Activation Characteristics of the Primary Motor (M1) and Supplementary Motor (SMA) Areas during Robust Unilateral Finger Tapping Task

AHMAD NAZLIM YUSOFF, MAZLYFARINA MOHAMAD, KHAIROH ABDUL HAMID, AINI ISMAFAIRUS ABD HAMID, HANANI ABDUL MANAN & MOHD HARITH HASHIM

ABSTRACT

This study investigated the functional specialisation characteristics of brain in multiple right-hand dominant subjects pertaining to the activation of the cerebral motor cortices evoked by unilateral finger tapping, especially in primary motor (M1) and supplementary motor (SMA) areas. This multiple-subject study used unilateral (UNIright and UNIleft) self-paced tapping of hand fingers to activate the M1 and SMA. Brain activation characteristics were analysed using statistical parametric mapping (SPM). Activation for UNIright and UNIleft showed the involvement of contralateral and ipsilateral M1 and SMA. A larger activation area but with a lower percentage of signal change (PSC) were observed in the left M1 due to the control on UNIright (4164 voxels at \(\alpha = 0.001\), PSC = 1.650) as compared to the right M1 due to the control on UNIleft (2012 voxels at \(\alpha = 0.001\), PSC = 2.377). This is due to the influence of the tapping rate effects which is greater than what could be produced by the average effects of the dominant and sub-dominant hands. The significantly higher PSC value observed in the right M1 (p < 0.05) is due to a higher control demand used by the brain in coordinating the tapping of the sub-dominant fingers. The findings obtained from this study showed strong evidence of the existence of brain functional specialisation and could be used as baseline references in determining the most probable motor pathways in a sample of subjects.

Keywords: Finger tapping; random-effects analysis; statistical parametric mapping

INTRODUCTION

In spite of a vast number of research conducted in studying how uni- and bilateral motor action are coordinated by the brain (Grefkes et al. 2008; Kasess et al. 2008; Walsh et al. 2008), questions still arise about the exact mechanism underlying the existence of activation clusters in the contralateral as well as in the ipsilateral regions and their functional relationships. These are pertaining, in particular, to the height and spatial extent of activation of the activated areas and their connectivity, not only in one hemisphere but also with the ones on the opposite hemisphere.

In a novel works on motor activation and network in humans, Walsh et al. (2008) reported that the dominant hemisphere is responsible in initiating the control over bilateral movement. They also discovered that bilateral activation is not the sum of the right and left unilateral activation from which it was later indicated that the left and right unimanual
movements differ significantly in terms of the activation of and connectivity between the areas involved.

It has been established that the primary motor area (M1) in the precentral gyrus (PCG) and the supplementary motor area (SMA) in the medial dorsal wall are involved in movement preparation and execution of motor action (Toga & Thompson 2000). The understanding of how these areas interact in normal people is important so that the study on plasticity or reorganisation of brain function in motor-impaired patients can be precisely conducted. Such decisions are of great practical relevance in diagnosing the function or wellness of motor areas for pre or post treatment or surgery.

Previous finger tapping studies (Latz et al. 2005; Aramaki et al. 2006; Grekès et al. 2008) relied on systematically constrained instruction visually or verbally given to the subjects. The externally triggered stimuli evoked responses not only in motor areas but also in areas related to vision and hearing, which in turn complicate the study of connectivity between motor areas. These were not considered in those studies. Furthermore, externally triggered methods are lacking in robustness and discount generalization. Therefore, in order to exclude areas not related to motor function and to impose robustness, this study are conducted in which the subjects are instructed to perform self-paced finger tapping at moderate tapping force and speed.

This study is a continuation of our previous work on a single subject (Ahmad Nazlim Yusoff et al. 2006c) and multiple subjects (Ahmad Nazlim Yusoff et al. 2010). In this study, the brain functional specialisation was investigated on multiple subjects with regards to the activation in the cerebral motor cortexes evoked by finger tapping which was robustly done by the subjects. First, group analyses were conducted by means of random (RFX) effects analysis and inferences based on the group responses were made onto the whole subject. Secondly, conjunction analysis was performed to search for common activated areas among multiple subjects. The ROIs were the activation clusters obtained from the subjects. Thirdly, the group’s percentage of signal change in the ROIs, in particular the left and right M1 and SMA were computed. Finally, a conclusion is made with regards to the activation characteristics in the contralateral and ipsilateral regions.

