Comparison of Unilateral and Bilateral Complex Finger Tapping-Related Activation in Premotor and Primary Motor Cortex

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Abstract: Sixteen healthy right-handed subjects performed a complex finger-tapping task that broadly activates the motor and premotor regions, including primary motor (M1), ventral premotor (PMv), and dorsal premotor (PMd) cortex. This task was performed with the right hand only, left hand only and both hands simultaneously. Behavioral performance and the possibility of mirror movements were controlled through the use of MRI-compatible gloves to monitor finger movements. Using spatially normalized ROIs from the Human Motor Area Template (HMAT), comparisons were made of the spatial extent and location of activation in the left and right motor regions between all three tasks. During unilateral right and left hand tapping, ipsilateral precentral gyrus activation occurred in all subjects, mainly in the PMv and PMd. Ipsilateral M1 activation was less consistent and shifted anteriorly within M1, towards the border of M1 and premotor cortex. Regions of ipsilateral activation were also activated during contralateral and bilateral tasks. Overall, 83%/70%/58% of the ipsilaterally activated voxels in M1/PMd/PMv were also activated during contralateral and bilateral tapping. The mean percent signal change of spatially overlapping activated voxels was similar in PMv and PMd between all three tasks. However, the mean percent signal change of spatially overlapping M1 activation was significantly less during ipsilateral tapping compared with contra- or bilateral tapping. Results suggest that the ipsilateral fMRI activation in unilateral motor tasks may not be inhibitory in nature, but rather may reflect part of a bilateral network involved in the planning and/or execution of tapping in the ipsilateral hand. *Hum Brain Mapp* 30:1397–1412, 2009. © 2008 Wiley-Liss, Inc.

Key words: brain; physiology; MRI; echo-planar imaging; motor activity; hand; fingers; dominance, cerebral; functional laterality; motor skills

INTRODUCTION

The motor control regions of the brain have been studied extensively with functional MRI (fMRI) and PET, and the somatotopic organization of the primary sensorimotor cortex has been demonstrated in vivo with these functional imaging techniques. During a unilateral hand motor task, strongly right-handed subjects demonstrate the largest region of activation overlying the contralateral primary motor (M1) and sensory (S1) cortex. This activation is centered over the “hand notch” (or “knob”), which can be identified visually in the axial plane [Yousry et al., 1997]. Activation of the ipsilateral precentral gyrus in normal

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adults has also been reported in a wide variety of PET [Kawashima et al., 1993], fMRI [Cramer et al., 1999; Hanakawa et al., 2005; Kim et al., 1993; Rao et al., 1993; Verstynen et al., 2005], MEG [Salmelin et al., 1995], and EEG [Toma et al., 2002] studies. There is a consensus in the fMRI literature that the ipsilateral precentral gyrus activation is shifted anterior, ventral and lateral, with respect to the M1 activation that occurs during a contralateral hand task [Cramer et al., 1999; Hanakawa et al., 2005; Verstynen et al., 2005]. Although many of the earlier studies considered ipsilateral precentral gyrus activation to be M1, more recent studies have suggested that this activation is more likely premotor [Hanakawa et al., 2005; Verstynen et al., 2005].

Two hypotheses for the functional significance of ipsilateral precentral gyrus activation have been proposed. Ipsilateral precentral gyrus activation may represent neuronal activity in uncrossed descending motor pathways [Cramer et al., 1999; Hanakawa et al., 2005; Kim et al., 1993; Rao et al., 1993; Verstynen et al., 2005]. This concept was originally based on nonhuman primate data demonstrating ipsilateral motor representations in M1 [Aizawa et al., 1990; Tanji et al., 1988]. Further support for this hypothesis is provided by transcranial magnetic stimulation (TMS) data in humans demonstrating ipsilateral motor evoked potentials (MEPs) following M1 stimulation in healthy children [Muller et al., 1997] and following stimulation of the precentral gyrus ventral, lateral, and anterior to the “hand knob” region in healthy adults [Ziemann et al., 1999]. Alternatively, it has been proposed that ipsilateral precentral gyrus activation may correspond to transcallosal inhibitory signals from the contralateral motor regions [Kobayashi et al., 2003; Verstynen et al., 2005]. These inhibitory signals would aid in the generation of dexterous hand movements by inhibiting unwanted neural activity in the ipsilateral motor cortex. This hypothesis is supported by data showing that transcallosal inhibition, detected using TMS, was highly correlated to the presence of BOLD activation in the ipsilateral precentral gyrus [Kobayashi et al., 2003]. Because BOLD activation can be secondary to inhibitory or excitatory dendritic inputs [Logothetis et al., 2001], the authors of this combined fMRI/TMS study suggest that the ipsilateral precentral gyrus activation seen on fMRI is a correlate of the transcallosal inhibitory signals observed with TMS.

The purpose of the present study is twofold. First, we will determine whether ipsilateral precentral gyrus activation during a unilateral hand task is predominantly situated within the primary motor (M1) or premotor cortices. Second, we will investigate whether this activation likely represents task-related activity from a bilateral motor network involved in the control of complex movements, or if it relates to transcallosal inhibitory signals arising from the contralateral hemisphere. We hypothesize that if the ipsilateral precentral gyrus activation is a correlate of transcallosal neuronal inhibition, then this activity should not be present during the contralateral and bilateral finger tap-

ping tasks. However, if the ipsilateral activation represents part of a bilateral network for control of complex finger movements, then these same cortical regions will be activated during the bilateral and contralateral tasks.

METHODS AND MATERIALS

Subjects

Sixteen healthy adults (four males and 12 females; ages 30–57) participated in this study. All subjects were strongly right-handed as assessed by the Edinburgh inventory [Oldfield, 1971]. The study was compliant with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the institutional review board of the Cleveland Clinic. Informed consent explaining the risks and benefits of the study was obtained from all subjects prior to enrollment.

Behavioral task

Subjects performed a complex finger tapping task in a standard block paradigm. Fingers were tapped sequentially in the following order: thumb, middle, pinky, index, and ring finger. The task was self-paced, and subjects were instructed to continually repeat the sequence as fast as possible without making mistakes. Subjects were trained for 5–10 min prior to MR scanning. Task performance was recorded with an MR compatible data glove (Fifth Dimension Technologies, Irvine, CA), consisting of two fiber-optic strain gauges in each of the four fingers and in the thumb. The voltage output from each gauge is proportional to the flexion of the underlying joint and was sampled at 25 Hz. Timeseries from the data gloves were analyzed for the presence of peaks corresponding to finger movements. For each individual sensor, a model waveform was built by averaging together multiple responses (finger taps). The model finger tap was used as a sliding window and the cross correlation between the model and each segment of the timeseries was computed. The cross correlation values for each window were plotted over time and a putative finger tap was said to occur at each local maximum with an amplitude greater than 0.5. A height threshold was then applied to remove putative finger taps of small amplitude. For each sensor, the threshold was defined as 20% of the amplitude of the largest detected putative finger tap. It was necessary to use a different height threshold for each sensor because the data glove employs an auto-gain mechanism which scales the signal from each sensor independently.

