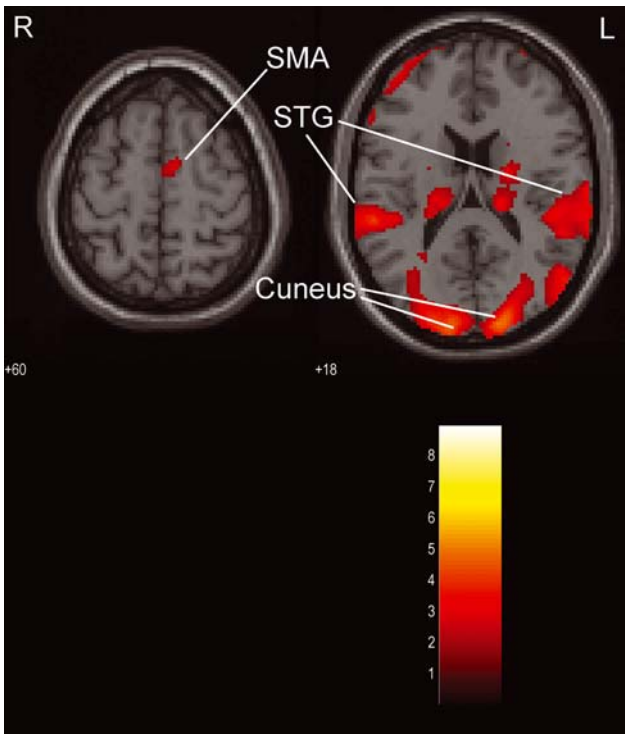

Fig. 6 Differences between the WALK and the STAND stimuli. Besides visual-related areas, activations were chiefly seen in the SMA and bilateral superior temporal gyrus. *SMA* supplementary motor area, *STG* superior temporal gyrus

behavior in another individual (di Pellegrino et al. 1992; Gallese et al. 1996). In addition to action understanding, the mirror-neuron system plays a fundamental role in action imitation (Craighero et al. 2007; Iacoboni and Mazziotta 2007; Rizzolatti and Craighero 2004). Moreover, during the observation of object-related actions, a somatotopically organized pattern of activation can be observed (Buccino et al. 2001). The cortical mirror neuron circuit is formed by the rostral part of the inferior parietal lobule, the lower part of the precentral gyrus, and the posterior part of the inferior frontal gyrus (Rizzolatti and Craighero 2004). Together, these three areas form a core circuit for imitation. Specifically, the superior temporal gyrus provides a higher-order visual description of the action, whereas the inferior parietal lobule is concerned with the kinesthetic copy of the imitated action. Finally, the frontal component is concerned with the goal of the imitated action (Iacoboni and Dapretto 2006; Iacoboni et al. 1999).

In this study, we propose a novel paradigm to elicit patterns of cortical activations that are similar to those observed during normal motor execution. Our model was based on the concept of shared motor representations, which hypothesizes a functional equivalence between intending, simulating, observing, and performing an action (Grezes and Decety 2001). To minimize the interindividual differences in motor imagery, our paradigm was based on mirror neuron responses to action observation. In this regard, previous studies have shown that brain activity during observation of actions can be significantly modulated by instructions related to the observation task (Zentgraf et al. 2005). In contrast, observation with the intent to imitate has been associated with activations in the regions involved in the planning and in the generation of actions (Decety et al. 1997). In our paradigm, there was an instruction to imitate before each individual stimulus.

The control session: execution versus observation plus imitation

As can be seen in Fig. 2, activation patterns were observed in left SMA and dorsal premotor area during the visual task using motor related imagery. SMA, which is chiefly related to motor execution, appears to have direct connections with the primary motor cortex and spinal cord (Picard and Strick 2001). Dorsal premotor cortex has often been associated with selection of an appropriate learned response to visual, auditory, and somatosensory cues (Chouinard and Paus 2006). These areas are both involved during action generation and action simulation (Grezes and Decety 2001). Moreover, they play an important role in early stage premovement activity, in the Bereitschaftspotential (or readiness potential), (Cunnington et al. 2003; Shibasaki and Hallett 2006), as well as in the preparation and readiness for voluntary movement.

The virtual task we created, which prompted the activation of the mirror neuron system, closely mimics the activation of cerebral areas as in the real motor task. Accordingly, the intention to act may be necessary in establishing a functional and an anatomical link between perception and action (Grezes and Costes 1998; Johnson et al. 2002). Our current data show that the observation of an action combined with mental imitation can closely mimic the activation patterns of cortical areas as observed during a simple hand movement task. The observed activations in bilateral inferior frontal gyrus, inferior parietal lobule and superior temporal gyrus suggest the involvement of mirror neuron system.

As can be seen in Fig. 3, significant differences were noted in the pattern of activation of bilateral primary sensorimotor cortex when the HAND MOVE stimulus was compared with the HAND IMAGE stimulus. This finding could be related to the cortical mechanism of motor execution and the proprioceptive feedback evoked by the moving limbs (Mima et al. 1999). The involvement of the primary motor and somatosensory areas during the mental simulation is still a matter of debate. It is likely that an

activation of the sensorimotor cortex can occur, although, the extent of activation during mental simulation is significantly lower compared to that observed during an actual execution (Grezes and Decety 2001). Thus, the differences in the patterns of activation of sensorimotor cortex between the HAND MOVE and the HAND IMAGE stimuli as observed in our study are likely to be ascribed to the effects of movement execution.