MATERIALS AND METHODS

Functional magnetic resonance imaging (fMRI) examinations were performed on 16 right-handed healthy male and female subjects. The subjects were conveniently sampled based on Desmond & Glover (2002). They suggested that for a liberal significant level of 0.05, about 12 subjects were required to achieve 80% power at the single voxel level for typical activation. In anticipating for non activated brain regions, 16 subjects were selected. The subjects were given informed consent and screening forms as required by the Medical Research Ethical Committee of the Universiti Kebangsaan Malaysia (UKM). The subjects were interviewed on their health condition prior to the scanning session and were confirmed to be healthy. Prior to the fMRI scans, the subjects’ handedness is tested using the Edinburgh handedness inventory (Oldfield 1971). All subjects were confirmed to be right-handed.

Functional magnetic resonance imaging (fMRI) scans were conducted in the Department of Radiology, Universiti Kebangsaan Malaysia Hospital. Functional images were acquired using a 1.5 tesla magnetic resonance imaging (MRI) system (Siemens Magnetom Vision VB33G) equipped with functional imaging option, echo planar imaging (EPI) capabilities and a radiofrequency (RF) head coil used for signal transmission and reception. The imaging parameters for the structural (T1) and functional (T2*) scans have been described elsewhere (Ahmad Nazlim Yusoff et al. 2006c).

The subjects were instructed on how to perform the motor activation task and were allowed to practice prior to the scanning. The subjects had to press all four fingers against the thumb beginning with the thumb-index finger contact and proceeding to the other fingers in sequence which would then begin anew with contact between thumb and index finger. This study used a robust self-paced finger movement. The tapping of the fingers would approximately be two times in one second (using an intermediate force between too soft and too hard). A six-cycle active-rest paradigm which was alternately cued between active and rest was used with each cycle consists of 10 series of measurements during active state and 10 series of measurements during resting state. The tapping of the fingers were done unilaterally (UNIright or UNIleft); see Ahmad Nazlim Yusoff et al. (2006c) for details.

The functional (T2* weighted) and structural (T1 weighted) images were sent to Universiti Kebangsaan Malaysia Hospital (HUKM) MedWeb and were later retrieved in the Functional Image Processing Laboratory (FIPL), Diagnostic Imaging & Radiotherapy Programme, Faculty of Allied Health Sciences, UKM Kuala Lumpur for further analyses. Image analyses were performed using a personal computer (PC) with a high processing speed and large data storage. The MATLAB 7.4 – R2006a (Mathworks Inc., Natick, MA, USA) and Statistical Parametric Mapping (SPM5) (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College of London) software packages were used for that purposes. Activated voxels were identified by the general linear model (GLM) by estimating the parameters of the model and by deriving the appropriate test statistic (T statistic) at every voxel. Statistical inferences were finally obtained on the basis of SPM and the Gaussian random field theory (Brett et al. 2004; Friston 2004). The inferences were made using the T-statistic at uncorrected ($\alpha = 0.001$) significant level, whereas for the analysis of conjunction, the significant level is taken at $\alpha = 0.1$. Steps taken in data analyses using SPM have been completely described in various similar studies (Ahmad Nazlim Yusoff et al. 2005, 2006a, 2006b & 2006c).

The region of interest (ROI) analyses were performed in order to compare the response of the brain due to lateralisation (left and right) and task (UNIleft and UNIright). The ROIs were the activation clusters obtained from the subjects’ activation map defined using automated anatomical labelling (AAL) (Tzourio-Mazoyer et al. 2002)
and WFU Pick Atlas (Maldjian et al. 2003) at $\alpha = 0.1$. The two selected ROIs were bilateral precentral gyrus (PCG) and supplementary motor area (SMA). Small volume correction was performed within the predefined ROIs (Worsley et al. 1996). Group’s fixed-effects (FFX) percentage of signal change (PSC) relative to the baseline for all ROIs was extracted from a 4-mm radius sphere with the peak coordinates as the centre using MarsBar toolbox for SPM (Matthew Brett et al. 2002).