Behavioral performance was analyzed for the number of finger taps per scan, error rate, and left/right asymmetry during the bilateral task. An error was defined as any tap occurring outside the prescribed sequence and the error rate was defined as the (total number of errors)/(total number of finger taps). The asymmetry score, defined as the absolute value of $((1 - \text{error rate left hand}) - (1 -$

error rate right hand))/((1 - error rate left hand) + (1 - error rate right hand)), was calculated based on the error rates from the bilateral finger tapping task. For unilateral tasks, movement data from the contralateral glove was inspected to evaluate for potential mirror movements, i.e., contralateral finger movements during unilateral task performance.

MRI Data Acquisition

Data were acquired on a Siemens Trio 3T whole-body scanner (Siemens Medical Solutions, Erlangen) using the standard transmit/receive circularly polarized head coil (USA Instruments, Aurora, Ohio). The following data were obtained in a single session for each subject.

Scan 1: 3D whole brain T1

T1-weighted inversion recovery turboflash (MPRAGE), 120 axial slices, thickness 1.2 mm, Field-of-view (FOV) 256 mm × 256 mm, TI/TE/TR/flip angle (FA) 1900/1.71/900 ms/8°, matrix 256 × 128, receiver bandwidth (BW) 32 KHz.

Scan 2: fMRI activation study-right hand tapping

One hundred sixty volumes of 31–4-mm thick axial slices were acquired using a prospective motion-controlled [Thesen et al., 2000], gradient recalled echo, echoplanar acquisition with TE/TR/FA = 29 ms/2000 ms/80°, matrix = 64 × 64, FOV = 256 mm × 256 mm, BW = 125 KHz. 4[1/2] cycles of a paradigm consisting of 32 s rest followed by 32 s complex finger tapping.

Scan 3: fMRI activation study-left hand tapping

Same prescription as scan 2.

Scan 4: fMRI activation study-bilateral hand tapping

Same prescription as scan 2.

The order of scans 2–4 was randomized for each subject. For scans 2–4, the prospective motion correction realignment parameters [Thesen et al., 2000] for each volume were recorded for data quality control methods described below.

fMRI Post-Processing

The first four volumes from each fMRI timeseries were discarded. The remaining data were spatially filtered using a 64-point, radially symmetric 2D Hamming filter in the Fourier domain, which has been shown to increase BOLD contrast to noise ratio with minimal loss of spatial resolution [Lowe and Sorenson, 1997]. The data were then retrospectively motion corrected using AFNI [Cox and Hyde, 1997]. Data were analyzed for activation by least squares fitting the timeseries for each pixel to a boxcar reference

function plus a slope [Lowe and Russell, 1999]. For each pixel, the percent signal change was calculated by dividing the amplitude of the fitted boxcar reference function by the mean of the pixel's timeseries. Resulting Student's *t* maps were overlaid onto high-resolution T₁-weighted images for viewing purposes.

Subject Head Motion

To quantify the amount of head motion, the mean total head displacement (THD) during each fMRI scan and the maximum THD (during any single volume acquisition) were calculated for each subject from the prospective motion correction rotation and translation parameters [Jiang et al., 1995]. In addition, for every subject, each Student's *t* map was visually inspected for evidence of motion corruption by three independent observers. Observers looked primarily for (1) large positive and negative rings of activation that occurred along the edge of the brain parenchyma superiorly in the cortex, where the outer surface of the brain has high curvature, (2) large amounts of artifact subcortically in slices through the superior aspect of the lateral ventricles and body of the corpus callosum, and (3) large amounts of artifact in the anterior temporal lobes and temporal poles. Following visual inspection each data set was given a score using a 4-point rating scale: 1 = no motion, 2 = some motion artifact but acceptable study, 3 = lots of motion artifact, possibly corrupted, 4 = motion corrupted study. The scores from each observer were averaged together, and studies with an average motion score > 3.33 during any of the three fMRI scans were discarded from further analysis.

fMRI Activation and ROI Analysis

Student's *t* maps and MPRAGE of each subject were transformed into the standard stereotaxic space defined by Talairach and Tournoux [Talairach and Tournoux, 1988] using AFNI [Cox and Hyde, 1997]. Group averaged activation maps were then constructed, averaging voxel-by-voxel the Student's *t* maps from each subject, according to task. The resulting maps were overlaid onto the Talairach transformed MPRAGE from a representative subject and displayed using radiologic convention. ROI analysis was performed using the Human Motor Area Template (HMAT), a set of ROI masks that defines the following regions in Talairach space: primary motor cortex (M1), primary sensory cortex (S1), dorsal premotor cortex (PMd), ventral premotor cortex (PMv), and supplemental motor area (SMA) [Mayka et al., 2006]. For the group averaged data sets, additional, functionally defined ROI masks were drawn around the activation in the thalamus, basal ganglia (BG) consisting of the putamen and globus pallidus, the inferior parietal lobule (IPL) consisting mainly of BA40, the superior parietal lobule (SPL) consisting mainly of BA7, and in the cerebellum. The Talairach coordinates and Student's *t* of the maximally activated voxel within each

ROI were recorded. Please note that we have reported the *xyz* coordinates of group averaged cerebellar activation in Talairach space, even though this is not a technically correct methodology. There is a wide variety in the shape of the posterior fossa among subjects that results in differences in the angulation between the cerebellum and the cerebral cortex that is not accounted for during routine Talairach transformation. Therefore cerebellar structures may not be appropriately aligned prior to group averaging. Because of this, we also report in the text of the results section cerebellar activation using broad anatomic definitions according to a 3D MRI-based cerebellar atlas [Schmahmann et al., 1999].