Cortical activation during standing

Interestingly, we noted an activation of bilateral superior parietal lobules during standing. This region is located on the dorsal stream of the dorsal visual system. Its major functional role is the "on line" control of actions; moreover, it plays a crucial role in visually guided motor tasks (Rizzolatti and Matelli 2003). Slobounov et al. (2006) have previously shown that visual recognition of postural instability of a virtual person may activate the parietal cortex bilaterally. These findings support the functional role of this region in the perception of egomotion and postural instability. Smaller additional activations during standing were also observed in the bilateral dorsal premotor areas. Notably, these areas have been associated with movement planning and executions. These findings actually support the growing evidence that the act of standing is a more active process than originally thought. In a PET study, Malouin et al. (2003) have provided evidence that the imagery of standing activates the bilateral dorsal premotor areas. Using the mobile gantry PET system, Ouchi et al. (1999) have shown that actual standing activates the cerebellar anterior lobe and the right visual cortex (BA 18/19). The authors, however, were unable to show significant activations of the upper part of the hemisphere due to the restricted axial field of view. Therefore, only the areas from the middle frontal gyrus to the lower part of the cerebellum can be investigated, compared the current study.

Cortical activations during walking

As can be seen in Fig. 5, activations in motor-related areas were evident during the imaginary of bipedal walking. Specifically, activations were seen in the SMA, bilateral precentral gyrus, left dorsal premotor and in the cingulate motor area. Activations in SMA and bilateral precentral gyrus are in keeping with previous findings obtained in SPECT and NIRS studies of actual walking (Fukuyama et al. 1997; Miyai et al. 2001). It is worth noting that activations in the left dorsal premotor and cingulate motor areas were not reported in previous studies. This could be ascribed to differences in the sensitivity of the imaging techniques used. In SPECT and NIRS studies of human walking, an extensive activation in bilateral sensorimotor cortices was evident. Only small activations in these areas could be shown in our study, chiefly restricted to a small strip in the bilateral precentral gyrus. This discrepant finding can be explained by differences between motor execution and motor imagery.

The activation in precentral gyrus as observed in our study was located more distantly from the motor areas reported to be activated in studies using actual or imagined foot movements (Dobkin et al. 2004; Kapreli et al. 2006; Sahyoun et al. 2004). Activations in the current study were more laterally located compared to the foot and ankle areas, and more anteriorly than the motor area. The area activated in this study was closely located to the anterior part of the medial sensorimotor regions, which have been found to be activated during gait and gait imagery, but not during foot movements (Miyai et al. (2001). Thus, activation in the precentral gyrus is likely to be associated with gait-specific activities. It is suggested that a simple foot movement is an inadequate paradigm for the complex act of human walking.

Malouin et al. (2003) used $H_2^{15}O$-PET to investigate brain activation during the imagination of locomotor-related tasks. In the imagery conditions, the study subjects were asked to imagine the motor tasks illustrated in the video prior to PET scanning. The results revealed a common pattern of activation involving the pre-supplementary motor area (pre-SMA) rather than SMA. In general, activations of SMA and pre-SMA are commonly seen in motor imagery and execution tasks. Pre-SMA is specifically activated during the preparation and ready-to-go stages of an action. In contrast, the caudal SMA has been shown to be activated in the movement execution stage (Cunnington et al. 2006). The strong activation in SMA as observed with the use of our paradigm is likely to be elicited by the combined tasks of mirror neuron system and motor-related imagery. Accordingly, this paradigm can be functionally related to movement execution.

Comparison between walking and standing

When the WALK stimulus was compared to the STAND stimulus, we found significant activation in SMA. SMA is known to be active during motor execution and encodes a discrete movement sequence (Ashe et al. 2006). Walking and standing share many features including the maintenance of upright posture and the activation of similar group of muscles. However, the differences in motor programs are likely to contribute to different patterns of cortical activation.

During the WALK task, subjects were required to watch a video clip of walking legs. On the other hand, a static image was shown during the STAND task. Additionally, more visual information is required for walking compared

to standing. In this context, extensive activations of visual-related areas are not surprising. Activations in bilateral superior temporal gyrus and bilateral inferior parietal lobule may reflect the demanding nature of the cortical process required in a walking imitation task. In this regard, walking is likely to require more visuospatial resources and kinesthetic information as compared to standing.

Conclusion

In this study, we propose a novel paradigm to study the cortical control of gait in healthy humans using fMRI. Specifically, the task used in this study—involving both mirror neurons and mental imagery—provides a new feasible model to be used in functional neuroimaging studies in this area of research. Our model may be particularly useful for patients with walking impairments, such as those with Parkinson's disease or higher-level gait disorders. In this regard, further studies are warranted in clinical cohorts to expand our findings obtained in a healthy, nonclinical sample.

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