RESULTS

Demographical data for all the subjects are depicted in Table 1. The mean age and its standard deviation for the subjects was $22.31 \pm 2.65$ years old. Four (25%) male and (75%) female subjects participated in this study.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Age</th>
<th>Race</th>
<th>Handedness</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>Female</td>
<td>24</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S2</td>
<td>Male</td>
<td>23</td>
<td>C</td>
<td>Right</td>
</tr>
<tr>
<td>S3</td>
<td>Female</td>
<td>19</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S4</td>
<td>Female</td>
<td>22</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S5</td>
<td>Female</td>
<td>23</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S6</td>
<td>Male</td>
<td>24</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S7</td>
<td>Male</td>
<td>24</td>
<td>C</td>
<td>Right</td>
</tr>
<tr>
<td>S8</td>
<td>Female</td>
<td>26</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S9</td>
<td>Female</td>
<td>23</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S10</td>
<td>Female</td>
<td>19</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S11</td>
<td>Female</td>
<td>28</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S12</td>
<td>Female</td>
<td>19</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S13</td>
<td>Male</td>
<td>22</td>
<td>C</td>
<td>Right</td>
</tr>
<tr>
<td>S14</td>
<td>Female</td>
<td>20</td>
<td>C</td>
<td>Right</td>
</tr>
<tr>
<td>S15</td>
<td>Female</td>
<td>22</td>
<td>M</td>
<td>Right</td>
</tr>
<tr>
<td>S16</td>
<td>Female</td>
<td>19</td>
<td>C</td>
<td>Right</td>
</tr>
</tbody>
</table>

Table 1. Demographical data for all subjects

Figure 1 is the statistical parametric maps (SPMs) obtained from random-effects (RFX) analysis showing contralateral and ipsilateral brain activations due to (a) UNI$_{right}$ and (b) UNI$_{left}$. The crossing of the hair-line indicates the point of maximum intensity which occurred at (-32, -22, 50) and (38, -20, 62) in the left and right hemispheres, respectively. In order to illustrate several ipsilateral region, Figure 1 was taken at $\alpha = 0.01$. Some RFX statistical data, MNI coordinates at the point of maximum intensity in each respective cluster and the anatomical areas in which the maxima in the brain activation due to UNI$_{right}$ and UNI$_{left}$ occur are summarised in Table 2.

For UNI$_{right}$, seven significant clusters survive a height threshold of uncorrected $\alpha = 0.001$ and a spatial threshold of 50 voxels. This is due to the fact that the other clusters are believed to be generated by factors not included in the experimental paradigm such as aliased biorhythm and mild responses of the brain during the experiment. There is a total of 4164 activated voxels ($t > 3.73$) in the main cluster which covers parts of the left post and precentral gyrii and left SMA. The eight highest peaks are at Talairach-MNI coordinates of (-32, -22, 50), (-42, -18, 52), (-42, -24, 52), (-26, -16, 64), (-36, -12, 64), (-42, -36, 46), (-46, -16, 48) and (-6, 6, 48). The results indicate that 29.8% of the main cluster is in the left BA6 (27.8% activated), 9.7% of cluster is in the left BA2 (44.6% activated), 7.8% of cluster is in the left BA3b (50.9% activated) and 7.1% of cluster is in the left BA4p (52.5% activated).

For UNI$_{left}$, five significant clusters survive the uncorrected height threshold of $\alpha = 0.001$. The main activation cluster in the precentral gyrus consists of 5 maxima. Their Talairach-MNI coordinates are (38, -20, 62), (42, -24, 62), (36, -32, 60), (46, -16, 58) and (48, -22, 58). A number of 2012 voxels are activated ($t > 3.73$); 35.0% of cluster is in the right BA6 (16.0% activated), 13.5% of cluster is in the right BA1 (32.7% activated), 10.2% of cluster is in...
the BA3b (22.5% activated) and 8.7% of cluster is in the right BA4a (15.2% activated).

The results obtained from the analysis of conjunction on the present UNIright and UNIleft datasets indicate that all subjects show common activation areas in the primary motor area. For UNIright, 3 activation clusters are detected in the left postcentral gyrus and precentral gyrus. The main cluster which has 64 activated voxels ($t > 1.28$) with the point of maximum activation at (-34, -22, 54), shows that 55.1% of cluster is in the left BA4p (6.3% activated), 25.6% of cluster in the left BA4a (1.3% activated), 10.7% of cluster in the left BA6 (0.2% activated) and 8.6% of cluster is in the left BA3b (0.9% activated).

For UNIleft, the analysis of conjunction at significant level of $\alpha = 0.1$, reveals 1 cluster of activation which is in the right precentral gyrus. The cluster consists of 95 activated voxels ($t > 1.28$) and has 5 maxima with the highest two at (36, -20, 62) and (40, -14, 56). 89.9% of the cluster is in the right BA6 (1.9% activated), 8.2% is in the right BA4a (0.7% activated), 0.5% of cluster is in the right BA4p (0.1% activated) and 0.3% of cluster is in the right BA3b (0.1% activated).