The HMAT ROI masks corresponding to M1, PMv, and PMd were also overlaid onto the Talairach transformed activation maps of each subject. The number of activated (Student's $t > 3.5$, one-sided, uncorrected $P < 3 \times 10^{-4}$) and deactivated (Student's $t < -3.5$, one-sided, uncorrected $P < 3 \times 10^{-4}$) voxels and the *xyz* coordinates of the maximally activated voxel within each ROI were determined for each subject. Differences in activation volume between tasks and hemisphere were assessed using a two-way ANOVA with task condition (ipsilateral, contralateral, bilateral) and hemisphere (right, left) as factors for each ROI. Shift of the maximally activated voxel within each ROI during the ipsilateral task (relative to the contralateral and bilateral tasks) was assessed using a paired t -test to compare the *xyz* coordinates between task conditions. For both hemispheres, the ROI containing the maximally activated motor or premotor voxel was determined for all three tasks. To demonstrate that the spatial filtering technique used for generating the activation maps did not bias the study findings, the above ROI analysis was repeated using Student's t maps generated from unfiltered time-series data. The differences in activation volume and spatial location of the maximally activated voxels were determined between the filtered and unfiltered datasets.

Spatial Overlap of Ipsilaterally and Contralaterally Activated Voxels

For each individual subject, we compared the spatial overlap of ipsilateral activation within the M1, PMv, and PMd ROIs to the activation that occurred in these same regions during the contralateral task (I-C comparison) and during the bilateral task (I-B comparison). For each hemisphere, we identified the percentage of ipsilaterally activated M1, PMd, and PMv voxels (Student's $t > 3.5$, one-sided, uncorrected $P < 3 \times 10^{-4}$) that had spatial overlap with activation from the contralateral and bilateral tasks. We then compared the mean percent signal change of the spatially overlapping, activated voxel populations using a paired t -test and visually inspected the overlapping and nonoverlapping regions to determine if there were any unique brain areas activated only during the ipsilateral task. To better understand results from the spatial overlap analysis, 2D scatter plots of the x vs. y , x vs. z , and y vs. z

coordinates for every voxel activated in M1, PMd, and PMv were generated for each subject. Visual inspection of these scatter plots allowed a qualitative assessment of the spatial position of the ipsilateral activation relative to the corresponding contralateral and bilateral activations. The spatial overlap analysis was repeated using both higher (Student's $t > 5.0$) and lower (Student's $t > 1.95$) thresholds for determining voxel activation in order to demonstrate that the chosen threshold for voxel activation was not biasing the results.

RESULTS

Quality Control Measures: Handedness, Head Motion and Task Performance

One subject had an Edinburgh Handedness Inventory < 0.6 and was discarded. Four additional subjects had significant motion corruption, as determined from visual inspection, during one or more of the task conditions and were also discarded from the analysis. For the remaining 11 subjects, the mean Edinburgh Handed Inventory was 0.90 ± 0.10 (range 0.75–1.0), the mean total head displacement (THD) during the right/left/bilateral (R/L/B) tasks was (0.37 ± 0.17) mm, (0.34 ± 0.17) mm, and (0.33 ± 0.11) mm, respectively, and the maximum THD during any single volume acquisition for the R/L/B tasks was (0.80 ± 0.28) mm, (0.74 ± 0.32) mm, and (0.70 ± 0.23) mm, respectively. All 11 subjects had acceptable finger tapping and error rates. The mean number of finger taps for the R/L/B tasks were 202 ± 54 , 197 ± 53 , and 199 ± 56 , respectively. The mean error rates for the R/L/B tasks were 0.05 ± 0.03 , 0.06 ± 0.06 , and 0.07 ± 0.05 , respectively. The mean asymmetry score for the bilateral task was -0.01 ± 0.03 . During unilateral tasks, no detectable movements of the contralateral hand, i.e., mirror movements, occurred.

Group Averaged Activation Maps

The *xyz* coordinates and mean Student's t of the maximally activated voxel for each brain region are shown in Table I. In the group averaged data sets, significant cortical activation ($t > 3.5$, corrected, one-sided $P < 2 \times 10^{-12}$) occurred in the contralateral M1, S1, PMd, PMv, SMA, SPL (BA5/BA7), IPL (BA40) (see Fig. 1). Two distinct regions of activation occurred in the ipsilateral precentral gyrus (see Fig. 1). The first activation is located primarily within the PMv ROI. It is situated lateral and ventral to the "hand knob" and extends inferiorly to the roof of the Sylvian fissure. The superior border of this PMv activation spreads into the lateral portion of PMd ROI, and posterior border of the PMv activation spreads into the M1 ROI. The second ipsilateral precentral gyrus activation is located medial and dorsal to "hand knob" and straddles the border of the PMd and M1 ROIs. However, it occurs in a location that is clearly distinct from the large contralateral M1 activation. (see Fig. 1).

TABLE I. Student's t and location of the maximally activated voxel for each ROI in the group averaged activation maps

ROI	Right hand task		Left hand task		Bilateral task	
	R hemisphere: max Student's t (xyz)	L hemisphere: max Student's t (xyz)	R hemisphere: max Student's t (xyz)	L hemisphere: max Student's t (xyz)	R hemisphere: max Student's t (xyz)	L Hemisphere: Max Student's t (xyz)
SMA	8.3 (1, -8, 55)	8.7 (-4, -9, 55)	9.4 (1, -9, 56)	9.1 (-1, -8, 56)	9.9 (1, -8, 56)	10.1 (-4, -9, 55)
M1	5.6 (26, -15, 52)	12.4 (-36, -26, 53)	13.6 (35, -27, 53)	6.9 (-31, -13, 57)	12.5 (34, -26, 53)	13.4 (-38, -25, -51)
S1	3.2 (32, -37, 45)	13.0 (-38, -27, 52)	13.5 (36, -27, 53)	4.5 (-56, -24, 38)	12.3 (35, -27, 52)	13.8 (-37, -26, 51)
PMd	5.8 (26, -14, 52)	8.3 (-27, -14, 53)	8.0 (25, -15, 53)	6.8 (-31, -12, 56)	7.4 (27, -14, 62)	8.1 (-28, -13, 55)
PMv	4.12 (50, -5, 39)	4.9 (-55, -3, 36)	4.7 (51, -7, 39)	4.3 (-55, -3, 36)	4.2 (50, -7, 39)	4.9 (-55, -2, 34)
IPL	4.3 (38, -42, 42)	12.2 (-38, -34, 56)	10.0 (38, -34, 55)	5.5 (-35, -39, 40)	9.2 (34, -33, 47)	12.0 (-37, -33, 52)
SPL	2.6 (13, -64, 53)	4.1 (-20, -68, 52)	3.0 (14, -69, 52)	3.6 (-19, -69, 51)	3.4 (13, -64, 53)	5.4 (-19, -69, 50)
Put/GP	3.7 (16, 0, 13)	5.0 (-25, -5, 10)	5.1 (22, -5, 15)	5.0 (-24, -6, 13)	4.5 (24, -7, 8)	5.1 (-25, -7, 12)
Th	3.4 (11, -16, 10)	5.7 (-14, -20, 9)	5.6 (13, -18, 10)	3.9 (-14, -18, 11)	5.2 (13, -19, 11)	4.9 (-15, -21, 12)
Cer-S	13.5 (18, -50, -16)	7.1 (-31, -49, -19)	8.5 (22, -52, -17)	14.1 (-22, -48, -16)	14.4 (18, -50, -15)	13.5 (-21, -48, -16)
Cer-I*	4.4 (16, -48, -43)	3.8 (-28, -44, -46)	3.4 (27, -46, -39)	6.8 (-27, -44, -42)	4.4 (18, -43, -43)	5.8 (-27, -44, -42)

The xyz coordinates (in Talairach space) and the Student's t of the maximally activated voxel in each ROI are listed for every task condition. Note that the group averaged Student's t -values for the Cer-I (inferior cerebellar hemisphere) are artificially low because this brain region was not completely included in the field-of-view of all the fMRI exams.

Significant ipsilateral parietal activation is also seen in BA7 and in BA 40 (extending from the hand knob inferiorly to the roof of the Sylvian fissure). Of note, there is an island of activity in the posterior portion of the SPL (BA 7), which demonstrates left hemisphere greater than right hemisphere activation for all tasks (see Fig. 1). This region was centered in Talairach space at $xyz = -20, -68, 50$.

In the deep grey nuclei, contralateral greater than ipsilateral activation occurred in the BG and TH (see Fig. 2). Ipsilateral greater than contralateral activation was present in the superior cerebellar hemisphere (centered over lobules IV,V,VI) and inferior cerebellar hemisphere (centered over lobules VIIb and VIIa and VIIb) (see Fig. 2). Additional ipsilateral greater than contralateral cerebellar activation was also seen along the vermis. Because of variations in brain size and head position among subjects, portions of the inferior cerebellum were excluded from the field-of-view in the fMRI scans of some subjects. Therefore, no further analysis was performed on the cerebellar activation.

M1/PMd/PMv ROI Analysis in Individual Subjects

Activation and deactivation volumes are shown (see Fig. 3). The ANOVA showed that M1 activation volume showed a significant effect for task ($P < 0.0001$) but not for hemisphere. For the PMd and PMv, there were no significant effects of task or hemisphere from activation volumes.

The mean (across all subjects) Student's t and xyz coordinates of the maximally activated voxel are listed (Table II). The spatial locations of the maximally activated RH and LH PMd and PMv voxels were not statistically different on a paired t -test for any of the three tasks. However, the maximally activated M1 voxel was shifted approximately 10 mm anteriorly during ipsilateral finger tapping, relative to its location during the contralateral (RH: $P < 7 \times 10^{-3}$; LH: $P < 8 \times 10^{-6}$) and bilateral (RH: $P < 2 \times 10^{-3}$; LH: $P < 2 \times 10^{-6}$) tasks. There was a significant lateral shift in the position of the RH M1 activation during ipsilateral vs. contralateral tapping ($P < 0.04$) and a significant ventral shift of right M1 activation during ipsilateral vs. contralateral ($P > 0.02$) and ipsilateral vs. bilateral ($P < 7 \times 10^{-3}$) tapping and in the left M1 activation during ipsilateral vs. contralateral ($P < 0.05$) tapping. Several subjects demonstrated a shift in ROI location of the maximally activated precentral gyrus voxel from M1 during contralateral (and bilateral) tapping to a premotor region during ipsilateral tapping. For the left hemisphere the maximally activated voxel was located in the M1/PMd/PMv in 9/1/1 subjects, respectively for the contralateral hand task and in 5/4/2 subjects, respectively, for the ipsilateral hand task. For the right hemisphere, the maximally activated voxel was located in the M1/PMd/PMv in 11/0/0 subjects, respectively, for the contralateral hand task and in 5/2/4 subjects, respectively, for the ipsilateral hand task.

The above ROI analyses were repeated using activation maps generated from unfiltered timeseries data. The main effect was that activation volumes were reduced by

Figure 1.

~45–55% in the unfiltered Student's t maps, depending on the ROI and task condition. However, the group averaged spatial location of the maximally activated voxel in each ROI remained stable. For all tapping conditions and all ROIs, the difference in xyz coordinates of the maximally activated voxels in the filtered vs. unfiltered data was less than the standard deviation of the group mean coordinates calculated using either the filtered or unfiltered datasets.

Significant deactivation ($t < -3.5$) also occurred, but was highly variable from subject to subject. On visual inspection, ipsilateral deactivation in the hand knob region of the sensorimotor cortex was noted in 4/11 subjects during left hand tapping and in 8/11 subjects during right hand tapping. Despite partially falling in the M1 HMAT ROI in some subjects, this deactivation was located entirely within the postcentral gyrus and did not extend anterior to the central sulcus. There was no deactivation in this region during the contralateral or bilateral tasks. Significant deactivation also occurred in the medial bank of the SMC of most subjects, overlying the pre- and postcentral gyri directly posterior to the SMA. This activation did not appear to be task specific and occurred with equal frequency in all three tasks. In 6/11 subjects, there was also bilateral deactivation ventrally within the postcentral gyrus, directly posterior to the PMv, that also occurred with equal frequency during all three tasks.

Spatial Overlap of Ipsilaterally and Contralaterally Activated Voxels

To investigate whether ipsilateral motor and premotor activation is spatially distinct from activation in the same hemisphere during contralateral and bilateral finger tapping, we calculated the percentage of ipsilaterally activated voxels that demonstrated spatial overlap with the activation that occurred during the contra- or bilateral tasks (Table III). Ipsilateral activation within M1/PMd/PMv had an 83%/70%/58% spatial overlap with activation of these regions during the contra- and bilateral tasks. For the I-C comparison, spatial overlap within M1 greater than 70% occurred in 9/10 subjects for the right hemisphere (Subject 2 had no ipsilateral M1 activation) and 8/11 subjects for the left hemisphere. Spatial overlap greater than 70%

occurred in the PMd in 8/11 subjects (RH) and 7/11 subjects (LH) and in the PMv of 5/11 subjects for both hemispheres. The majority of nonoverlapping voxels (activated only during the ipsilateral task) were located along the borders of the activation seen during the other task conditions and did not constitute unique areas of ipsilateral activation (see Fig. 4). The spatial overlap analysis was repeated using higher ($t > 5.0$) and lower ($t < 2.0$) thresholds for determining voxel activation to confirm that the results were not biased by the choice of threshold for determining voxel activation. Though there were subtle changes in the percentage of overlapping voxels when using different thresholds, the main observation that the majority of activated voxels in these regions overlapped in all tasks was stable.