Figure 2 is the plot of adjusted fitted responses and the corresponding error term calculated at the group peak coordinates for all subjects in (a) left M1 during UNIright and (b) right M1 during UNIleft. Subjects’ responses at peak coordinates are well fitted into the model but with a large variability between subjects. It can be seen that the M1 peak intensity is roughly higher during UNIleft than during UNIright. The percentage of change in signal intensity (PSC) that had occurred in the left and right M1 and SMA are tabulated in Table 3 for UNIright and UNIleft. For UNIright, M1(L) and SMA(L) show higher PSC values as compared to the ipsilateral M1(R) and SMA(R). Similarly, the PSC values for UNIleft are higher in M1(R) and SMA(R) as compared to the ipsilateral M1(L) and SMA(L). The PSC results for M1 are in good agreement with the fitted responses mentioned earlier. As opposed to number of activated voxels, the tapping of the left hand fingers generate higher signal change in M1(L) than in M1(R) during the tapping of right hand fingers. The effect is however incomparable in SMA.

**DISCUSSION**

Based on Figure 1 and Table 2, it is quite interesting to see that the left side of the brain (triggered by the tapping of the hand) is activated more during UNIright and the right side of the brain is activated more during UNIleft. This is in agreement with the fitted responses mentioned earlier. The results obtained from the analysis of conjunction on the present UNIright and UNIleft datasets indicate that all subjects show common activation areas in the primary motor area. For UNIright, 3 activation clusters are detected in the left postcentral gyrus and precentral gyrus. The main cluster which has 64 activated voxels ($t > 1.28$) with the point of maximum activation at (-34, -22, 54), shows that 55.1% of cluster is in the left BA4p (6.3% activated), 25.6% of cluster in the left BA4a (1.3% activated), 10.7% of cluster in the left BA6 (0.2% activated) and 8.6% of cluster is in the left BA3b (0.9% activated).

The results obtained from the analysis of conjunction on the present UNIright and UNIleft datasets indicate that all subjects show common activation areas in the primary motor area. For UNIright, 3 activation clusters are detected in the left postcentral gyrus and precentral gyrus. The main cluster which has 64 activated voxels ($t > 1.28$) with the point of maximum activation at (-34, -22, 54), shows that 55.1% of cluster is in the left BA4p (6.3% activated), 25.6% of cluster in the left BA4a (1.3% activated), 10.7% of cluster in the left BA6 (0.2% activated) and 8.6% of cluster is in the left BA3b (0.9% activated).

The results obtained from the analysis of conjunction on the present UNIright and UNIleft datasets indicate that all subjects show common activation areas in the primary motor area. For UNIright, 3 activation clusters are detected in the left postcentral gyrus and precentral gyrus. The main cluster which has 64 activated voxels ($t > 1.28$) with the point of maximum activation at (-34, -22, 54), shows that 55.1% of cluster is in the left BA4p (6.3% activated), 25.6% of cluster in the left BA4a (1.3% activated), 10.7% of cluster in the left BA6 (0.2% activated) and 8.6% of cluster is in the left BA3b (0.9% activated).

The results obtained from the analysis of conjunction on the present UNIright and UNIleft datasets indicate that all subjects show common activation areas in the primary motor area. For UNIright, 3 activation clusters are detected in the left postcentral gyrus and precentral gyrus. The main cluster which has 64 activated voxels ($t > 1.28$) with the point of maximum activation at (-34, -22, 54), shows that 55.1% of cluster is in the left BA4p (6.3% activated), 25.6% of cluster in the left BA4a (1.3% activated), 10.7% of cluster in the left BA6 (0.2% activated) and 8.6% of cluster is in the left BA3b (0.9% activated).
TABLE 3. Percentage of signal change of the peak coordinates of the right and left M1 and SMA for UNIright and UNIleft

<table>
<thead>
<tr>
<th></th>
<th>M1(L)</th>
<th>M1(R)</th>
<th>SMA(L)</th>
<th>SMA(R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNIright</td>
<td>1.650</td>
<td>0.633</td>
<td>0.860</td>
<td>0.670</td>
</tr>
<tr>
<td></td>
<td>(-32, -20, 52)</td>
<td>(36, -10, 62)</td>
<td>(-6, -2, 54)</td>
<td>(8, 6, 52)</td>
</tr>
<tr>
<td>UNIleft</td>
<td>0.713</td>
<td>2.377</td>
<td>0.739</td>
<td>0.793</td>
</tr>
<tr>
<td></td>
<td>(-36, -8, 56)</td>
<td>(40, -20, 66)</td>
<td>(-6, 4, 52)</td>
<td>(10, 4, 50)</td>
</tr>
</tbody>
</table>