The mean percent signal change of spatially overlapping voxels was determined for both the I-C and the I-B comparisons (Table III). In M1, the mean percent signal change of the overlapping voxel population was significantly less for the ipsilateral task compared with the contralateral task (RH: $P < 3 \times 10^{-3}$, LH: $P < 0.02$) and when compared with the bilateral task (RH: $P < 6 \times 10^{-4}$, LH: $P < 7 \times 10^{-3}$). However, there was no significant difference in mean percent signal change of the spatially overlapping, activated voxels in the PMd and PMv during any of the three tasks.

To visualize the spatial relationship between ipsilateral and contralateral motor and premotor activation, 2D scatter plots were made demonstrating the x vs. y and x vs. z coordinates of every activated voxel for both right and left hand tapping (see Fig. 5). The ipsilaterally activated M1 voxels were well centered over the contralateral activation in 4/10 subjects. In the other six subjects, the ipsilateral M1 activation was centered over the anterior portion of the corresponding contralateral activation. In the two subjects with poor M1 overlap, the 2D scatter plots demonstrate that nonoverlapping voxels were situated anterior to the contralateral activation in the region of the "hand knob" and also ventrally along the shared M1/PMv border. Activation patterns in the premotor regions were highly variable from subject to subject. Some subjects demonstrated bilaterally symmetric activation in the premotor regions during all tasks, while some greater bilateral

Figure 1.

Group Average Data: Cortical Activation. The Talairach transformed data sets from every subject were averaged together voxel-by-voxel to generate averaged activation maps for each task condition. Axial slices of these maps are overlaid onto a representative anatomic dataset. For the unilateral tapping conditions, there is robust contralateral activation in the SMC, as well as bilateral activation in the SMA (not labeled), PMd, PMv, and BA40 (IPL). The PMd and PMv can be seen budding off of the SMC activation and clearly represent distinct regions of activation. PMd activation extends superiorly to the dorsal convexity

whereas PMv activation extends inferiorly along the precentral gyrus to the roof of the Sylvian fissure. Also note the left greater than right hemisphere activation in BA7 (SPL) for all three tasks. FMRI datasets are thresholded using a minimum Student's $t > 3.5$ (one-sided, corrected $P < 2 \times 10^{-12}$). The color bar saturates at a Student's $t = 15$. The yellow number in the upper left corner of each image represents the slice position in Talairach space, S = superior). All images are shown in radiological convention.

Figure 2.

premotor activation during left hand tapping compared with right hand tapping in some subjects, or because of a paucity of premotor activation in others.

DISCUSSION

Prior fMRI studies have demonstrated that ipsilateral precentral gyrus activation occurs in normal subjects following unilateral hand motor tasks [Cramer et al., 1999; Hanakawa et al., 2005; Kim et al., 1993; Rao et al., 1993; Verstynen et al., 2005]. This activation has been shown to be shifted ventral, anterior and lateral to the activation that occurs in the “hand knob” region of M1 during a contralateral task [Cramer et al., 1999; Hanakawa et al., 2005; Verstynen et al., 2005]. However, its functional significance and whether it’s anatomic location is primary motor or premotor cortex remains unclear. The purpose of the present study was to determine the spatial distribution of ipsilateral motor and premotor activation in normal controls performing a complex finger tapping task and to investigate whether this activation relates to the planning and/or execution of ipsilateral hand movements or to inhibition from the contralateral hemisphere.

Simple motor paradigms involving repetitive flexion-extension [Cramer et al., 1999; Rao et al., 1993; Verstynen et al., 2005] or abduction-adduction [Kobayashi et al., 2003] finger movements require very little cognitive effort and result in very small ipsilateral activation volumes. This ipsilateral activation does not occur in all subjects [Kobayashi et al., 2003; Rao et al., 1993] and is more prominent following movements with the nondominant hand [Hanakawa et al., 2005; Kim et al., 1993; Kobayashi et al., 2003]. More recently, it has been demonstrated that increasing task difficulty results in greater ipsilateral motor-related activation volume. Specifically, Harrington et al. demonstrated that during right hand tapping task, the number of finger transitions in a sequence (i.e., moving one finger then another) positively correlated with increased ipsilateral PMd activation [Harrington et al., 2000]. Verstynen et al. demonstrated that tapping out a sequence results in greater ipsilateral activation then tap-

ping out chords, where multiple fingers are moved simultaneously, and that both of these tasks produced greater ipsilateral activation then simple finger tapping [Verstynen et al., 2005]. Consistent with these results, our motor task required subjects to repeatedly tap out a sequence, thumb-middle-pinky-index-ring finger, producing robust ipsilateral motor-related activation in all subjects for both right and left hand tapping.

To determine whether the ipsilateral fMRI activation was located in the primary motor or premotor cortex, we used predefined ROI masks from the Human Motor Area Template (HMAT) to distinguish between M1, PMv, and PMd. The HMAT defines M1, PMd, and PMv in Talairach space and creates an objective, nonbiased segmentation of the precentral gyrus. HMAT ROI boundaries are determined from activation likelihood estimate (ALE) statistical maps. Therefore activation located centrally within the ROI has 95% likelihood of belonging to that functionally defined ROI, while activation at the edge of the ROI has only 50% likelihood. When interpreting the results of the HMAT analysis, it is important to recognize that some degree of voxel misclassification will occur, especially at the borders.

During both the right and left hand tasks, the group averaged Student’s *t* maps show large contralateral activations centered about the “hand knob” region of M1 (see Fig. 1). Two additional frontal motor regions are activated bilaterally for both right hand and left hand tapping (and during bilateral tapping). The first region is anterior and medial to the large contralateral M1 activation and straddles the border of the HMAT M1 and PMd ROIs (see Fig. 1). This activation is seen clearly in the ipsilateral hemisphere due to a lack of ipsilateral M1 activity. In the contralateral hemisphere, though it merges with the large M1 activation, it can clearly be seen budding off as a separate region of activity. According to the HMAT, this activation has a 50% likelihood of being contained within the PMd and a 50% likelihood of being contained within M1. Alternatively it could be a mixture of activation from the two brain regions. The Talairach (*xyz*) coordinates of the maximally activated voxel during ipsilateral tapping (RH *x* = 26, *y* = -13, *z* = 52, LH: -28, -12, 54) are similar to those

Figure 2.