The right hand fingers shows a larger number of activated voxels and higher activation intensity as compared to the right side of the brain (triggered by the left-hand finger tapping), as opposed to our previous study on a single male subject (Ahmad Nazlim Yusoff et al. 2006c), despite the fact that all the subjects are right handed. This shows the reliability of multiple subject analyses in making inference over a population. Moreover, group results indicate the existence of ipsilaterality accompanying the expected contralaterality. The analyses conducted were focused on two anatomical regions that are known to be involved in controlling motor movement which are the primary motor cortex in the precentral gyrus (will be named as M1) and SMA which is also known to be involved in planning complex movements and in coordinating movements involving both hands (Walsh et al. 2008). The primary motor cortex (PMC) is not included in the present study due to the inconsistency of the activation in the respective pre-motor area for all subjects, which resulted in lack of activation in group results. This could be due to the nature of task done by the subjects that does not involve the integration of sensory information which is one of the functions of PMC (Grefkes et al. 2008). M1 and SMA were found to be activated at different significant level in all participating subjects but the coordinates of the activation peaks differ by a few millimeters from subject to subject.

The typicality of the effects of the right and left unilateral tapping of fingers in all subjects was investigated using conjunction analysis. Conjunction analysis, as described by Friston (2004) provides a way to locate common features of functional anatomy between subjects under the same experimental condition. The results obtained from the analyses of conjunction on the present UNI and UNIL datasets indicate that all subjects show common activation areas in precentral gyrus (M1). However, the SPM results generated at significant level of \( \alpha = 0.1 \) indicate significant activation only at voxel level. Both the set and cluster level inferences about the activation clusters revealed insignificant brain activation.

In our previous study on a single right-handed male subject (Ahmad Nazlim Yusoff 2006c), the activated motor areas in the right hemisphere due to UNIleft showed a higher signal intensity and larger activation area as compared to that in the left hemisphere due to UNIright. The findings obtained from our single subject study are in good agreement with a multiple subject fMRI study on unilateral and bilateral sequential movement in right-handers (Jäncke 1998). They found that the right hemisphere showed more activation than the left hemisphere in both unilateral and bilateral task at two tapping frequencies. They also concluded that faster movement rates will cause higher activation both in terms of signal intensity and number of activated voxel, the so called “rate effects.” Their interpretations are that right-handers expend more effort to perform with their non-preferred hand. A stronger activation pattern in the right hemisphere is the result of trying to perform with a system that is slightly less competent with the implication that the more skilled and competent system will expend less effort and will therefore provide a weaker activation. As for the rate effects, they concluded that faster movement involves the recruitment of more motor units and will therefore activate a greater
neuronal activation in motor area of one hemisphere suppresses neuronal activity of the same area in the opposite hemisphere. Inhibitory has been shown to be either in terms of activated volume or percentage of signal change (Newton et al. 2005). Inhibition is not observable in this study since tapping style is kept constant. However, as can be seen from Figure 1 and Table 3, ipsilaterality did occur in both M1 and SMA and the effects are asymmetrical and these shows possible evidence of inhibitory of activation in the ipsilateral areas.

CONCLUSION

The results obtained from this multiple-subject study on right-handed male and female subjects showed that the observed brain activation for UNI_right and UNI_left fulfill contralaterality behavior of motor coordination. Brain activations are also presented in the ipsilateral regions indicating important roles of brain regions that are located on the same side of movement. Dominant hand has been found to produce stronger tapping rate effects (larger activation area) for this group of right handers as compared to subdominant hand and the influence is greater than what would be produced by the average effects of the dominant and sub-dominant hand. However, the higher percentage of signal change observed in the right M1 that controls UNI_right is due to a higher control demand used by the brain in coordinating the tapping of the sub-dominant hand fingers.

ACKNOWLEDGEMENT

The authors would like to thank Sa’don Samian, the MRI Technologist of the Universiti Kebangsaan Malaysia Hospital (HUKM), for the assistance in the scanning and the Department of Radiology, Universiti Kebangsaan Malaysia Hospital for the permission to use the MRI scanner. The authors were also indebted to Professor Karl J. Friston and the functional imaging group of the University College of London for valuable discussions on experimental methods and data analyses. This work is supported by the research grants IRPA 09-02-02-0119EA296, the Ministry of Science, Technology and Innovation of Malaysia and and UKM-GUP-SK-07-20-205, Universiti Kebangsaan Malaysia.

REFERENCES


Ahmad Nazlim Yusoff, Mohd Harith Hashim, Mohd Mahadir Ayob & Iskandar Kassim. 2006a. Analisis data pengimajen resonans magnet kefungsian: Prapemprosesan ruang menggunakan kaedah pemetaan statistik berparameter (Functional magnetic resonance data analyses: Spatial pre