Group Average Data: Basal Ganglia and Cerebellar Activation. The Talairach transformed data sets from every subject were averaged together voxel by voxel to generate averaged activation maps for each task condition. Axial slices through the Put/GP and Th and coronal slices through the cerebellum are overlaid onto a representative anatomic dataset. For the unilateral tapping conditions, there is robust contralateral greater than ipsilateral activation in the putamen, globus pallidus, and thalamus. In the ventral putamen, activation is less during the bilateral task then during the corresponding contralateral Put/GP activation that occurs during unilateral tapping. Also note the PMv (BA6) activation that is present in the roof of the Sylvian Fissure. Ipsi-

lateral greater than contralateral cerebellar activation was seen in the superior hemisphere (Cer-S), the inferior hemisphere (Cer-I), and in the midline along the vermis. Note that the Cer-I activation has a lower Student’s *t* because this region of the cerebellum only partial included in the field-of-view during the fMRI scans. FMRI datasets are thresholded using a minimum Student’s *t* > 3.5 (corrected $P < 2 \times 10^{-12}$). The colorbar saturates at a Student’s *t* = 15. The yellow number in the upper left corner of each image represents the slice position in Talairach space, S = superior, P = posterior). All images are shown in radiological convention.

Figure 3.

Activation and Deactivation Volumes: Bar graphs showing the mean activation and deactivation volumes for each ROI, broken down according to task and hemisphere. The errorbars denote one standard deviation from the mean. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

TABLE II. Mean Student's t and mean xyz coordinates of the maximally activated voxel from the M1, PMd, and PMv of each individual subject

	Right hand task			Left hand task			Bilateral task		
	$T_{\max}$	X	Y	Z	$T_{\max}$	X	Y	Z	$T_{\max}$
R M1	10.3 ± 4.2	42.8 ± 11.0	-13.4 ± 6.9	46.9 ± 7.7	17.5 ± 4.7	36.0 ± 7.6	-23.0 ± 6.4	54.6 ± 8.4	17.1 ± 6.5
L M1	17.2 ± 5.9	-34.2 ± 4.9	-23.5 ± 4.6	57.6 ± 6.1	11.7 ± 3.1	-39.8 ± 8.9	-12.6 ± 3.1	53.3 ± 6.6	16.9 ± 5.3
R PMd	10.7 ± 4.7	30.6 ± 13.7	-9.6 ± 5.0	50.6 ± 7.7	12.7 ± 4.5	28.7 ± 8.6	-11.9 ± 4.1	55.2 ± 8.4	11.6 ± 4.6
L PMd	12.9 ± 5.7	-26.2 ± 9.6	-12.4 ± 3.3	54.8 ± 8.1	11.6 ± 3.8	-34.5 ± 13.2	-9.1 ± 4.6	52.2 ± 8.3	12.4 ± 5.0
R PMv	9.6 ± 4.0	52.1 ± 6.2	-0.6 ± 4.9	29.8 ± 10.1	9.7 ± 3.6	51.1 ± 5.7	0.7 ± 6.4	30.3 ± 8.3	9.6 ± 3.4
L PMv	9.7 ± 3.6	-53.6 ± 5.8	0.2 ± 6.0	30.0 ± 6.5	10.6 ± 3.5	-54.2 ± 6.9	3.4 ± 7.3	29.1 ± 7.1	9.7 ± 2.7

For each subject, the volume of activation (mm^3) was calculated by determining the number of voxels (in Talairach space) with a Student's $t > 3.5$ (one-sided, uncorrected $P < 3 \times 10^{-4}$). There was clear ipsilateral M1 activation in 6/11 studies for right hand tapping and 6/11 studies for left hand tapping. Four additional subjects for each task showed lesser amounts of ipsilateral activation that occurred at the border of the M1 and premotor ROIs. This activation likely represents partial volume averaging of the adjacent PMd/PMv activation. In all subjects, ipsilateral SMC activation was confined to the precentral and did not involve the postcentral gyrus (S1). Note the relatively bilateral activation that occurs in the PMd and PMv during all tasks.

reported for the ipsilateral PMd activation by Harrington et al. (31, -6,52) [Harrington et al., 2000] and Baraldi et al. (RH: 34, -10,54; LH: -32, -15,51) [Baraldi et al., 1999]. As in those studies, this region was activated bilaterally during unilateral tasks. Harrington et al. speculate that activation in this region is related to the high number of finger transitions during a finger tapping sequence, a feature that is also true of our finger tapping task.

The second precentral gyrus region activated bilaterally during right and left hand tapping is situated ventral and lateral to the "hand knob" region of M1 and extends inferiorly to roof of the Sylvian fissure. This activation is located primarily within the PMv ROI but it extends superiorly into the PMd ROI and posteriorly into the M1 ROI. The authors of the HMAT comment that within the lateral aspect of the PMv, there is evidence suggesting that its superior border is actually more dorsal than reported in their atlas. They suggest that while the superior border of PMv is +40 mm above the AC-PC line medially, it may be as high as +50 mm laterally [Mayka et al., 2006]. This claim is supported by our group averaged activation maps, which show continuous PMv activation in the lateral precentral gyrus that extends superiorly to +50 mm in the z-dimension. At this slice level, the PMv activation can be seen budding off of the large M1 activation as a separate region of activity (see Fig. 1). During ipsilateral tapping, the maximally activated voxel of this activation (RH: 54, 5, 42, LH: -49, 2, 46) was similar in location to a region identified by Hanakawa et al. in a study comparing precentral gyrus activation during real and imagined finger and face movements [Hanakawa et al., 2005]. Hanakawa et al. conclude that this activation is likely PMv and not M1 because it lacked the somatotopic features associated with M1 and was activated during imaginary as well as actual finger movements.

To better understand the behavior of the ipsilateral precentral gyrus activations identified on the group-averaged activation maps, ROI analysis using the HMAT ROIs for the PMd, PMv, and M1 was performed in each individual subject. This analysis revealed that the ipsilateral M1 activation had a significantly lower max t -score and significantly smaller activation volume relative to the M1 activation in the contralateral hemisphere during the same task (and relative to the activation within the same M1 during the contralateral/bilateral tasks). Consistent with prior studies [Cramer et al., 1999; Hanakawa et al., 2005; Verstynen et al., 2005], the maximally activated ipsilateral M1 voxel was shifted anteriorly (by 10 mm), relative to the contra- and bilateral task conditions. Detailed examination of each subject's activation map reveal that this anterior shift of ipsilateral M1 activation volume is caused by a combination of two factors. First, while contralateral SMC activation covered both the precentral and postcentral gyri, ipsilateral SMC activation was confined to the precentral gyrus. Therefore, postcentral gyrus voxels that fell within the HMAT M1 ROI and were activated during the contralateral task, were no longer activated during ipsilateral

TABLE III. Spatial Overlap Analysis

	RH: Ipsi vs. Contra			RH: Ipsi vs. Bilat			LH: Ipsi vs. Contra			LH: Ipsi vs. Bilat		
	Overlap (%)	% Signal change		Overlap (%)	% Signal change		Overlap (%)	% Signal change		Overlap (%)	% Signal change	
		Ipsi	Contra		Ipsi	Bilat		Ipsi	Contra		Ipsi	Bilat
M1 Mean	87	0.54	0.81	88	0.54	0.91	77	0.57	0.89	80	0.58	1.05
M1 Std	14	0.19	0.34	8	0.19	0.21	24	0.19	0.50	17	0.19	0.49
PMd Mean	75	0.55	0.67	73	0.56	0.73	66	0.54	0.62	66	0.57	0.72
PMd Std	21	0.26	0.38	25	0.26	0.33	34	0.25	0.36	30	0.24	0.31
PMv Mean	62	0.60	0.61	54	0.60	0.63	62	0.54	0.52	51	0.55	0.58
PMv Std	25	0.18	0.16	29	0.20	0.12	23	0.16	0.18	21	0.18	0.09

A spatial overlap analysis was performed to determine if the M1, PMd, and PMv voxels activated during the ipsilateral task condition represent a unique neuronal population or if they are part of a bilateral network involved in the control of complex finger movements. The percentage of ipsilaterally activated voxels that were also activated during the contralateral or bilateral task (% Overlap) and the mean percent signal change of these voxels are reported. Note that for M1, the mean percent signal change of overlapping voxels is significantly greater for contralateral and bilateral tapping conditions, but for the PMV and PMd, the percent signal change of overlapping voxels is similar across all tasks.

tapping. Second, while some ipsilateral M1 activation was observed in the vicinity of the “hand knob” and along the central sulcus, the majority of the ipsilaterally activated M1 voxels were contiguous with the PMd/PMv activations and not directly adjacent to the central sulcus. This suggests that they may in fact represent premotor activation, despite being situated within the boundaries of the HMAT M1 ROI. Furthermore, not only was the maximally activated voxel in M1 shifted anteriorly during ipsilateral tapping, the maximally activated voxel in the region of the precentral gyrus was shifted anteriorly from the M1 ROI to a premotor ROI in half the studies.

Further evidence that ipsilaterally activated voxels with the M1 ROI may be functionally related to premotor activation comes from our spatial overlap analysis. While the percent signal change of the overlapping PMd and PMv voxels was relatively unchanged during ipsilateral tapping (in comparison to the contra- and bilateral tasks), the percent signal change of the overlapping M1 voxels was significantly reduced during ipsilateral finger tapping. The mean percent signal change of the overlapping voxels in the ipsilateral M1 (range 0.53–0.61%) more closely resembles the mean percent signal change observed in the bilateral premotor regions (0.47–0.65%) than in the contralateral M1 (0.80–0.95%).

The hypothesis that the anteriorly placed precentral gyrus voxels, in what has traditionally been considered M1, are in fact premotor is consistent with most current concepts of motor organization. It has been recognized that the hand region of the precentral gyrus contains multiple zones of somatotopy [Geyer et al., 1996; Naito et al., 1999]. One zone is located in the depth of the central sulcus while the other is located on the crest or convexity of the gyrus. A recent fMRI publication examining the unimanual and bimanual object manipulation suggests that zone within the depth of the central sulcus is activated mainly in response to contralateral hand movements

and receives tactile sensory input, while the crestal zone contains a more bimanual representation that deals mainly with the sensorimotor integration of proprioceptive information [Theorin and Johansson, 2007]. This view of precentral gyrus organization is also consistent with the most recent primate data demonstrating that only neurons within the depth of the central sulcus make monosynaptic connections to the motoneurons of the finger muscles [Rathelot and Strick, 2006].

The functional imaging literature has proposed two possible roles for ipsilateral precentral gyrus activation during unilateral finger tapping. The activation may be part of a bilateral network related to the planning and execution of finger movements or it may represent transcallosal inhibitory signals that are suppressing unwanted movements in the ipsilateral hand. This second hypothesis comes from a combined TMS/fMRI study demonstrating that the presence of transcallosal inhibition detected using TMS was highly correlated to the presence of ipsilateral precentral gyrus activation.

To study this question indirectly, we hypothesized that if the ipsilateral fMRI activation was a correlate of the transcallosal inhibition observed with TMS, then the voxels activated during the ipsilateral task should be spatially distinct from the task-related activation and should not be activated during the contralateral and bilateral tasks. Therefore, we performed a spatial overlap analysis to determine if there were any unique areas of the precentral gyrus activated only during the ipsilateral task. Ipsilateral M1 activation showed strong spatial overlap in most subjects. The spatial overlap of premotor activation was more variable, but the studies demonstrating poor overlap did not show any consistent evidence for a spatially unique area of ipsilateral activation. Overall, the nonoverlapping ipsilateral activated voxels tended to occur at the borders of the contralateral and bilateral activations and did not represent unique areas of activity (see Fig. 3).

Figure 4.

Spatial Overlap Analysis: For every subject, we compared the spatial overlap of ipsilaterally activated voxels in the M1, PMd, and PMv to the activation in these same regions that occurred in the contralateral and bilateral tapping conditions. Activation occurring outside the M1, PMv or PMd ROIs has been masked out. Results shown are for a representative subject. Yellow represents voxels activated during the ipsilateral task only. Blue represents voxels activated during the contralateral (or bilateral) task only. Red represents the intersection of both voxel populations (i.e., voxels activated during both tasks). Across all subjects, approximately 83%/70%/58% of ipsilaterally activated voxels

in the M1/PMd/PMv were also activated during the contra- and bilateral tasks (see Table III for details). This analysis was performed using minimum threshold of Student's $t > 3.5$ (uncorrected $P < 3 \times 10^{-4}$). The voxels activated during the ipsilateral task only (orange voxels) tend to occur around the edges of the intersecting population (yellow voxels) and do not constitute a unique population of activity. Note also the strong contralateral M1 activation (blue voxels) in the region of the hand knob at slice position S45. (Number in top left corner of each image refers to slice position (i.e., the z-coordinate in Talairach space). All images are shown in radiological convention.

Figure 5.

Spatial Overlap Analysis: 2D Scatter Plots of Activated Voxel Coordinates. To help visualize the spatial extent of the primary motor and premotor activation during ipsilateral tapping relative to contralateral tapping, we produced 2D scatter plots of the x vs. y coordinates and x vs. z coordinates of every voxel activated in the M1, PMv and PMd. We then overlaid the scatter plots from right hand tapping on top of the scatter plots from left hand tapping. Displayed in this figure are the results from 2 representative subjects, Subject 2 who had poor overlap in all 3 brain regions and Subject 4 who had good overlap in all 3 brain regions. In the M1 region, subject 2 did not have any ipsilateral activation in the right hemisphere. In the left hemisphere, ipsilateral activation (in red) can be seen overlapping the main contralateral activation (blue). This activation is centered around $x = 40$, $y = 2$, $z = 50$ and is located in the region of the hand knob. Note how the ipsilateral activation extends anterior to the contralateral activation. There is also a separate, spatially distinct

region of ipsilateral M1 activation anterior, ventral and lateral to the “hand knob,” adjacent to the PMv, that was not activated during the contralateral task. Subject 4 displays good spatial overlap of M1 activation, note how the ipsilateral activation is situated within the anterior portion of the corresponding contralateral activation (more pronounced in LH). In the premotor regions of PMd and PMv, note for Subject 2 how there is considerably more bilateral activation during left hand tapping (green and red) compared to right hand tapping (black and blue). This difference could be due to differences in premotor recruitment when using the non-dominant hand or could be due to differences in head motion and noise artifacts that affect the overall level of activation in the brain. For Subject 4, there is good spatial congruence between ipsi and contra activation and that the majority of non-overlapping ipsilateral voxels occur at the edges of the contralateral activation and likely represent different noise characteristics between scans.

This conclusion is inconsistent with results of Kobayashi et al. [Kobayashi et al., 2003]. In a combined fMRI/TMS study, they reported significant interhemispheric inhibition of the left motor cortex by the right motor cortex only in those subjects displaying left hemisphere ipsilateral precentral gyrus fMRI activation. The discrepancy in the results between this study and Kobayashi's may reflect differences in the behavioral task. Kobayashi et al. used a relatively simple metronome-paced index finger abduction/adduction task that only produced ipsilateral precentral gyrus activation in 5/10 subjects with the nondominant hand and 0/10 subjects with the dominant hand. The present study employed a self-paced complex finger tapping sequence that produced strong bilateral activation of PMv and PMd regardless of which hand was used. This bilateral premotor activation may have obscured any fMRI correlates of the interhemispheric inhibition seen with TMS.

Another fMRI study by Newton et al. reported ipsilateral deactivation of the pre- and post-central gyrus that the authors suggest is related to interhemispheric inhibition [Newton et al., 2005]. Our task also produced ipsilateral SMC deactivation in many of the subjects. Ipsilateral SMC deactivation was more posterior, located over the postcentral gyrus, while ipsilateral SMC activation tended to be more anterior, situated directly over the central sulcus or over the precentral gyrus at the level of the hand knob. Interestingly, some subjects demonstrated simultaneous ipsilateral precentral gyrus activation and ipsilateral postcentral gyrus deactivation. It is possible that these deactivations are markers of transcallosal/interhemispheric inhibition of the ipsilateral SMC by the contralateral SMC. It may be possible to delineate differences in interhemispheric connectivity based on correlation of low frequency bold fluctuations that occurs in subjects with ipsilateral activations compared with subjects demonstrating ipsilateral deactivations.

The spatial overlap analysis revealed that the spatial pattern of premotor activation was highly variable from subject to subject. While the overall premotor activation volumes were relatively bilateral across all subjects and all task conditions, some subjects demonstrated stronger bilateral premotor activation during one unilateral task compared with the other. This effect is possibly related to differences in processing that occurs when using the dominant versus the nondominant hand, but more likely it is related to differences in head motion and noise characteristics across fMRI scans that effect the global level of fMRI activation in the brain. Other subjects demonstrated trends towards left hemisphere greater than right hemisphere premotor activation regardless of task condition, though no such effect was seen at the level of group analysis.

Lateralization of left hemisphere premotor activation has been reported in multiple prior fMRI studies [Haaland et al., 2004; Theorin and Johansson, 2007; Verstynen et al., 2005]. Haaland et al. reported that left hemisphere dominance of activation in the PMd and in the caudal superior parietal lobe that increases with increasing task difficulty.

They speculate that the left hemisphere is specialized for learning motor sequences [Haaland et al., 2004]. Theorin et al. also report the presence of a bilateral frontal parietal network whose activity is biased towards the left hemisphere [Theorin and Johansson, 2007]. They point out that while there is much evidence indicating a critical role of the left hemisphere in activating sensorimotor engrams to control skilled movements, it remains unclear which specific task characteristics promote this left lateralized activity. Our group averaged datasets did show left lateralized caudal superior parietal activation, similar to that reported by Haaland et al., but we saw no such effect in the PMd. One possible explanation is that our motor paradigm did not rely on auditory or visual cues. The paradigms used in the aforementioned studies required the subject to interpret a visual cue and then respond appropriately from a set of predetermined motor tasks. Furthermore, our subjects were trained 5–10 min prior to scanning, just long enough for the sequence to be memorized and to insure consistent finger tapping across subjects. It may be that since task was internally generated and required no decision making on the subject's part, we were less likely to engage the motor learning or motor engram selection networks that show a bias towards left hemisphere activation.

CONCLUSION

We present the first fMRI study of complex bimanual and unimanual finger tapping. Activation of the precentral gyrus and adjacent frontal cortex could be clearly separated into M1, PMd and PMv activation. Our results suggest that during complex finger tapping, ipsilateral M1 is sparsely activated and that the majority of ipsilateral precentral gyrus activation is located in premotor cortex (PMv and PMd). Furthermore, the results from this study suggest that the spatial distribution of M1 is more highly restricted within the bank of the central sulcus, than what is typically assumed during the analysis methods employed by most functional imaging studies. Our analysis also revealed that individual subjects have highly variable patterns of premotor activation following complex finger tapping, and that these individual variations are obscured during analysis at the group level. Furthermore, spatial overlap analysis failed to identify unique regions of ipsilateral precentral activation that could be an fMRI correlate of transcallosal/interhemispheric inhibitory input. The results suggest that the observed ipsilateral motor and premotor activation represent part of a bilateral network for the control of complex finger movements rather than reflecting BOLD activation related to transcallosal inhibition.

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